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Automatic detection of microaneurysms in colour fundus images for diabetic retinopathy screening

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Abstract Regular eye screening is essential for the early detection and treatment of the diabetic retinopathy. This paper presents a novel automatic screening system for diabetic retinopathy that focuses on the detection of the earliest visible signs of retinopathy, which are microaneurysms. Microaneurysms are small dots on the retina, formed by ballooning out of a weak part of the capillary wall. The detection of the microaneurysms at an early stage is vital, and it is the first step in preventing the diabetic retinopathy. The paper first explores the existing systems and applications related to diabetic retinopathy screening, with a focus on the microaneurysm detection methods. The proposed decision support system consists of an automatic acquisition, screening and classification of diabetic retinopathy colour fundus images, which could assist in the detection and management of the diabetic retinopathy. Several feature extraction methods and the circular Hough transform have been employed in the proposed microaneurysm detection system, alongside the fuzzy histogram equalisation method. The latter method has been applied in the preprocessing stage of the diabetic retinopathy eye fundus images and provided improved results for detecting the microaneurysms.

Keywords Diabetic retinopathy · Eye screening · Colour fundus images · Image processing · Microaneurysms

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1 Introduction

Diabetic retinopathy (DR) is one of the systemic complications of diabetes mellitus. The retinopathy means damage to the retina, a thin layer of light-sensitive tissue that lines the back of the eye. It happens due to the long-standing of diabetes mellitus, and as a result, the blood vessels become blocked, leaky and grow haphazardly. Diabetic retinopathy is asymptomatic; it does not interfere with sight until it reaches an advanced stage. Therefore, screening for diabetic retinopathy is essential for an early detection and early treatment of this disease.

Diabetes mellitus is a disorder caused by sustained hyperglycaemia of varying severity, secondary to lack or diminished efficacy of endogenous insulin [1]. Diabetes is a lifelong condition that causes a person's blood sugar level to become too high [2]. It happens when the pancreas does not produce enough insulin or because cells do not respond to the insulin produced. Insulin is a peptide hormone, produced by the beta cells of the pancreas, a large gland which is located behind the stomach. Diabetes mellitus is an epidemic due to longer lifespan, modern lifestyle (urbanisation) and also environmental and social factors, such as diet, obesity and lack of physical activity [1]. In addition to that, some of the risk factors for the diabetes mellitus are the uncontrolled hypertension and smoking [3].

The diabetes epidemic is leading to an increasing number of acute and chronic complications, including sight-threatening. Diabetes mellitus left untreated can cause many health problems. Systemic complications of the diabetes mellitus are represented by stroke, cardiovascular disease, diabetic neuropathy, diabetic nephropathy and also diabetic retinopathy [1]. The clinical manifestations of the retinopathy are due to two basic pathophysiologic mechanisms, which are the increased capillary permeability and also the closure of retinal capillaries [3]. Diabetic retinopathy is a complication of the diabetes mellitus that damages blood vessels inside the retina. It commonly affects both eyes and can lead to vision loss if it is not treated [4].

Diabetes mellitus is a major public health concern. Wild et al. [5] reveals that the global prevalence of the diabetes mellitus in 2000 was estimated to be 2.8 % (171 million diabetics) and projected to rise to 4.4 % (366 million diabetics) in 2030. The results show that the estimated number of people with diabetes will increase between 2000 and 2030, not only for developed countries, but for developing countries in the world as well.

Screening is defined as testing on a population in order to identify individuals exhibiting attributes that could be early symptoms or indicators of predisposition associated with a particular condition [7]. The main purpose of diabetic retinopathy screening is to detect whether the individuals require follow-up or referral for further treatment, in order to prevent blindness. Besides this main purpose, there are other purposes for diabetic retinopathy screening, which include: identifying the disease at an early stage; possibly detecting a requirement for blood pressure and blood sugar treatment; educating the population on the diabetic retinopathy causes and on the ways to reduce the retinopathy risk; and potentially identify non-diabetic conditions through the screening process [7]. According to Taylor and Batey [7], one major problem is that the diabetic eye disease does not interfere with sight until it reaches an advanced stage. Laser treatment can save sight, but only if it is used at an early stage and, hence, regular screening is essential. This shows the importance of regular screening, which can help detect the diabetic patients at an early stage of the diabetic retinopathy. Furthermore, earlier identification of any retinopathy signs can allow change in blood pressure or blood glucose management in order to slow the rate of the disease progression. In addition, Taylor and Batey considered the digital retinal imaging as one of the main screening choices and underlined five principles of retinal screening, comprising of regular screening assurance, robust screening system availability, eye screening practice as part of the diabetes care, the ophthalmologist participation in the screening system planning and operation and, finally, the quality control of the screening process [7]. Four steps have been recommended in systematic screening programmes developed for the sight-threatening diabetic retinopathy; firstly, effective treatment, opportunistic as well as systematic screening, and, finally, full quality assurance and coverage screening [36]. As a conclusion, regular screening can help identify early signs of diabetic retinopathy and, most importantly, can help save sight.

Amongst the features detected in the diabetic retinopathy diagnosis are the microaneurysms, retinal haemorrhages, hard exudates, cotton-wool spots, abnormal new vessels, venous beadings, dilations and segmentations. Diabetic retinopathy is broadly divided into two stages, i.e. non-proliferative diabetic retinopathy (NPDR) and proliferative diabetic retinopathy (PDR).

This paper is focusing on the detection of microaneurysms, as they are the first important indication of the diabetic retinopathy. One of the earliest signs of diabetic retinopathy is the dilation of the veins in the retina. The small capillaries may also undergo early changes, leading to occlusion. This results in small bulges in the vascular walls, called microaneurysms. At this early stage, which is referred to as the minimal non-proliferative diabetic retinopathy (MNPDR), sight may be affected. Part (a) of Fig. 1 shows a diagrammatic representation of a microaneurysm, formed by ballooning out of a weak part of the capillary wall, which appears as a dot to the observer [7], while part (b) shows the fundus photograph image of the eye with diabetic retinopathy showing microaneurysms [25]. The microaneurysms are the small red dots on the retina, and they represent the earliest visible sign of the diabetic retinopathy. So, the detection of microaneurysms at an early stage is the first step in preventing diabetic retinopathy.

The paper is organised as follows. Section 2 presents previous related work on automatic methods for retinopathy sign detection, with emphasis on microaneurysm detection methods, while Sects. 3 and 4 explain the proposed approaches used in the development of the different versions of the microaneurysm detection system. Section 5 details the conclusions and the future work plan.

2 Previous related work

Diabetic retinopathy screening is a popular research area and a lot of researchers focus on and contribute towards the advancement of study in this area. Automated methods for diabetic retinopathy screening were proposed in order to address the manual screening issues, such as low sensitivity, high cost, time consuming and low human detection ability. The goal of automated methods for screening is to identify the needs of referral for further treatment [37]. Abramoff and Niemeijer [37] reviewed the available

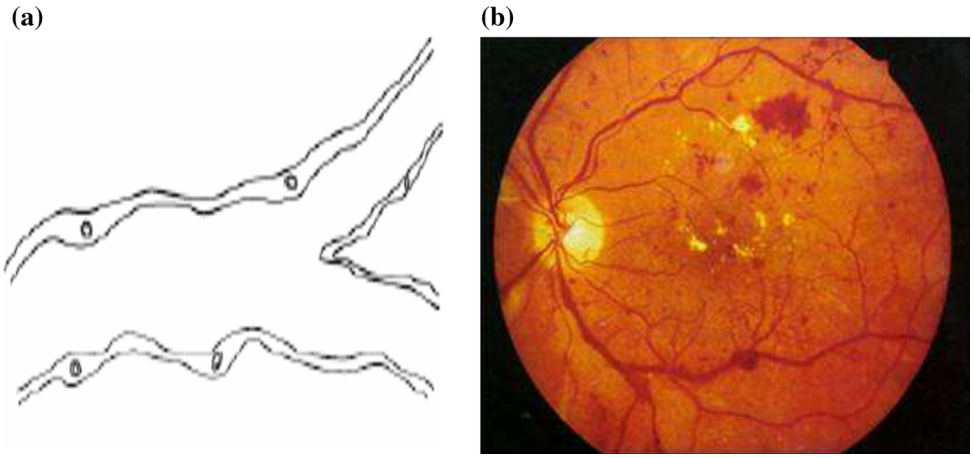


Fig. 1 Microaneurysm representation

automated methods for diabetic eye disease screening, besides highlighting the issues of higher sensitivity and high productivity in mass screening using automated methods. Donsa et al. [40] highlighted several problems and challenges of decision support systems and machine learning methods for diabetes treatment.

Automatic detection systems for the earliest signs of diabetic retinopathy, i.e. the microaneurysms, have been proposed in [8, 10–12, 14–20, 29, 30, 43–47, 53]. The automatic detection of exudates, which are defined as small white or yellowish-white deposits with sharp margins [36], has been proposed in [38, 48, 49, 53, 55]. Meanwhile, researchers have proposed various methods for the detection of other signs of diabetic retinopathy, such as haemorrhages [53, 54] as well as neovascularisation, caused by abnormal new vessels [50–52, 55].

An automated grading system with image processing methods that detect two diabetic retinopathy features, which are the dot haemorrhages and microaneurysms, was developed by Larsen et al. [29]. Jelinek et al. [30] developed an effective tool for detecting microaneurysms, in order to identify the diabetic retinopathy presence in rural optometric practices. A comparison of the automated system used with optometric and ophthalmologic assessment was performed by calculating the sensitivity and specificity of both methods.

In addition, Priya and Aruna [31] investigated and proposed a computer-based system for identifying normal, non-proliferative diabetic retinopathy (NPDR) and proliferative diabetic retinopathy (PDR) cases. The proposed system uses colour fundus images, where the features are extracted from the raw image by using various image processing techniques and fed into a support vector machine (SVM) for classification. The system has been later enhanced by combining two types of classifiers, a probabilistic neural network (PNN) and a support vector machine [32].

The detection of the diabetic retinopathy disease by using a radial basis function neural network (RBFNN) classification method has been proposed in [33]. The Aravind diabetic retinopathy screening (ADRES) 3.0, developed and presented by Permalsamy et al. [34], is a software for reading and grading the diabetic retinopathy. This simple tool is used to assist in the detection of the diabetic retinopathy, and it is offered as an additional checking method to a usual clinical examination by an ophthalmologist.

2.1 Microaneurysm detection methods

Different types of methods have been proposed and used for detecting the microaneurysms in order to produce an efficient and reliable detection system. Abdelazeem proposed the blood vessel removal and circular Hough transform as main techniques to be used in the detection of microaneurysms [8]. The proposed improvement in the detection of microaneurysms is based on the removal of blood vessels from the image and then the classification of all detected circular objects of whether they are microaneurysms or not. The proposed scheme was applied to the retinal fluorescein angiographic images. There are various modes of fundus photography examination, such as colour, red-free and angiography. Retina illuminated by white light and examined in full colour is called the colour mode, while red-free or monochromatic mode is where the imaging light is filtered to remove red colours, which helps improve the contrast of vessels and other structures. In the angiography mode, vessels are brought into high contrast by intravenous injection of a fluorescent dye, which produces a very high-contrast image of the vessels. The Hough transform proved to be an effective method for detecting circular features in pictures [9]. Since the microaneurysms are circular in shape, the circular Hough transform is suitable to be used to locate and detect objects of circular

shapes. Amiri et al. [10] proposed the use of circular Hough transform for the detection of microaneurysms in retinal angiography images. The proposed algorithm for detecting microaneurysms in retinal images started with a preprocessing stage, to eliminate pseudo-imaging and noise by using an average filter. The next tasks are finding the centres related to microaneurysms by using the circular Hough transform, applying region growing process to detect the points and scope of microaneurysms and, eventually, the postprocessing stage to eliminate false-positive region.

An automated detection of microaneurysms in digital red-free photographs for diabetic retinopathy screening has been proposed by Hipwell et al. [11]. Candidate microaneurysms are extracted after the image has been modified to remove large-scale differences between images, caused by changes in the illumination conditions, with the "shade-corrected" method, and also by removing other large features such as vessels and haemorrhages. The subsequent classification is performed based on the shape and size features of the microaneurysms. Antal and Hajdu [12] have suggested an improvement of microaneurysm detection in colour fundus images by using an optimal combination of preprocessing methods and candidate extractors. The selected preprocessing methods used are the contrast-limited adaptive histogram equalisation, the Walter-Klein contrast enhancement and the vessel removal and extrapolation. The results showed that the accuracy of the individual candidate extractors is increased by applying these preprocessing methods.

The retinopathy online challenge (ROC) presents an online competition for numerous methods in microaneurysm detection to compare with each other on the same data [13]. The data set consists of 50 training images of colour fundus photographs with available reference standard, and 50 test images where the reference standard was withheld by the organisers. The overall results show that microaneurysm detection has been a challenging task for both automatic methods and the human experts. One of the proposed methods for this challenge is using the optimal wavelet transform for the detection of microaneurysms in retina photographs [14]. The second method proposed is the use of mixture model-based clustering and logistic regression for automatic detection of microaneurysms in retinal images [15]. The third method that has been presented using the ROC data set is the hierarchical detection of red lesions in retinal images by multiscale correlation filtering [16]. The automated microaneurysm detection method based on double-ring filter in retinal fundus images has been proposed by Mizutani et al. [17]. Besides these methods, there are several other proposed methods for the detection of microaneurysms using the ROC data set. Adal et al. [18] proposed the automated detection of microaneurysms using robust blob descriptors, while Lazar and Hadju [19] presented the retinal microaneurysm detection based on intensity profile analysis. Hatanaka et al. [20] extended the use of double-ring filter with feature analysis, for the automatic microaneurysm detection in retinal fundus images.

There are several developed systems to detect and diagnose diabetic retinopathy [29, 30, 34]. General detection systems for diabetic retinopathy detect the diabetic retinopathy by classifying into general detection categories, such as normal (no apparent retinopathy) or abnormal (retinopathy presence) [21, 35, 57]. In addition, there are some developments on automatic systems that provide a more detailed classification of diabetic retinopathy stages, namely normal, non-proliferative diabetic retinopathy (NPDR) and proliferative diabetic retinopathy (PDR) [31–33, 56]. Some developed systems focus on the detection of diabetic retinopathy features, such as microaneurysms, exudates and haemorrhages. The automatic detection of microaneurysms is still considered to be a very challenging task, and further exploration is needed to find techniques suitable for this purpose. The main contribution of this paper is in using different preprocessing techniques, different features and different classifiers in a diabetic retinopathy screening system. The results on the application of these different techniques are compared and offer an insight into their suitability for utilisation in an automatic diabetic retinopathy screening system.

3 Diabetic retinopathy screening system and automatic detection of microaneurysms in colour fundus images using feature extraction and classification

System I represents the preliminary classification and screening of diabetic retinopathy using fundus images. It is a general detection system of diabetic retinopathy screening. System II focuses on the detection of the earliest signs of diabetic retinopathy, which are the microaneurysms. Both systems are using a popular public database for the system training and evaluation, i.e. the standard diabetic retinopathy database calibration. System I is evaluated by using the standard diabetic retinopathy database calibration level 0 (DIARETDB0), which consists of 130 colour fundus images [6], of which 20 are normal and 110 contain signs of diabetic retinopathy (hard exudates, soft exudates, microaneurysms, haemorrhages and neovascularisation). System II is evaluated by using the standard diabetic retinopathy database calibration level 1 (DIARETDB1). The database consists of 89 colour fundus images [22], of which 5 are normal and 84 contain signs of diabetic retinopathy (exudates, microaneurysms and haemorrhages). The fundus

images are of size 1500 × 1152 in PNG format. There are 75 images with microaneurysm, and the remaining 14 images were identified as showing no microaneurysm signs.

Both systems present a combination of different techniques, such as different preprocessing techniques, different feature parameters and different classifiers in a diabetic retinopathy screening system, which are different from systems proposed by other researchers.

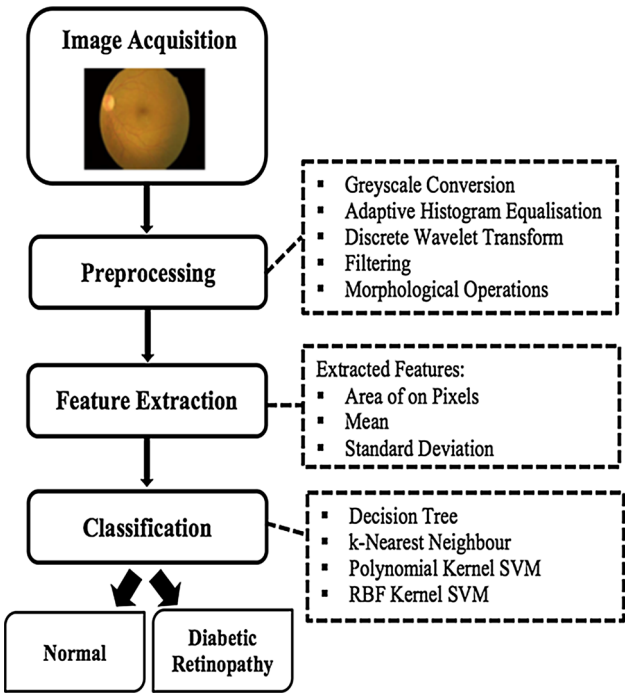
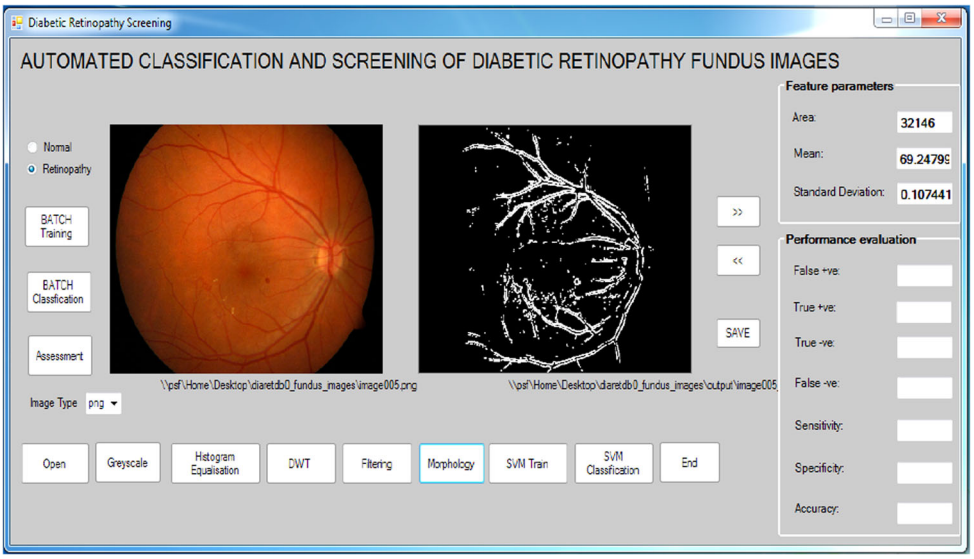


Fig. 2 Block diagram of the proposed automatic screening and classification of diabetic retinopathy

3.1 System I: Preliminary system for automatic screening and classification of diabetic retinopathy fundus images

A preliminary classification and screening of diabetic retinopathy using fundus images is presented in [21]. The developed general detection system contains four main parts, namely the image acquisition, the image processing, the feature extraction and, finally, the classification by using several machine learning techniques. Figure 2 presents the block diagram of the proposed system, while Fig. 3 shows a user interface snapshot of the proposed developed system. The proposed system starts with the image acquisition process to select images for further processing. The selected images will undergo preprocessing in order to improve the image contrast as well as perform other enhancements. After that, feature extraction takes place where the preprocessed images will be used to extract a number of features, such as the area, the mean and the standard deviation of on pixels. Four nonlinear classifiers, namely a binary decision tree, a *k*-nearest neighbour classifier and two support vector machines (SVM), are then trained on the training data to find an optimal way to classify images into their respective classes. The 1-nearest neighbour rule (1-NN) is used in the particular implementation of the system. Two different types of kernel functions provided for SVM classification were used, i.e. the second-order polynomial kernel SVM and the radial basis function kernel SVM. The results show that the RBF kernel outperformed the results obtained with the second-order polynomial kernel. Finally, in the prediction phase, the images are classified into two main groups: normal and diabetic retinopathy.

Fig. 3 Snapshot of the proposed system user interface



The experimental results presented in our previous preliminary work [21] show that the four classifiers, and especially the *k*-nearest neighbour, are able to identify well the normal and the diabetic retinopathy classes. Since our previously developed system is a general detection system, it can be extended to get more details on the diabetic retinopathy classification, namely to classify into no apparent retinopathy, mild non-proliferative, moderate non-proliferative, severe non-proliferative and proliferative diabetic retinopathy cases, or focusing on the detection of diabetic retinopathy features, such as microaneurysms, exudates and haemorrhages.

3.2 System II: Automatic detection of microaneurysms in colour fundus images using vessel segmentation and features extraction

The system for automatic detection of microaneurysm diabetic retinopathy consists of four main parts, namely the image acquisition, the image preprocessing, the feature extraction and the classification by using several machine learning techniques.

The initial stage of the proposed system is the image acquisition process, followed by the preprocessing process. The preprocessed images are then used to extract a number of features. Four nonlinear classifiers, namely a binary decision tree, a *k*-nearest neighbour classifier and two support vector machines, using radial basis function and polynomial function kernels, respectively, are then trained on the training data to find an optimal way to classify images into their respective classes. Finally, in the classification phase, the images are classified of whether microaneurysms are present or not. The overall process of microaneurysm detection is shown in Fig. 4.

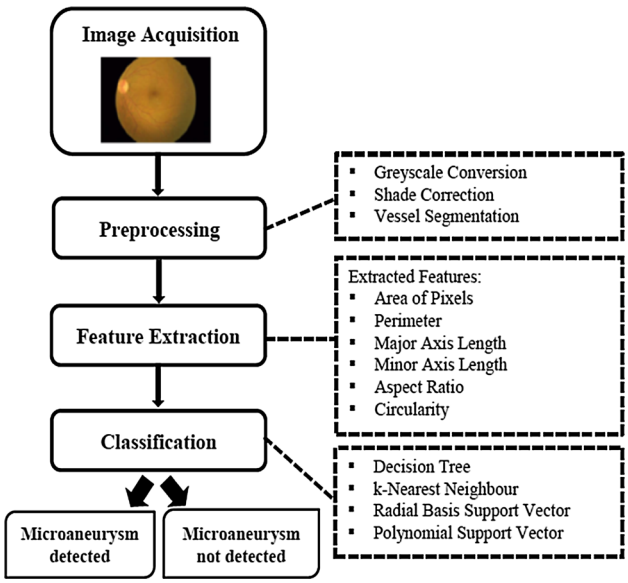


Fig. 4 Block diagram of the proposed automatic detection of microaneurysm diabetic retinopathy

3.2.1 Image preprocessing

Preprocessing is used for image improvement. Greyscale conversion and shade correction are the preprocessing techniques used in the proposed system.

First of all, the colour fundus image is converted into the greyscale format for better contrast. The second technique is the shade correction, where the background image is estimated and later subtracted from the original image. The nonuniform illumination in the image has to be corrected if the microaneurysm in this area has to be detected correctly. The first step is to estimate the background. The morphological opening technique is used in order to estimate the background. The function *imopen* in MATLAB is used to perform morphological opening on the greyscale image (with the structuring element of 12 pixels and disc shape). The second step is to subtract the background image from the original image (by using the *imsubtract* function). The shade correction process is then continued, by increasing the image contrast (using the function *imadjust*), followed by thresholding the image (by using *im2bw* function), and then by the removal of the background noise (using *bwareaopen*). As a result, the thresholded image is inverted and the final output, which only shows the fundus image area, is obtained.

After the greyscale conversion and shade correction, vessel segmentation is performed. The vessels are extracted from the shade-corrected image using a morphological operation. The image is closed using a disc-shaped structuring element of 5 pixels. The shade-corrected image is filled to eliminate holes in the vessels. Later, the filled image is subtracted from the closed image to give a vessel difference image. The image is thresholded to get the binary images containing the vessels. The binary image is subtracted from the Gaussian-filtered image so that the final image has vessel-free candidates.

Besides the two main preprocessing methods, the greyscale conversion and shade correction, some other image preprocessing techniques may be implemented as well, such as the green channel conversion, the median filter, the Gaussian filter and the contrast-limited adaptive histogram equalisation. In addition, four of the blood vessel extraction techniques can be implemented, including the Kirsch Template, Frangi Filter, Local Entropy and Entropic Thresholding. Figure 5 shows the output after the preprocessing operations are done on a selected image.

3.2.2 Feature extraction

After performing the preprocessing tasks, feature extraction takes place in order to obtain relevant features from the

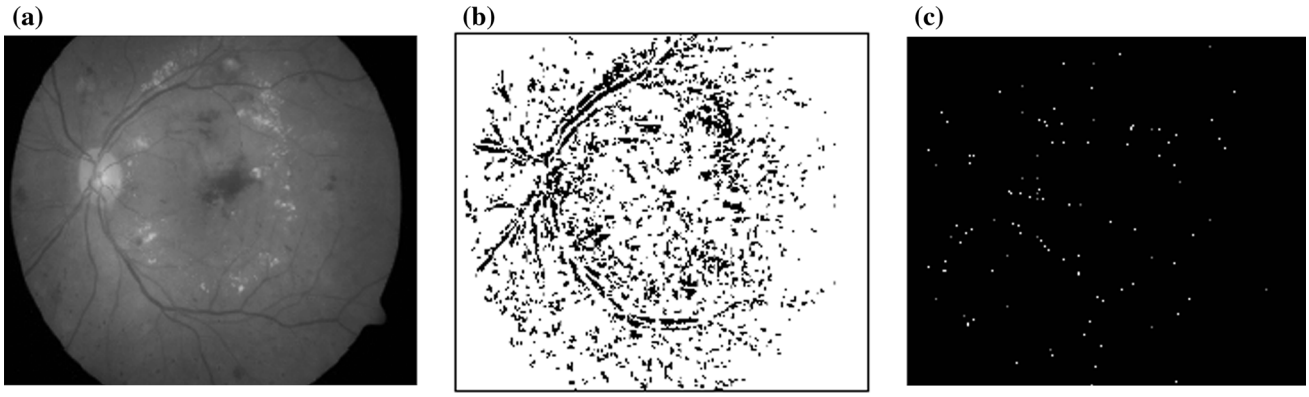


Fig. 5 Preprocessing the output image. **a** Greyscale conversion, **b** shade correction, **c** vessel segmentation

Table 1 Feature extraction in the proposed microaneurysm detection system

Feature	Description
Area of pixels in the candidate	The actual number of pixels in the region
Perimeter of the object	The distance around the boundary of the region
Major axis length of the candidate	The length (in pixels) of the major axis of the ellipse that has the same normalised second central moments as the region
Minor axis length of the candidate	The length (in pixels) of the minor axis of the ellipse that has the same normalised second central moments as the region
Aspect ratio	Major axis length divided by the minor axis length
Circularity	Roundness of the candidate $[(4 \times \pi \times \text{area})/(\text{perimeter}^2)]$

given images. Since a microaneurysm has specific features, such as circular shape and red colour, appropriate features should be extracted to ensure a reliable feature extraction and classification performed. Sopharak et al. [23] listed some useful features for microaneurysm detection based on shape, pixel intensity, Fourier descriptor and colour. Features such as the area of the pixels, perimeter of the object, major axis length, minor axis length, aspect ratio and circularity have been chosen and extracted in our second system for microaneurysm detection purposes. Table 1 presents the details of the features extracted in our system.

3.2.3 Classification

The implementation of the classification part was done using the PRTools package [24] in MATLAB. In the second system presented in this section, the classifiers selected and implemented for image classification purposes were as follows: the binary decision tree classifier, the 1-nearest neighbour rule (1-NN) classifier, the radial basis function kernel-based support vector classifier and the second-order polynomial kernel-based support vector classifier.

3.2.4 System results

Figure 6 shows the user interface snapshot of the proposed developed system. The performance (misclassification error) of the four classifiers is presented in Table 2. Since the data set is imbalanced, containing 75 images with microaneurysm signs and only 14 normal images, therefore, the minority class was oversampled by one-time duplication in order to avoid having a very imbalanced data set. The DIARETDB1 data are split randomly into 90 % for training and the remaining 10 % for testing. The process is repeated ten times in a cross-validation procedure in order to generate unbiased results. The average results on the ten runs for each of the four classifiers are reported.

The accuracy, sensitivity and also the specificity of the individual classifiers are presented in Table 2 above to measure the classification performance. The accuracy of the four classifiers, i.e. the binary decision tree and the 1-nearest neighbour, is 0.9091, while the radial basis function kernel-based support vector classifier and the second-order polynomial kernel-based support vector classifier are 0.7273. The experimental results show that the four classifiers are able to identify both classes, i.e. the "microaneurysms detected" and "no microaneurysms" classes. The binary decision tree and the *k*-nearest neighbour classifiers yielded very good results.

4 Automatic detection of microaneurysms in colour fundus images using circular Hough transform

In this section, two other versions of the proposed automatic general detection system are presented. For both proposed systems, 40 fundus images (of three different

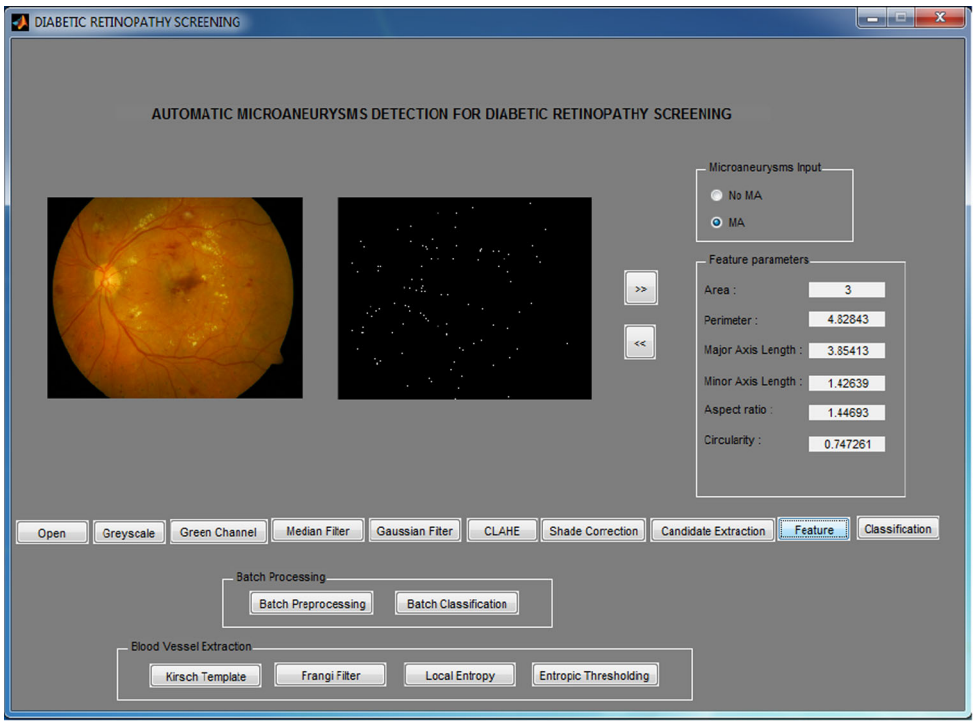


Fig. 6 Snapshot of the proposed system user interface

Table 2 Average results when using the four classifiers

	Binary decision tree	*k*-nearest neighbour	RBF kernel SVM	Polynomial kernel SVM
Misclassification error	0.0909	0.0909	0.2727	0.2727
Accuracy	0.9091	0.9091	0.7273	0.7273
Specificity	1	1	0.3333	0
Sensitivity	0.875	0.875	0.875	1

sizes: 768 × 576, 1058 × 1061 and 1389 × 1383) from the retinopathy online challenge (ROC) public database have been used for evaluation [13].

Both systems implement the combination of the preprocessing techniques and the circular Hough transform for the localisation and detection of the microaneurysms in colour fundus images. The circular Hough transform technique has been previously proposed for the detection of microaneurysms in two types of photography modes, i.e. in retinal fluorescein angiographic images [8] and also in digital red-free photographs [11]. Therefore, we explore the application of the circular Hough transform for the microaneurysm detection in another type of fundus photography modes, which is the colour mode. The detection of microaneurysms in colour fundus images is more challenging compared to the angiography and red-free types. In addition, the fourth system proposes the implementation of a fuzzy preprocessing technique, which is the fuzzy histogram equalisation. The fuzzy preprocessing techniques were used for contrast enhancement in the medical digital images, such as pathology images [42] and also other non-medical images [41]. The performance of the fuzzy preprocessing techniques reported in previous work is promising. We investigate the suitability of the fuzzy preprocessing technique for the diabetic retinopathy screening using the colour fundus images.

4.1 System III: Automatic detection of microaneurysms in colour fundus images using a combination of image preprocessing techniques and circular Hough transform

The third system proposed here is an automatic detection of microaneurysms in colour fundus images. The initial stage of the proposed system is the image acquisition process, followed by the preprocessing process. After that, the detection of the microaneurysm is performed by using the circular Hough transform method. Finally, in order to test the accuracy of the microaneurysm detection system compared to the ROC annotation, statistical tests are performed for result analysis. The overall process of microaneurysm detection is presented in Fig. 7.

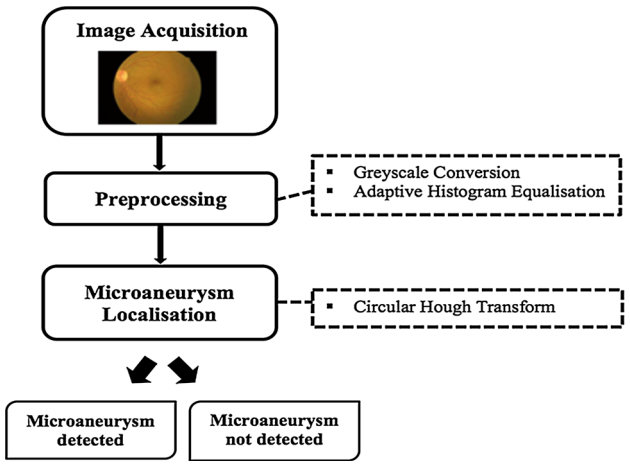


Fig. 7 Block diagram of the proposed automatic detection of microaneurysms using the CHT

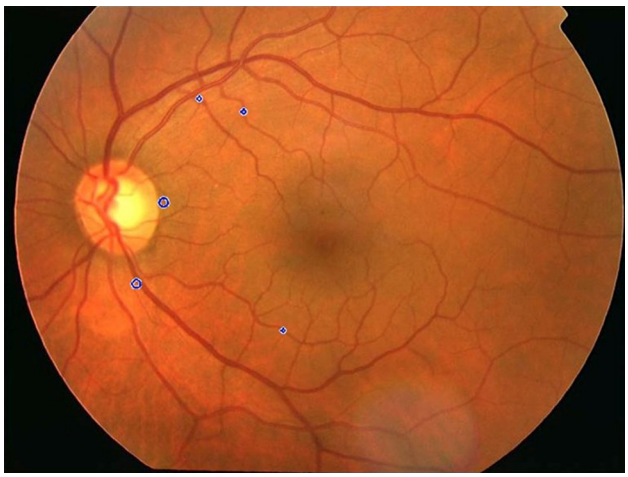


Fig. 8 Microaneurysm detection by using the circular Hough transform

4.1.1 Image preprocessing

A combination of preprocessing techniques, i.e. a greyscale conversion and contrast-limited adaptive histogram equalisation, are used in the system development. The proposed preprocessing techniques are used to help increase the contrast of the colour fundus images. The uses of the colour fundus images are more challenging compared to the other modes of fundus photography examination, which have been previously explained in Sect. 2.1: angiography and red-free. Therefore, appropriate techniques need to be implemented in order to improve the contrast of the fundus images for better visualisation and detection.

4.1.2 Circular Hough transform

The circular Hough transform (CHT) is implemented in the proposed system to locate the microaneurysms, due to the circular shape of the microaneurysms. In addition, CHT is also useful to detect the optic disc in a diabetic retinopathy screening system.

The Hough transform can be used to detect lines, circles or other parametric curves. The Hough transform can be used to determine a circle when a number of points that fall on the perimeter are known. A circle with radius R and centre (a, b) can be described with the parametric equations [26]:

$$x = a + R\cos(\theta)$$
$$y = b + R\sin(\theta)$$

The objective is to find the (a, b) coordinates of the centres at (x, y) on a circle of radius R. The Hough transform offers some advantages, such as being simple, easy to implement, handling missing and occluded data effectively, and that it can also be adapted to many types of forms other than lines. However, the limitation of the Hough transform is the complex computation involved for objects with many parameters, one single type of object detection, and the difficulty to determine the length and position of a line segment and, finally, that it cannot separate collinear line segments [27].

Firstly, the radius of the microaneurysms in the fundus images is calculated (using the function *imdistline*). Based on the radius range specified, the system will find the circles in the fundus images using the CHT (by using the *imfindcircles* function). Finally, after finding the circles in the image based on the radius range, the circle is created onto the current axes (using the function *viscircles*).

The Hough transform has been used for optic disc localisation by Noronha et al. [28]. Meanwhile, the same method was used to detect the early signs of diabetic retinopathy, represented by the microaneurysms [8]. The output of the microaneurysms' localisation and detection of the third proposed system is shown in Fig. 8.

4.1.3 System results

Figure 9 shows the user interface snapshot of the proposed developed system. The performance analysis of the system and expert annotation are presented in Tables 3 and 4, respectively. The number of microaneurysms detected by the expert and the system are calculated and compared. The presence of any number of microaneurysms is represented as diabetic retinopathy (microaneurysms detected), and if there is no microaneurysm detected, it is considered as normal (microaneurysm not detected). Two types of statistical tests were performed to test the system performance compared to the expert diagnosis. T test is used to test the differences in mean between the annotated images and the

Fig. 9 Snapshot of the user interface of the third proposed system

Table 3 *T* test analysis ($n = 40$)

	Mean	Standard deviation	Standard error mean	*p* value
Pair tested				0.253
Expert	1.78	0.423	0.067	
System	1.88	0.335	0.053	

n = number of fundus images diagnosed by the expert and the system

system output, and the results are presented in Table 3. The fundus images (forty in total) diagnosed by the expert and the system on the other hand were then compared with the *T* test analysis. Firstly, a descriptive statistical analysis was conducted, and the results, as shown in Table 3, indicate that there is only a small difference in the mean for the annotated images and that of the system (1.78 and 1.88, respectively). The inferential statistical analysis (i.e. *T* test) result indicates a *p* value of 0.253. This shows that the means of the annotated images and the system output are not significantly different.

The Chi-square test was also used to compare the two groups (i.e. the expert diagnosis and the system diagnosis). In addition, the Chi-square test was used to explore the relationship between these two categorical variables, as the results will help determine whether the system findings are more likely to be different from the expert findings, or in this case whether the expert is more likely or not to better identify diabetic retinopathy than the system. The results generated by the Chi-square test are shown in Table 4, where the Chi-square test indicates a *p* value of 0.239. Thus, it can be concluded that the system findings are more likely not to be different from the expert findings. In addition, Table 4 also shows the results of a cross-tabulation generated to descriptively compare the methods of assessment between two groups: expert and system diagnosis for both normal and diabetic retinopathy categories. The results show the expert diagnosed 9 images as normal and 31 images as diabetic retinopathy, while the developed system diagnosed 5 images as normal and the balance 35 images as diabetic retinopathy category, providing a further indication of the similarities between the two sets of diagnosis.

Table 4 Chi-square analysis ($n = 80$)

	Classification			Chi-square test statistic
	Normal *n* (%)	DR *n* (%)	Total *n*	
Method of assessment				χ^2 (1, $n = 80$) = 1.385, $p = 0.239$
Expert	9 (22.5)	31 (77.5)	40	
System	5 (12.5)	35 (87.5)	40	

n = number of fundus images diagnosed by the expert and the system

4.2 System IV: Automatic detection of microaneurysms in colour fundus images using fuzzy image processing

The fourth system applies a fuzzy technique for image preprocessing in the detection of microaneurysms. As explained before in Sect. 4.1.1 for the third system, the colour fundus images are more challenging compared to the other modes of fundus photography examination. Therefore, in order to get better visualisation and accurate detection, contrast enhancement should be implemented. Fuzzy histogram equalisation is used as the preprocessing method within this system.

Contrast enhancement produces better image than the original by changing the pixel intensities [41]. There are several contrast enhancement techniques available, i.e. histogram equalisation (HE), contrast-limited adaptive histogram equalisation (CLAHE), histogram stretching and brightness preserving histogram modification approaches. Histogram equalisation is a technique for adjusting image intensities in order to enhance contrast, where it distributes the grey-level values uniformly. Adaptive histogram equalisation, a more advanced version of histogram equalisation, divides the image into smaller tiles, applies histogram equalisation to each tile, and then interpolates the results. Adaptive histogram equalisation includes limits on how much the contrast is allowed to be changed, called the contrast-limited adaptive histogram equalisation, CLAHE.

Sheet et al. [41] proposed a modified technique of the brightness preserving equalisation called brightness preserving dynamic fuzzy histogram equalisation (BPDFHE). The representation and processing of images in the fuzzy domain allow the technique to handle the inexactness of grey-level values in a better way in order to improve the performance [41]. The technique proposed by Sheet et al. [41] is used for contrast enhancements in digital pathology images [42]. The performance of this technique has been compared with HE and CLAHE, and as a result, the BPDFHE preserved the image brightness better than the other two techniques. Good performance of the BPDFHE technique especially in the medical images such as pathology images is reported in [42]. This technique has been explored as a preprocessing technique for the proposed microaneurysm detection in diabetic retinopathy screening.

The first stage of the proposed system is the image acquisition process, secondly, the preprocessing process, thirdly, the detection of microaneurysms using the circular Hough transform method and, finally, in order to test the accuracy of the microaneurysm detection system with the ROC annotation, the statistical tests are used for analysis. System IV (a) is similar with the third system presented in Sect. 4.1, which implemented the greyscale conversion, contrast-limited adaptive histogram equalisation and circular Hough transform. The difference between these systems is that the third system presented is based on the nominal input, which categorised as normal or diabetic retinopathy, while the System IV (b) is analysed based on the scale input, which is the number of microaneurysms detected. The overall process of microaneurysm detection is presented in Fig. 10.

4.2.1 Image preprocessing

A combination of preprocessing techniques, a greyscale conversion and contrast-limited adaptive histogram equalisation (CLAHE) are implemented for the first system, while for the second system, a combination of a greyscale

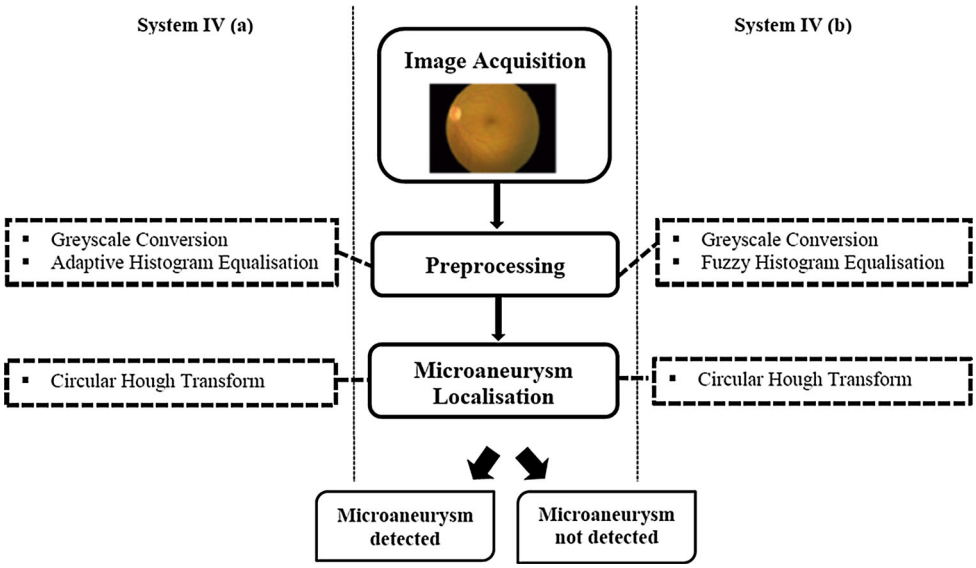


Fig. 10 Block diagram of the fourth proposed automatic detection of microaneurysms

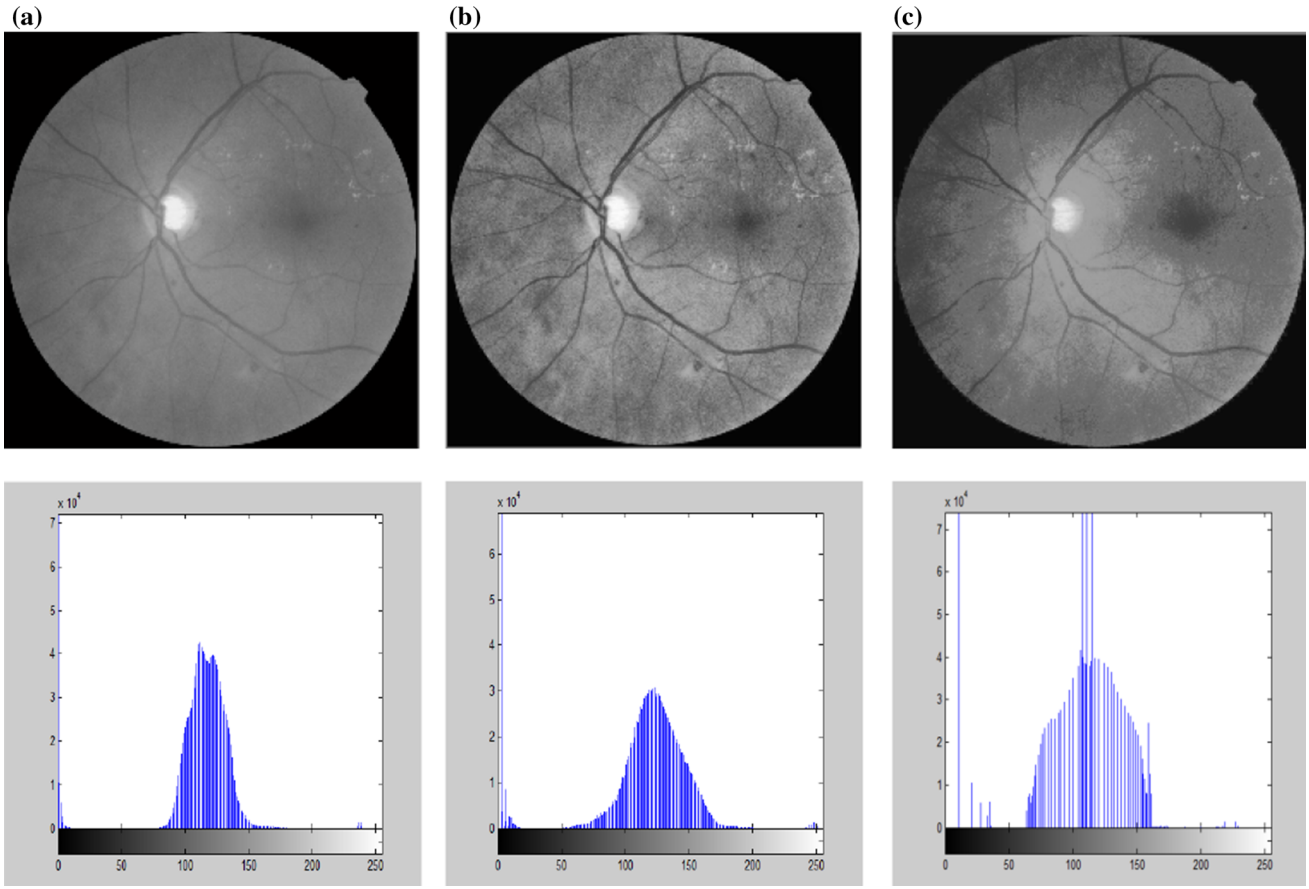


Fig. 11 Preprocessing the output image. **a** Greyscale conversion, **b** contrast-limited adaptive histogram equalisation, **c** fuzzy histogram equalisation

conversion and fuzzy histogram equalisation is proposed. Figure 11 shows the output and also the histogram for the intensity fundus image after the preprocessing techniques are applied, i.e. greyscale conversion, CLAHE and fuzzy histogram equalisation.

4.2.2 Microaneurysm detection

Circular Hough transform technique is implemented in the fourth system to detect the microaneurysms, as this technique has good ability to detect circular shapes. The explanation of circular Hough transform technique is presented in Sect. 4.1.2.

4.2.3 System results

Figure 12 shows the user interface snapshot of the proposed developed system. Generally, the interfaces for both systems are similar, but the implementation of the preprocessing techniques is different, as mentioned in Sect. 4.2.1 above.

The statistical result comparisons for both systems are presented in Table 5. The *T* test and the ANOVA test were performed to test the differences in mean between the annotated images and the system results based on the number of microaneurysms detected by the expert and the system. The first system, using a combination of greyscale conversion and contrast-limited adaptive histogram equalisation, shows that the means of the annotated images (7.48) and the system output (18.98) are significantly different. On the other hand, the second system, which implemented the greyscale conversion and fuzzy histogram equalisation, shows that the means of the annotated images (7.48) and the system (9.33) are not significantly different. The inferential statistical analysis (i.e. *T* test) result indicates a *p* value of 0.006 and 0.484 for the first and the second system, respectively. Meanwhile, the results generated by the ANOVA test are also shown in Table 5, where the ANOVA test indicates a *p* value of 0.380 for the first system and 0.961 for the second system. Based on the results presented, it can be concluded that the implementation of the fuzzy preprocessing technique provides better

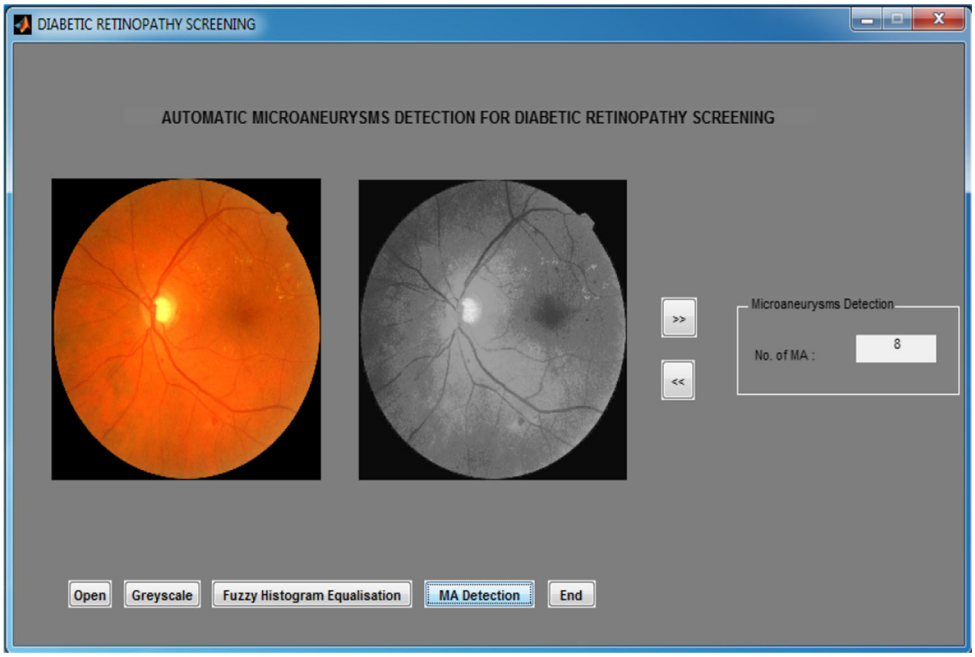


Fig. 12 Snapshot of the user interface of the fourth proposed system

Table 5 Summary results for Systems IV(a) and IV(b)

Features	System IV (a)	System IV (b)
Techniques	Greyscale conversion, contrast-limited adaptive histogram equalisation, circular Hough transform	Greyscale conversion, fuzzy histogram equalisation, circular Hough transform
Number of fundus images diagnosed	40	40
Confidence interval	95 %	95 %
T test *p* value	0.006	0.484
T test mean		
Expert	7.48	7.48
System	18.98	9.33
T test standard deviation		
Expert	10.268	10.268
System	21.021	11.425
T test standard error mean		
Expert	1.624	1.624
System	3.324	1.806
ANOVA test *p* value	0.380	0.961

contrast enhancement for fundus images, and hence, it greatly assists in detecting the microaneurysms, providing a more efficient and reliable performance of the diagnosis system.

5 Conclusions and future work

Several methods have been proposed and used in our developed systems for diabetic retinopathy screening, which were presented and contrasted in the above sections. Different techniques have been implemented for the proposed system in order to either detect general retinopathy signs (i.e. having retinopathy or not) or to detect more specific signs of retinopathy, such as the microaneurysms. The first and the second systems highlighted the uses of feature extraction and classification methods. The preliminary system for the general detection of diabetic retinopathy screening was extended by using more reliable features for the microaneurysm detection in the second system. The other two extensions of our system proposed the use of the circular Hough transform to detect the

microaneurysms in another mode of fundus photography, which are colour fundus images. Although the detection on the colour fundus images was challenging, the techniques proposed were able to improve the contrast and eventually improve the system performance. The fourth system proposed the implementation of a fuzzy preprocessing technique, which clearly provides better contrast enhancement for the fundus images, and it can greatly assist the detection of the microaneurysms.

In addition, different public data sets have been used, which contained a variety of colour fundus images. A good quality of the available fundus images can help in the process of localisation and detection of the retinopathy signs. Preprocessing techniques also play an important role and can help increase the quality of the fundus images to be used by the system.

The detection of microaneurysm is a really challenging problem due to the special characteristics of the microaneurysm in terms of shape, size and colour. Therefore, appropriate techniques must be considered in the system development for microaneurysm detection in order to produce better sensitivity, specificity and accuracy. A reliable and efficient automatic system for microaneurysm detection will help detect the early retinopathy signs and, indirectly, reduce the burden borne by the diabetic retinopathy screening team. Such system will facilitate the future medicine goal related to modelling the complexity of patient needs in order to tailor medical decisions, health practices and therapies to the individual patient [39].

In our future work, we will explore enhancements of the above described system by utilising other preprocessing techniques such as the optic disc localisation, vessel segmentation and the fuzzy circular Hough transform for microaneurysm detection. The proposed system can be a benchmark for the development of detection systems for other retinopathy signs, such as exudates, haemorrhages and neovascularisation. In addition, the system could be also extended in order to get more details on the diabetic retinopathy classification, namely to classify into no apparent retinopathy, mild non-proliferative, moderate non-proliferative, severe non-proliferative and proliferative diabetic retinopathy cases, based on the retinopathy signs detected. A complete and accurate automatic system would help the diabetic retinopathy screening in a more effective way. Moreover, it can help achieve the overall aim of the screening process, which is to detect earlier the sight-threatening diseases and to ensure a timely treatment in order to prevent vision loss.

Currently, we are developing a new database of fundus images, which have been collected from the Eye Clinic of the Department of Ophthalmology, Hospital Melaka, Malaysia. The data set, which consists of colour fundus images from 2401 patient's folders, offers a good representation of South-east Asian population, particularly Malaysian. As a future plan, the techniques presented in this paper for the microaneurysm detection will be tested with the new data set.

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