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Abstract. The contrast enhancement of retinal image plays a vital role for the detection of microaneurysms (MAs), which are an early sign of diabetic retinopathy disease. A retinal image contrast enhancement method has been presented to improve the MA detection technique. The success rate on low-contrast noisy retinal image analysis shows the importance of the proposed method. Overall, 587 retinal input images are tested for performance analysis. The average sensitivity and specificity are obtained as 95.94% and 99.21%, respectively. The area under curve is found as 0.932 for the receiver operating characteristics analysis. The classifications of diabetic retinopathy disease are also performed here. The experimental results show that the overall MA detection method performs better than the current state-of-the-art MA detection algorithms. © 2016 Society of Photo-Optical Instrumentation Engineers (SPIE) [DOI: 10.1117/1.JMI.3.1.014502]

Keywords: medical image analysis; diabetic retinopathy; retinal image; microaneurysms; exudates; optic disk; retinal blood vessels.

Paper 15045RR received Mar. 3, 2015; accepted for publication Dec. 18, 2015; published online Feb. 9, 2016.

1 Introduction

The development of a reliable method for early detection of diabetic retinopathy (DR) disease is still an open issue in medical image analysis. The DR is an ocular disease that originates from diabetes mellitus and also a major cause of adult blindness in developing countries if not detected and treated in time.¹ Early detection of DR has been clinically proven to reduce the chances of vision loss by 90% and also slow down the progression of DR very effectively. According to medical experts, the small (diameter 10 to 100 μm) circular red spot on retina called microaneurysms (MAs) are the first sign of DR. Hence, one of the essential parts for early detection of DR is the proper detection of MAs. Clinical study shows that automated MA detection may reduce the workload of ophthalmologist because manual screening is a time-consuming and resource-demanding process.² Additionally, in cases of low-contrast, noisy retinal images, the detection of MAs becomes difficult. Therefore, prior to the medical analysis, contrast enhancement of retinal image is an essential step.³ Here, contrast enhancement improves the quality of the retinal images and brings out the finer details of the image. This enhanced retinal image can serve either for improved human perception or as an input to further automated screening system. Generally, contrast enhancement schemes may be categorized into global histogram equalization (GHE) and adaptive histogram equalization (AHE). In GHE, the enhancement is based on the equalization of the histogram of the entire image. So using only global information is often not enough to achieve good contrast enhancement. To overcome this

problem, AHE may be applied that considers local window for each individual pixel and computes new intensity values based on local window. If there is a small intensity range, the noise in that region gets more enhanced. To limit the noise, contrast limited AHE (CLAHE) may be applied.⁴ In CLAHE, the adaptive property usually improves the image quality but is unable to preserve the mean brightness of the retinal fundus images. The preservation of mean brightness of the input image is essential for medical image analysis. To overcome this limitation, many brightness-preserving techniques were introduced earlier. Dynamic histogram equalization (DHE) is one of them, where mean image brightness is more or less varied due to histogram peak remapping.⁵ In this research paper, at the preprocessing stage, the fuzzy statistics of the digital image is applied, which enable handling of the intensity values in better ways for enhancement of retinal images. The proposed contrast enhancement does not have missing intensity levels and provides a smooth histogram. Experimental results with performance analysis show that the proposed contrast enhancement method produces better quality images and also is able to preserve the mean brightness satisfactorily, and as a result it indeed improves the overall MA detection method. The rest of the paper is presented as follows: in Sec. 2, review work is given. In Sec. 3, proposed methods for retinal image contrast enhancement is presented. The overall MA detection method is given in Sec. 4, and in Sec. 5, the criteria for grading of DR image presented. The brightness preserving ability of the proposed method is described in Sec. 6. In Sec. 7, the method for performance analysis is given. The results and discussion are provided in Sec. 8. Finally, the conclusion of the paper is given in Sec. 9.

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2 Review Work

In retinal fundus images, the background pixel intensities are very similar to the pixel intensities of dark lesion. Hence, prior to MA detection, retinal image preprocessing for contrast enhancement becomes an essential step. The literature review shows that a dark lesion has the highest contrast in a green plane.² Thus, a lot of research papers for MA detection have been published considering the green plane. Histogram equalization (HE) and histogram matching are the most common contrast enhancement methods that are applied for MA detection. Salem and Nandi⁶ and Hijazi et al.⁷ applied this method. In this method, a high-quality retinal image is selected as reference image. Then an image contrast-enhancement technique is applied to other images with the goal of changing the intensity to be similar to the reference image histogram. It is not a good method for contrast enhancement because the mean brightness of the image is not preserved. If the reference image does not contain a lesion, the effect of lesion is also removed from other images. Yun et al.⁸ applied GHE for the identification of different stages of DR disease. Here, GHE expands the histogram of an image to a full range of gray-scale images, and as a result, the washed-out effect appeared on the output image. Feng et al.⁹ had shown the limitation of GHE on retinal images. Spencer et al.¹⁰ applied the shade correction method at preprocessing stage. A median filter with large window size was applied there and the size of window would be larger than the largest vessel size. Frame et al.¹¹ also applied the similar technique but normalization of the image was done in such a way that resultant image showed similar maximum and minimum gray levels as the initial image. Cree et al.¹² applied the shade correction method for each plane of the image to correct the intrainage variations. The main problem of the shade correction method is that bright lesion turns into sharp edges, and these lead to false-positive points in candidate detection process. Neimenjer et al.¹³ eliminated this drawback by omitting bright lesions from the image. This method had also the limitations of preserving the mean brightness of the retinal input images. Miri and Mahloojifar¹⁴ used matched filtering to enhance the blood vessels contrast. The limitation of this method is that computations become complex when the image size is large enough. Matched filtering technique is useful for global contrast enhancement, but does not produce good results on nonproliferative DR (NPDR) image analysis. Foracchia et al.¹⁵ and Garcia et al.¹⁶ applied contrast normalization method on retinal images. This technique is useful only on HSV color model. Antal et al.¹⁷ used CLAHE-based method for the detection of MAs. Here, the main disadvantages are that noise amplification occurs in flat regions and ring artifacts appear at the edges. In DHE, the image histogram partitioned using the position of local minima. This method is not good enough for preserving the mean brightness due to the fact that remapping of histogram peaks caused mean brightness to also vary. Ibrahim and Kong⁵ proposed the brightness-preserving DHE (BPDHE) to avoid the peak remapping of histogram. This method applies the crisp histograms to enhance the contrast of the image but this technique does not take any consideration of inexact gray values. So, mean brightness significantly changes. The current state-of-the-art shows that GHE and CLAHE methods are very popular for contrast enhancement of the retinal images. Still, to date, the researchers are not considering the effect of mean brightness on MA detection method. Previously no such image quality assessment technique has been applied prior to the medical image selection, which is

an essential part of the medical image analysis. In diabetic screening system (DSS), DR grading is an important issue, although all the authors are not considering the DR image gradation.

3 Proposed Method: Preprocessing Stage

The existing DHE method⁵ is unable to consider the inexact gray level values of retinal images. Here, the scheme is modified using fuzzy statistics of digital images which will be appropriate for retinal image contrast enhancement. The proposed contrast enhancement method consists of following operational stages:

- Step 1.** Green plane is selected from RGB color plane.
- Step 2.** Fuzzy histogram is calculated.
- Step 3.** Partition the image histogram.
- Step 4.** Equalize the intensity level of subhistogram.
- Step 5.** Equalize the brightness difference of input and output images.

The following sections are representing the details of each step.

Step 1: In the preprocessing stage, the green plane is chosen from the RGB color plane as MAs have the maximum contrast with the background in this color plane^{2,3,13,18}

$$g = \frac{G}{R + G + B}, \quad (1)$$

where g is the component of green plane (G). R and B are red and blue planes, respectively.

Step 2: If $\tau(i)$ is the frequency of occurrence of gray level “around i ,” then fuzzy histogram is calculated as

$$\text{FuzzyH} = \tau(i) + \sum_x \sum_y \mu \hat{I}(x, y) i, \quad (2)$$

where $\mu \hat{I}(x, y) i$ is the fuzzy membership function defined as

$$\mu \hat{I}(x, y) i = \max \left(0, 1 - \frac{|I(x, y) - i|}{4} \right) \quad \text{and} \\ i \in \{0, 1, \dots, L - 1\},$$

where L is a real positive number, $I(x, y)$ is the gray value of image, and $\hat{I}(x, y)$ is the fuzzy number. Compare to the conventional GHE method, fuzzy computation is able to produce more smoothing histogram.

Step 3: In this step, the image histogram is partitioned into subhistograms to obtain the local maxima points. Here, the valleys are segmented by two consecutive local maxima points to form a segment. In the next stage when DHE of these portions is performed, the peaks of the histogram are not remapped, and as a result, the mean brightness is preserved. Here, partitioning of the image histogram is done using local maxima, which lie in between first- and second-order derivatives of the fuzzy histogram. First-order derivative of i 'th intensity level is

$$\frac{\tau(i)}{di} = \frac{d\tau(i)}{di} \triangleq \frac{\tau(i+1) - \tau(i-1)}{2}. \quad (3)$$

Second-order derivative of i 'th intensity level is

$$\overline{\tau(i)} = \frac{d^2\tau(i)}{di} \triangleq \tau(i+1) - 2\tau(i) + \tau(i-1), \quad (4)$$

where $\overline{\tau(i)} < 0$.

The second-order derivation is done to reduce the approximation error of the first-order derivative. The local maximum points (i_m) are those values of intensity level where zero crossing of the first-order derivative detected with a negative value at the second-order derivative. The ambiguity arises when perfect zero crossing does not take place at integral values of the intensity level. In such cases, two neighboring pairs are selected and detected as maxima. The ambiguity can be determined by preserving the point with the highest count among the neighboring pair of maxima

$$i_m = i \forall \{\overline{\tau(i+1)} \times \overline{\tau(i-1)} < 0\}, \quad (5)$$

where i_m points are applied to create partition on fuzzy histogram. Assume that the original fuzzy histogram spread in $[I_{\min} - I_{\max}]$ with $(n+1)$ intensity level of the corresponding local maxima denoted by $\{m_0, m_1, \dots, m_n\}$. The subhistograms are formed by partitioning the histogram as $\{[I_{\min}, m_0], [m_0 + 1, m_1], \dots, [m_n + 1, I_{\max}]\}$.

Step 4: In this step, when DHE of these portions is performed, the peaks of the histogram are not remapped and as a result, it preserves the mean brightness. Here, DHE is applied to equalize the intensity level of subhistogram. A spanning function is based on total number of pixels in the partition performs the equalization. The stages for DHE are given as

$$S_i = h_i - l_i, \quad (6)$$

$$f_i = S_i \times \log_{10} M_i, \quad (7)$$

$$R_i = \frac{(L-1) \times f_i}{\sum_{k=1}^{n+1} f_k}, \quad (8)$$

where h_i and l_i represent the highest and lowest intensity values in the i 'th input subhistogram, respectively. M_i is the total number of pixels in the partition. S_i , f_i , and R_i represent the dynamic range of the input subhistogram, the factor for DHE, and the output subhistograms, respectively. So, from Eq. (8) the dynamic range for the i 'th output subhistograms are as follows:

$$\text{start}_i = \sum_{k=1}^{i-1} R_k + 1, \quad (9)$$

$$\text{stop}_i = \sum_{k=1}^i R_k. \quad (10)$$

In Fig. 1, the red points are manually marked to realize the local maxima concept. The selection of local maxima is a completely software-based automated procedure. Hence,

Fig. 1 Local maxima points of fuzzy histogram.

the detection of local maxima is done effectively in case of noisy histogram also.

The dynamic range is calculated in Eqs. (9) and (10) and assigned on local maxima points. Then, each histogram partition is equalized and the i 'th subhistogram the remapped values are obtained by the following equation:

$$y(c) = s_i + R_i \sum_{k=s_i}^c \frac{h(k)}{D_i}, \quad (11)$$

where $y(c)$ is the new intensity level corresponding to the c 'th intensity level of the input image and $h(k)$ is the histogram values at the k 'th intensity level of the fuzzy histogram. The total population count in the i 'th partition of the fuzzy histogram, D_i , can be derived from Eqs. (9)–(11) as

$$D_i = \sum_{k=\text{start}_i}^{\text{stop}_i} h(k). \quad (12)$$

Step 5: The mean brightness, followed by DHE of each subhistogram, may differ slightly from the input image. Normalization is applied here to remove the brightness difference. DHE method partitions the image histogram into multiple segments using the position of local minima. Thereafter, the subhistogram is independently equalized. This method has the limitations of histogram peaks remapping, which leads to unavoidable changes on mean image brightness. To avoid the histogram peak remapping, brightness-preserving dynamic histogram equalization (BPDHE) has been introduced. Here, concept of smoothing a global image histogram is used by applying Gaussian kernel followed by segmentation of valley regions for their dynamic equalizations. Basically, BPDHE processes the crisp histograms of images for contrast enhancement. These crisp statistics of digital image processing do not take into consideration the inexactness of gray values. So, here for contrast enhancement of retinal images, the fuzzy statistics of digital images are used, as in a fuzzy histogram there are no random fluctuations or missing intensity levels. This last stage of the proposed contrast enhancement scheme ensures that the mean intensity of the image obtained after processing is the same as that of the input image.

Let, ϕ and ψ are the mean brightness level of input image and the image (F) is found after histogram equalization, respectively. If $f(x, y)$ is the output image then the gray level value at the pixel location (x, y) for image $f(x, y)$ is given by

$$f(x, y) = \frac{\phi}{\psi} F(x, y). \quad (13)$$

This image contrast enhancement method (Fig. 2, phase 1) is applied on MA detection algorithm. The next section describes the MA detection method.

4 Microaneurysm Detection: Early Detection of Diabetic Retinopathy

In this paper, automated software-based diabetic screening system (DSS) is developed using MATLAB[®] 10 software. The next few sections describe the intermediate steps for detection of MAs.

4.1 Input Images

Publicly available databases DRIVE, STARE, DIARETDB0, and DIARETDB1 are used as input for the DSS. The low-contrast, noisy retinal images collected from the hospital are also used here as input images. The green layer of retinal input image is shown in Fig. 3(a).

4.2 Retinal Image Contrast Enhancement

The proposed contrast enhancement method described in Sec. 3 is applied (Fig. 2, phase 1) on the input images prior to the MA detection. Then, quality assessment is made on the resultant image.

4.3 Image Quality Assessment

Here, in this paper, structural similarity index measurement (SSIM) is applied for the retinal image quality assessment. By definition, If $SSIM = 1$, the image is original and closer to 1; the image quality will be better.¹⁹ The performance of the SSIM using the MATLAB[®] 10 software is evaluated to examine the image quality (Fig. 4 and Table 1). A retinal image where SSIM value greater than or equal to 0.7 is selected for the detection of MAs otherwise processed the input image again. The details of the SSIM method are described as follows:

$$SSIM = L(p_1, p_2) \times C(p_1, p_2) \times S(p_1 \times p_2), \quad (14)$$

where p_1 and p_2 are the original and enhanced images, respectively. In SSIM, comparison is done on luminosity (L), contrast (C), and similarity (S) of input and resultant image. M and N are the dimensions of image. If μ and β are the mean and standard deviation of the corresponding images and C_1, C_2 , and C_3 are constants then

Fig. 2 DSS; phase 1: selection of image as input; phase 2: existing features detection and elimination; and phase 3: classification of eye as normal or diabetic diseased (with grading).

Fig. 3 (a) Green layer of retinal image, (b) preprocessed the image having SSIM = 0.76, (c) optic disk detection and elimination, (d) exudates detection, (e) image after closing from image (b), (f) filled in image, (g) difference image from (e) and (f), (h) image after eliminating the objects smaller than MAs. (i) Extended minima transformation with selected threshold value, (j) image after eliminating vessels and exudates from (d) and (g), (k) detected MAs on retinal fundus image, (l) superimposed image.

$$\mu p_1 = \frac{1}{M \times N} \sum_{y=0}^{M-1} \sum_{x=0}^{N-1} p_1(x, y), \quad (15)$$

$$\beta p_1 = \sqrt{\frac{1}{(M \times N - 1)} \sum_{y=0}^{M-1} \sum_{x=0}^{N-1} [p_1(x, y) - \mu p_1]^2}. \quad (16)$$

From Eq. (16)

$$\begin{aligned} \beta p_1 \beta p_2 &= \frac{1}{M \times N - 1} \sum_{y=0}^{M-1} \sum_{x=0}^{N-1} [p_1(x, y) - \mu p_1 \\ &\quad - \mu p_2][p_2(x, y) - \mu p_2]. \end{aligned} \quad (17)$$

According to the theory of SSIM

$$L(p_1, p_2) = \frac{2\mu p_1 \mu p_2 + C_1}{\mu^2 p_1 + \mu^2 p_2 + C_1}, \quad (18)$$

$$C(p_1 p_2) = \frac{2\beta p_1 \beta p_2 + C_2}{\beta^2 p_1 + \beta^2 p_2 + C_2}, \quad (19)$$

and

$$S(p_1 p_2) = \frac{\beta p_1 p_2 + C_3}{\beta p_1 \beta p_2 + C_3}. \quad (20)$$

Hence,

$$\text{SSIM}(p_1 p_2) = \frac{(2\mu p_1 \mu p_2 + C_1)(\beta p_1 p_2 + C_2)}{(\mu^2 p_1 + \mu^2 p_2 + C_1)(\beta^2 p_1 + \beta^2 p_2 + C_2)}. \quad (21)$$

Here, for the simplicity, let, $C_3 = C_2/2$, $C_1 = (K_1 L)^2$, and $C_2 = (K_2 L)^2$, where L is the dynamic range of the pixel values (255 for 8 bit gray scale images). According to the theory, K_1 (where $K_1 \ll 1$) and K_2 (where $K_2 \ll 1$) both are constant and assumed as $K_1 = 0.01$ and $K_2 = 0.02$, respectively.¹⁹ The performance of the SSIM using the MATLAB[®] VER10 software is evaluated to examine the image quality. A retinal image where SSIM value is equal to or greater than 0.7, selected for the detection of MAs otherwise process the input image again. Preprocessed image is shown in Fig. 3(b).

4.4 Feature Extraction of Retinal Input Image

Here, in the proposed method, MAs are the object, and other existing features such as optic disk, bright objects (exudates),

Fig. 4 Image quality (SSIM) comparison with GHE, CLAHE, and proposed method on (a) DIARETDB0 (no. of images: 130), (b) DIARETDB1 (no. of images: 89), (c) STARE (no. of images: 81), (d) DRIVE (no. of images: 40), (e) collected from hospital (no. of images: 247).

Table 1 Average SSIM values for different data set.

Image source	GHE	CLAHE	Proposed method
DIARETDB0	0.68	0.75	0.83
DIARETDB1	0.67	0.75	0.82
DRIVE	0.69	0.76	0.81
STARE	0.67	0.76	0.84
Hospital	0.58	0.72	0.82
Average	0.65	0.74	0.82
Std. Dev.	0.044	0.016	0.011

and retinal blood vessels are treated as noise. So, prior to the MA detection, noise is detected and eliminated. The next few sections describe the retinal feature selection and elimination applying mathematical morphological operations.

4.5 Optic Disk Detection

Optic disk is the largest-size high-contrast area in retina. In retinal images, the high-contrast blood vessels are also apparent, but the size is smaller than optic disk. So, here morphological closing operator (ϕ) on green channel image (f_g) will eliminate the vessels. This morphological operation is given as

$$X_1 = \phi^{(S_A)}(f_g), \quad (22)$$

where S_A is the morphological structuring element A of size S . S_A size varied as $S_A \in [6, 7, 8, 9, 10]$ for testing purpose. Then,

X_1 is binarized and the output image is applied as mask. All the pixels are reversed for the removal of bright features in the mask region. The resultant image is denoted as X_2 . Then, apply R (dilation) on X_2 and obtained image X_3 as

$$X_3 = Rf_g(X_2). \quad (23)$$

The difference between the original and the reconstructed image is threshold at gray level (α_A). It tested for $\alpha_A \in [0.6, 0.7, 0.8]$. As a result, high intensities are reconstructed while the rest are removed. Let, $Q = \{q_{\min} \dots q_{\max}\}$ be the ordered set of gray levels. The reconstructed image X_4 can be expressed as

$$X_4 = Q_{[\alpha, q_{\max}]}(f_g - X_3). \quad (24)$$

So, the optic disk is identified and dilation operator (d) is applied to ensure that all optic disk areas are detected. Here, X_5 is the resultant image, given as

$$X_5 = d^{(S_A)}[\text{area}_{\text{largest}}(X_4)]. \quad (25)$$

The optic disk detection and elimination are shown in Fig. 3(c).

4.6 Exudates Detection

Like optic disk detection, bright features such as exudates are detected. Here, high-contrast retinal blood vessels can be eliminated by applying closing operator. P_1 is the image after using a closing operator. At this stage the output $P_2(x)$ is expressed as

$$P_2(x) = \frac{1}{N-1} \sum_{i \in m(x)} [P_1(i) - \mu P_1(x)]^2, \quad (26)$$

where x is the set of all pixels in $m(x)$ subwindow, N is the number of pixels in $m(x)$, $\mu P_1(x)$ is the mean value of $P_1(i)$ and $i \in m(x)$. Window size 6×6 is applied here. The resultant image $P_2(x)$ is threshold at gray level α to get rid of all regions. Here, $\alpha = 0.5$ is selected. Dilation operator (d) is applied to ensure that all neighboring pixels are included into the candidate region. The resultant image $P_3(x)$ is represented as

$$P_3(x) = d^{(S_A)}[Q_{[\alpha, q_{\max}]}(P_2(x))]. \quad (27)$$

Thereafter, the existing holes are flood-filled as the exudates regions should not present only their borders

$$P_4(x) = P_3(x) - d^{(S_A)}(X_5). \quad (28)$$

In Eq. (28), $P_4(x)$ is used as a mask for all possible exudate regions and (X_5) is the optic disk region [Eq. (25)]. After that, a morphological dilation operation is performed for reconstruction of the image. The resultant image is $P_5(x)$ and it is subtracted from the original image at gray intensity level (α_B). Here, (α_B) varied as $\alpha_B \in [0.5, 0.6, 0.7]$. Finally, exudates (E_X) are obtained as

$$E_X = T_{[\alpha_B, t_{\max}]}[f_g - P_5(x)]. \quad (29)$$

The detected exudates are shown in Fig. 3(d).

4.7 Retinal Blood Vessel Detection

Clinically, MAs cannot occur on vessels; in addition to that, both MAs and blood vessels appear in reddish color. So, the blood vessels are removed prior to MA detection from the retinal fundus image. In the proposed method to detect retinal blood vessels, two intermediate images are generated. The first image generated from the green plane image (f_g) applying closing operator (ϕ) on it. This morphological operation removes the vessels from the image. Here, flat disk-shaped structuring element ($A_L = 12$) is applied. The second image is generated after removing small red objects and fill holes in the vessel. According to medical experts, the diameter of MA (λ) $< 125 \mu\text{m}$ and it lies in-between 10 and $100 \mu\text{m}$. In this proposed method, the size of MA is considered as 10 pixels. Here, the difference between first and second image is the vessel candidate area, given as

$$f_{v_{A_L}} = \phi^{(A_L)}(f_g) - \text{fill}(f_g), \quad (30)$$

where A_L is the morphological structuring element. The closing and filled in image are shown in Figs. 3(e) and 3(f), respectively. Then, applying threshold gray level (α_C), the candidate vessels are converted into binary values given as

$$f_v = T_{[\alpha_C, t_{\max}]}(f_{v_{A_L}}), \quad (31)$$

where $T = \{t_{\min}, \dots, t_{\max}\}$ are the ordered set of gray levels. The (α_C) is varied as $\alpha_C \in [0.4, 0.5, 0.6]$. The result is given in Fig. 3(g).

4.8 Microaneurysm Detection

Clinically, MAs are the reddish, circular pattern with diameter less than $125 \mu\text{m}$ and show high contrast in the green plane of the RGB image. Here, on the green plane f_g the extended minima transformation is applied. This threshold technique suppresses all the minima of the intensity image whose value is less than or equal to the predefined threshold. The resultant image is a binary image and collection of white pixels. The extended minima transformation on the green channel image is given as

$$f_{ge} = e_m(f_g, \alpha_D), \quad (32)$$

where f_{ge} is the output image. The overall performance of the MA detection is highly dependent on the threshold value selection. Here, $\alpha_D = 0.3$ is considered and best results are obtained, i.e., in performance analysis highest sensitivity and specificity are observed. For testing purpose, (α_D) is varied as $\alpha_D \in [0.1, 0.2, 0.3, 0.4, 0.5]$. In Fig. 3(i), the output image of the extended minima transformation is shown. Then, the detected bright features such as exudates [Eq. (29)] and retinal blood vessels [Eq. (31)] are removed from f_{ge} [Eq. (32)]. Thereafter, the resultant image f_M is shown the existing MAs on the retinal fundus image as follows:

$$f_M = f_{ge} - f_v - E_X. \quad (33)$$

The resultant image is given in Fig. 3(j). Subsequently, morphological operation is applied to select the object where the size is less than or equal to 10 pixels, which are consider as MAs. In proposed method, the objects with size smaller or

equal to 10 pixels are classified as MAs [Fig. 3(k)]. The parameter is varied as $MA_{size} \in [4, 7, 9, 10, 11, 12, 16]$. When the MA size selected as 4, 7, 9, and 10, the highest sensitivity and specificity are achieved, i.e., the maximum area under curve (AUC) in receiver operating characteristics (ROC) analysis is found. If the size of MA is greater than 10 pixels, the AUC is reduced, i.e., best result is not appeared. Hence, the size of MA is considered as less than or equal to 10 pixels, where the range for MA size is [4, 10]. Finally, the detected MAs are superimposed on the green layer of the retinal images in Fig. 3(l).

5 Grading of Diabetic Retinopathy Disease

The grading of DR disease primarily depends on the count of MAs.²⁰ The four stages of classification are no DR, mild DR, moderate DR, and severe DR as shown in Table 2. The proposed DSS counts the existing MAs on retinal images and grade the DR disease. Here, to grade the DR the hemorrhage (H) count is ignored, as there is no such significance of H count in grade 0 and grade 1. The H count is optional for grade 2 and grade 3.

6 Comparison of Brightness-Preserving Ability

In this paper, a brightness-preserving contrast enhancement method is presented for MA detection.

Absolute mean brightness error (AMBE) indicates how close the outputs mean brightness to the input mean brightness as follows:

$$AMBE = |X_o - X_i|, \quad (34)$$

where X_o and X_i represent the mean brightness of output and input images, respectively. The smaller value of AMBE is representing the better preservation of brightness property. The average AMBE is used for the proposed method is given by

$$AAMBE = \frac{1}{N} \sum_{i=1}^N |X_o - X_i|, \quad (35)$$

where N is the total number of test images.

7 Performance Analysis

The proposed method is tested for publicly available data sets DIARETDB0, DIARETDB1, DRIVE, and STARE. Subsequently the data sets of 247 nondilated retinal fundus images collected from hospital are also tested. The performance of the proposed MA detection method is evaluated by comparing the resultant extraction with the ophthalmologists hand drawn ground truth pixel-by-pixel. The captured image and

the superimposed images are compared by the ophthalmologist for evaluating the ground truth of the MA detection. A group of ophthalmologists make few changes by adding some missing MAs or eliminating some wrongly selected non-MA pixel. Here, the grading of DR is also verified by the ophthalmologists. In performance analysis, the sensitivity and specificity are the important parameters. This pixel-based evaluation considers four values, specifically, true positive (T_P), false positive (F_P), false negative (F_N), and true negative (T_N) (defined in Table 3, confusion matrix). Sensitivity is the percentage of the actual MA pixel those are detected by DSS. Specificity is the percentage of non-MA pixel which is correctly classified as non-MA pixels. All these parameters are calculated using Eqs. (36) and (37), respectively,

$$\text{Sensitivity} = \frac{T_P}{T_P + F_N} \times 100, \quad (36)$$

$$\text{Specificity} = \frac{T_N}{T_N + F_P} \times 100. \quad (37)$$

8 Results and Discussion

Here, to describe how the measurement was made, the results of the measurements are clearly described in Secs. 8.1 and 8.2.

8.1 Methods Used for Evaluation

The aim of this research work is to propose an effective contrast enhancement method for the detection of MAs on retinal images. The proposed contrast enhancement method is compared with GHE and CLAHE method because several papers opt for these two techniques prior to the MA detection. SSIM and AMBE methods are used here to test the retinal image quality. As clinically it is proved that MAs are the early sign of DR, so the focus of this research work is only on MA detection. During the input data set selection, high quality publicly available data set such as DIARETDB0, DIARETDB1, DRIVE, and STARE are selected. Subsequently, low-contrast, noisy retinal images collected from a hospital are also selected here as input data set. In this experiment, all the input images (no. of input images: 587) are tested by Pentium processor P6100 using software toolkit MATLAB[®] 10. Here, the results are tested by a group of ophthalmologists and finally the overall DSS is measured by applying ROC analysis. The software toolkit Graph Pad Prism version 6 is used for ROC analysis. The average rule with standard deviation is also applied to examine the variation of results for low contrast and high contrast retinal input images. Section 8.2 describes the overall experimental results of this research work. Here, in this research work, the overall procedure for MAs detection system is divided into

Table 2 Grading for DR disease.

DR stages	Criteria used for DR grading MA = microaneurysms, H = hemorrhage	
Grade 0	No DR	MA = 0
Grade 1	Mild DR	$1 < MA \leq 5$
Grade 2	Moderate DR	$5 < MA < 15$
Grade 3	Severe DR	MA > 15

Table 3 Confusion matrix (pixels evaluation).

Test result	Disease status	
	Present	Absent
Positive	True positive (T_P)	False positive (F_P)
Negative	False negative (F_N)	True negatives (T_N)

three fundamental steps. The first step consists of retinal image contrast enhancement on the green channel, as MAs have the maximum contrast with the background in this color plane, and subsequently image quality analysis is also performed. The second step detects all possible patterns corresponding to MAs. The last step classifies the normal and diabetic eye based on the presence of MA on the retinal image and grading of DR is also performed here.

8.2 Results

Experimental results for both retinal image contrast enhancement and overall MA detection are reported here. In Fig. 4, green lines (higher SSIM) are showing the SSIM values (image quality) obtained as an outcome of proposed contrast enhancement method. Red and blue lines are representing the SSIM values for GHE and CLAHE methods applied, respectively, on the same images. The image quality analysis (Fig. 4 and Table 1) shows that the proposed method can be more effective for low-resolution images (collected from hospitals, resolution: 480×512). When the input image is blurred, the output image produced by GHE and CLAHE methods is poor in quality (lower SSIM value). Figure 4 shows the effectiveness of the

proposed method. For the highest (DIARETDB0, resolution: 1500×1152) and lowest (hospital database, resolution: 480×512) resolution image database, the average SSIM is greater than 0.8. While in case of other conventional method like GHE, the average SSIM is less than 0.7. Similar results are observed for other databases [Figs. 4(b)–4(d)]. Using the AAMBE values, comparisons of the mean brightness preserving ability for the GHE, CLAHE, and proposed method are reported in Table 4. The proposed method produces satisfactorily results, so, at the preprocessing stage of DSS (Fig. 2) the said method may be applied. The performance analyses of the MA detection system are reported in Table 5. Overall 459 images are found as diseased images and 128 as the normal images. The performance of the proposed method is evaluated quantitatively by comparing the resultant extraction with ophthalmologists.¹⁸ In Fig. 5, some examples of ground truth evaluation are given. The average sensitivity and specificity revealed as 95.94% (Std.Dev. = 0.75505) and 99.21% (Std.Dev. = 0.304604), respectively. The ROC analysis is used here for appropriate performance analysis of the proposed DSS system. The ROC is to represent the tradeoff between the false negative (F_N) and false positive (F_P) for every possible cutoff. Table 6 represents the ROC analysis of the selected databases. The AUC is found as 0.932. The nature of the ROC curve is shown in Fig. 6.

The ROC raises rapidly toward upper left-hand corner of the graph, i.e., the false positive and false negative are low. So, the diagnostic test shows good results. When low contrast noisy retinal images (hospital database, resolution: 480×512) are used as input for the DSS, the AUC reaches at 0.9268 (red line at Fig. 6) which is quiet good result. The maximum AUC reaches at 0.9490 (95% confidence interval: 0.8339 to 1.064) for the DRIVE database and the minimum is 0.9165 (95% confidence interval: 0.8780 to 0.9550) for the DIARETDB0 database. The final AUC for the proposed MA detection method is 0.93252 (Std.Dev. = 0.01365). Here, the low standard deviation indicates that all the individual values are bunched up closely on either side of the mean. So, this proposed MA detection method is applicable for both good quality and low contrast noisy retinal images. Here, the average rule is applied to avoid for the computation providing extreme results, i.e., either bad or good. The high specificity of the proposed method

Table 4 Average AMBE values for different data set.

Image source (no. of image)	GHE	CLAHE	Proposed method
DIARETDB0(130)	10.087	8.058	0.014
DIARETDB1(89)	13.089	10.761	0.075
DRIVE(40)	24.005	24.071	0.003
STARE(81)	21.672	18.928	0.021
HOSPITAL(247)	34.852	32.082	0.002
Average	20.741	18.78	0.023
Std. Dev.	9.781	9.800	0.030

Table 5 Performance analysis of MA detection system (average rule).

Databases	Resolution	No. of images	Normal images	Diseased images	Sensitivity (%)	Std. Dev.	Specificity (%)	Std. Dev.	
DIARETDB0	1500 × 1152	130	20	110	95.52	3.68	99.09	0.86	
DIARETDB1	1500 × 1152	89	5	84	95.99	5.09	98.96	3.89	
STARE	768 × 584	81	31	50	95.70	6.45	99.51	0.46	
DRIVE	565 × 584	40	33	7	97.21	1.26	99.56	0.45	
Hospital	480 × 512	247	39	208	95.29	3.18	98.92	0.99	
Average	Considering all groups				95.94	—	99.21	—	
Minimum					95.29		98.92		
Maximum					97.21		99.56		
Std. Dev.					0.75505	0.304604			
Median					95.94	99.21

Fig. 5 Sample of performance analysis (such as TP and FN) done by ophthalmologists.

Table 6 ROC analysis of the proposed DSS method.

Databases	AUC	Std. error	95% confidence interval	<i>P</i> value	Best sensitivity/specificity
DIARETDB0	0.9165	0.01966	0.8780 to 0.9550	<0.0001	92.72/82.83
DIARETDB1	0.9259	0.02153	0.8837 to 0.9682	<0.0001	85.71/88.10
STARE	0.9444	0.02062	0.8339 to 1.064	<0.0049	90.00/86.00
DRIVE	0.9490	0.05869	0.8339 to 1.064	<0.0049	99.99/85.72
Hospital	0.9268	0.01346	0.9004 to 0.9532	<0.0001	88.94/88.95
Average	0.93252				
Std. Dev.	0.01365

Fig. 6 ROC analysis of the proposed method.

confirms that it does not identify a non-MA pixel as an MA pixel. Such high sensitivity and high specificity (close to 100%) cannot be achieved earlier as shown in Table 7. The overall ROC analyses are shown in Table 6. So, this proposed method is an optimum choice for detection of MAs. Here, the parameters are set using the values that provide highest sensitivity and specificity. $SA = 8$, $\alpha_A = 0.7$, $\alpha_B = 0.6$, $A_L = 12$, $\alpha_C = 0.5$, and $\alpha_D = 0.3$ produce a good balance between the number of detected MAs and the number of spurious object. In this context, the British Diabetic Association (Diabetes UK) has established standards for any DR screening programmed of at least 80% sensitivity and 95% specificity.²⁶ Obviously, the proposed method fulfills the minimum requirement. Here, the automated classification of DR is made by the DSS. The grading of DR disease is performed on low quality retinal images collected from hospital using the criteria reported in Table 2. The grading report is tested by ophthalmologists and comparative results are given in Table 8. The overall report for DR grading is very close with the ophthalmologists. The identical results are observed for grade 0 and 1 of DR disease at early stage.

Table 7 Comparison of performance analysis.

Author (year of publication)	Sensitivity (%)	Specificity (%)
Yun et al. (2008) ⁸	90	100
Spencer et al. (1996) ¹⁰	82	86
Frame et al. (2008) ¹¹	84	85
Cree et al. (1997) ¹²	82	Not given
Niemeijer et al. (2010) ¹³	100	87
Kose et al. (2012) ²¹	95.10	99.30
Dupas et al. (2010) ²⁰	88.47	Not given
Sinthanayothin et al. (2000) ²²	77.50	88.70
Zhang et al. (2010) ²³	95	89
Usher et al. (2004) ²⁴	95.10	46.30
Raman et al. (2004) ²⁵	70	70
Proposed method	95.94	99.21

Table 8 DR grading for hospital data set.

DR grade	Number of images (by proposed DSS method)	Number of images (verified by ophthalmologists)
Grade 0	39	39
Grade 1	156	156
Grade 2	31	30
Grade 3	21	22

9 Conclusion

The existence of MAs in retinal images is the early sign of DR and the automatic detection of MA is of recent clinical interest. The success rate of MA detection is highly dependent on the quality of input retinal images. In the proposed method, a new contrast-enhancement technique is presented that will generate a better quality of retinal image than the previously reported methods. To examine the retinal image quality, here, SSIM and AAMBE analyses are applied. The resultant images generated by the proposed contrast-enhancement method are encouraging and this preprocessing method increases the overall success rate of the MA detection system. In this screening process, 587 images are evaluated and AUC reaches at 0.932 with sensitivity and specificity close to 100% which are better than previously reported results. The DR grading of retinal images is also performed here and grading report is verified by a group of ophthalmologists. This automated MA detection method would be very effective to reduce the workload of ophthalmologist and would help to reduce the cost of the public health system effectively.

Acknowledgments

The authors acknowledge the K.P.C. Hospital, Kolkata, India, for their clinical support and the authority of publicly available data sets DRIVE, STARE, DIARETDB0, and DIARETDB1 for providing retinal images and data. The authors are thankful to the entire faculty member especially Professor Debasree Sarkar, Professor Sushanta Biswas, and Professor Partha Pratim Sarkar of DETS, University of Kalyani for continuous help in study.

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