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"Extraction of Microaneurysm in a Color Fundus Image of Retina using various ensemble frames and also grading system for diabetic retinopathy grading"

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Abstract: *We propose an ensemble-based framework to improve microaneurysm detection. Unlike the well-known approach of considering the output of multiple classifiers, we propose a combination of internal components of microaneurysm detectors, namely preprocessing methods and candidate extractors. We have evaluated our approach for microaneurysm detection in an online competition, where this algorithm is currently ranked as first, and also on two other databases.*
Keywords: *Diabetic retinopathy (DR) grading, ensemble-based systems, fundus image processing, microaneurysm (MA) detection.*

I. Introduction

Diabetic retinopathy (DR) is the most common cause of blindness in the developed countries. Microaneurysms (MAs) are early signs of this disease, so the detection of these lesions is essential in the screening process. DR can be prevented and its progression can be slowed down if diagnosed and treated early.. Microaneurysm appear as small circular dark spots on the surface of the retina .the most common appearance of microaneurysms is near thin vessels, but they cannot actually lie on the vessels. In some cases, microaneurysms are hard to distinguish from parts of the vessel system. A key feature to recognize DR is to detect microaneurysms (MAs) in the fundus of the eye. The importance of handling MAs are twofold. First, they are normally the earliest signs of DR; hence their timely and precise detection is essential.

II. Objective

In this paper we use ensemble based frame work. This is used to choose the best combination of preprocessing methods and candidate extractors

III. Existing System

DIABETIC retinopathy (DR) is a serious eye disease that originates from diabetes mellitus and is the most common cause of blindness in the developed countries. Therefore, much effort has been made to establish reliable computer aided screening systems based on color fund us images. In previous work "On combining computer-aided detection systems," showed that the fusion of the results of the several MA detectors leads to an increased average sensitivity measured at seven predefined false positive rates

3.1 Existing System Disadvantages:

a. In our earlier research on combining MA detectors did not provide reassuring results
b. The low Sensitivity of MA detectors originates from the candidate extractor part.

IV. Proposed System

In this paper, we propose an effective MA detector based on the combination of preprocessing methods and candidate extractors. We provide an ensemble creation framework to select the best combination. An exhaustive quantitative analysis is also given to prove the superiority of our approach over individual algorithms. We also investigate the grading performance of our method, which is proven to be competitive with other screening systems.

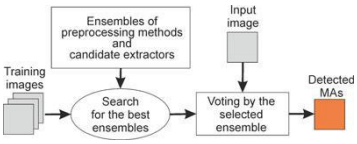


Fig- 1: Flow chart of the ensemble-based framework.

4.1.PROPOSED ADVANTAGES

a. The framework has high flexibility for different datasets.
b. The detector to provide sufficient sensitivity and specificity rate.

V. Diabetic Retinopathy

Diabetes is a disease that occurs when the pancreas does not secrete enough insulin or the body is unable to process it properly. Insulin is the hormone that regulates the level of sugar (glucose) in the blood. Diabetes can affect children and adults . Patients with diabetes are more likely to develop eye problems such as cataracts and glaucoma, but the disease's affect on the retina is the main threat to vision. Most patients develop diabetic changes in the retina after approximately 20 years. The effect of diabetes on the eye is called diabetic retinopathy. Over time, diabetes affects the circulatory system of the retina. The earliest phase of the disease is known as background diabetic retinopathy. In this phase, the arteries in the retina become weakened and leak, forming small, dot-like hemorrhages. These leaking vessels often lead to swelling or edema in the retina and decreased vision.

The next stage is known as proliferative diabetic retinopathy. In this stage, circulation problems cause areas of the retina to become oxygen-deprived or ischemic. New, fragile, vessels develop as the circulatory system attempts to maintain adequate oxygen levels within the retina. This is called neovascularization. Unfortunately, these delicate vessels hemorrhage easily. Blood may leak into the retina and vitreous, causing spots or floaters, along with decreased vision.

In the later phases of the disease, continued abnormal vessel growth and scar tissue may cause serious problems such as retinal detachment and glaucoma.

The affect of diabetic retinopathy on vision varies widely, depending on the stage of the disease. Some common symptoms of diabetic retinopathy are listed below, however, diabetes may cause other eye symptoms.

a. Blurred vision (this is often linked to blood sugar levels
b. Floaters and flashes
c. Sudden loss of vision

Diabetic patients require routine eye examinations so related eye problems can be detected and treated as early as possible. Most diabetic patients are frequently examined by an internist or endocrinologist who in turn works closely with the ophthalmologist.

The diagnosis of diabetic retinopathy is made following a detailed examination of the retina with an ophthalmoscope. Most patients with diabetic retinopathy are referred to vitreo-retinal surgeons who specialize in treating this disease.

Diabetic retinopathy is treated in many ways depending on the stage of the disease and the specific problem that requires attention. The retinal surgeon relies on several tests to monitor the progression of the disease and to make decisions for the appropriate treatment. These include: fluorescein angiography, retinal photography, and ultrasound imaging of the eye

Fig-2:Influence Of Diabetes On Vision

5.1 CLASSIFICATION OF DIABETIC RETINOPATHY

Diabetic retinopathy occurs when the blood vessels of the retina in the posterior part of the eye are damaged. Damages due to small vessels would be known as microvascular disease while damages due to the arteries would be macrovascular disease.

Generally, diabetic retinopathy is classified into two main stages, namely nonproliferative diabetes retinopathy (NPDR) and proliferative diabetes retinopathy (PDR).

5.1.1 NON-PROLIFERATIVE DIABETIC RETINOPATHY

In NPDR, depending on the presence and extent of the features such as hard exudates, microaneurysms or cotton wools spots due to leakage of fluid and blood from the blood vessels, can be classified to mild, moderate or severe stages as followings:

5.1.1.1. Mild NPDR:

This is the earliest stage of retinopathy and vision is usually normal except in some cases. However, deterioration of the blood vessels in the retina has already started. Blood vessels erupt when there is not enough oxygen in the blood because of high levels of glucose. Small swellings known as Micro-aneurysms or flame-shaped hemorrhages start to develop in the fundus quadrants.

5.1.1.2. Moderate NPDR:

As the disease progresses, some of the blood vessels that irrigate the retina become blocked. It is more than "mild" but less than "severe" stage. There will be micro-aneurysms or hemorrhages of greater severity in one to three quadrants and leakage might occur, resulting cotton wool spots and exudates etc to be present in the retina.

5.1.1.3. Severe NPDR:

As more blood vessels are blocked, those areas in the retina will be deprived of blood supply. Signals will then be sent to the body for the growth of new vessels in order to compensate for the lack of nourishment. The disease would be considered severe NPDR stage when any of the following criteria are met:

- Severe (more than 20) hemorrhages and micro-aneurysms in all four quadrants of the fundus
- Definite venous beading in at least two quadrants
- Severe damage to the small blood vessels in at least one quadrant but no signs of any proliferative diabetic retinopathy.

5.1.2 PROLIFERATIVE DIABETIC RETINOPATHY

PDR is the advanced stage whereby signals are sent by the retina to the body for the lack of blood supply and this triggered the growth of new blood vessels. These blood vessels can grow along the retina and the surface of the jelly-like substance (vitreous gel) which fills the centre of the eye. Although they are fragile and abnormal, they do not cause symptoms or vision loss. It is only when their thin and weak walls leak blood, severe visual loss or even irreversible blindness would occur.

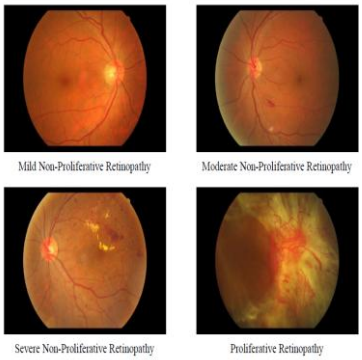


Fig-3: Retinal Images To Show The Different Stages Of Diabetic Retinopathy

VI. Methodologies

6.1 .PREPROCESSING METHODS:

The selection of the preprocessing method and candidate extractor components for this framework is a challenging task. Comparison of preprocessing methods dedicated to MA detection has not been published yet. Since preprocessing methods need to be highly interchangeable, we must select algorithms that can be used before any candidate extractor and do not change the characteristics of the original images (unlike, e.g., shade correction. We also found some techniques to generate too noisy images for MA detection (histogram equalization adaptive histogram equalization or color normalization.

6.1.1.Walter–KleinContrast Enhancement

This preprocessing method aims to enhance the contrast of fundus images by applying a gray level transformation using the following operator,

$$f' = \begin{cases} \frac{\frac{1}{2}(f'_{\max} - f'_{\min})}{(\mu - f_{\min})^r} \cdot (f - f_{\min})^r + f'_{\min}, & f \le \mu \\ -\frac{\frac{1}{2}(f'_{\max} - f'_{\min})}{(\mu - f_{\max})^r} \cdot (f - f_{\max})^r + f'_{\max}, & f \ge \mu \end{cases}$$

Where {fmin, . . . , fmax}, {f_ min, . . . , f_ max} are the intensity levels of original and the enhanced image, respectively, μ is the mean value of the original grayscale image and r ∈ R is a transition parameter.

6.1.2. Contrast Limited Adaptive Histogram Equalization

Contrast limited adaptive histogram equalization (CLAHE) is a popular technique in biomedical image processing, since it is very effective in making the usually interesting salient parts more visible. The image is split into disjoint regions, and in each region local histogram equalization is applied. Then, the boundaries between the regions are eliminated with a bilinear interpolation.

6.1.3. Vessel Removal and Extrapolation

We investigate the effect of processing images with the complete vessel system being removed based on the idea proposed. We extrapolate the missing parts to fill in the holes caused by the removal using the inpainting algorithm presented. MAs appearing near vessels become more easily detectable in this way.

6.1.4. Illumination Equalization

This preprocessing method aims to reduce the vignetting effect caused by uneven illumination of retinal images. Each pixel intensity is set according to the following formula:

$$f' = f + \mu_d - \mu_l$$

Where f, f' are the original and the new pixel intensity values, respectively, μ_d is the desired average intensity, and μ_l is the local average intensity. MAs appearing on the border of the retina are enhanced by this step.

6.1.5. No Preprocessing

We also consider the results of the candidate extractors obtained for the original images without any preprocessing. That is, we formally consider a "no preprocessing" operation, as well.

6.2 MA CANDIDATE EXTRACTORS:

Candidate extraction is a process that aims to spot any objects in the image showing MA-like characteristics. Individual MA detectors consider different principles to extract MA candidates.
In this section, we provide a brief overview of the candidate extractors involved in our analysis. Again, just as for preprocessing methods, adding new MA candidate extractors may lead to further improvement in the future. A summary on the key differences of the candidate extractor algorithms and their performance measured in the Retinopathy online challenge (ROC) training dataset

6.2.1.Walter et al.

In our approach, color images input from the fundus camera are initially resized to a standard size of 768 × 576 pixels while maintaining the original aspect ratio. We select the green channel for all our operations because retinal images are almost always saturated in the red channel and have very low contrast in the blue channel. A closing operation is performed on the green channel image using two different sizes of a structuring element (filter). Closing operation is defined as dilation (Max filter) followed by erosion (Min filter). The formulations of dilation and erosion for gray scale images are as follows.

Dilation:

$$A \oplus B = A_1(x, y) = \sup_{i,j \in b} (A(x-i, y-j) + B(i, j))$$

Erosion:

$$A \ominus B = A_1(x, y) = \sup_{i,j \in b} (A(x-i, y-j) + B(i, j))$$

Where A is the input image, B and B1 are the structuring elements or masks used for dilation and erosion respectively and b1 are grids over which the structuring elements are defined. Dilation in gray scale enlarges brighter regions and closes small dark regions. The erosion is necessary to shrink the dilated objects back to their original size and shape. The dark regions closed by dilation do not respond to erosion. Thus, the vessels being thin dark segments laid out on a brighter background are closed by such a closing operation. A subtraction of the closed images across two different scales (let S1 and S2 be the sizes of the structuring elements B1 and B2) will thus give the blood vessel segments of the green channel image. The operation is as follows:

We use a disk shaped structuring element for morphological operations. The radius of the larger disk (S2) is fixed at a high value (we use 6 pixels for an image of size 768 × 576 pixels) so that all the vessels including the main blood vessel get closed. The size of the structuring element is chosen based on which

describes the blood vessels to be ranging from 1.5-6 pixels in radius on an average. S1 is chosen adaptively as follows:

1. 1 or 2 pixels below S2 if we want to obtain only the thicker vessels emanating from the optic disk.
2. At least 4 pixels below S2 to obtain the entire blood vessel network. Criterion 1 is used for optic disk localization whereas criterion 2 is used in microaneurysms and hemorrhages detection.

The image C′ is threshold (90% of the maximum intensity) and median filtered to obtain the binary image of the blood vessels (U). Morphological thinning is then performed on U to obtain the skeleton of the blood vessel network. Thinning operation is implemented as $U - (U \ominus B1 - \overline{U} \ominus B2)$, where B1 and B2 are disjoint structuring elements and $\overline{U}$ is the complement of the image U. Noise can occur in the thinned image usually in the form of dots. A 2×2 median filtering operation is performed to remove the isolated specks of noise. The vessel segments being connected structures are unaffected by this operation. An additional source of noise in retinopathy images could be exudates, the removal.

6.2.2. Spencer et al.

From the input fundus image, the vascular map is extracted by applying 12 morphological top-hat transformations with 12 rotated linear structuring elements (with a radial resolution 15°). Then, the vascular map is subtracted from the input image, which is followed by the application of a Gaussian matched filter. The resulting image is then binarized with a fixed threshold. Since the extracted candidates are not precise representations of the actual lesions, a region growing step is also applied to them. While the original paper is written to detect MAs on fluorescein angiographic images, our implementation is based on the modified version published by Fleming et al.

6.2.3. Circular Hough-Transformation

Following the idea presented in, we established an approach based on the detection of small circular spots in the image. Candidates are obtained by detecting circles on the images using circular Hough transformation. With this technique, a set of circular objects can be extracted from the image.

6.2.4. Zhang et al.

In order to extract candidates, this method constructs a maximal correlation response image for the input retinal image. This is accomplished by considering the maximal correlation coefficient with five Gaussian masks with different standard deviations for each pixel. The maximal correlation response image is threshold with a fixed threshold value to obtain the candidates. Vessel detection and region growing is applied to reduce the number of candidates, and to determine their precise size, respectively.

6.2.5 Lazar et al

Pixel-wise cross-sectional profiles with multiple orientations are used to construct a multidirectional height map. This map assigns a set of height values that describe the distinction of the pixel from its surroundings in a particular direction. In a modified multilevel attribute opening step, a score map is constructed from which the MAs are extracted by thresholding.

6.3 ENSEMBLE CREATION:

In this section, we describe our ensemble creation approach. In our framework, an ensemble *E* is a set of *(*preprocessing method, candidate extractor) or shortly *(*PP, CE) pairs. The meaning of a *(*preprocessing method, candidate extractor) pair is that first we apply the preprocessing method to the input image and then we apply the candidate extractor to this result. That is, such a pair will extract a set of candidates *HE* from the original image. If an ensemble *E* contains more *(*preprocessing method, candidate extractor) pairs, their outputs are fused in the following way:

Take 10 training images (already disease affected images). Then we present the selected preprocessing methods, which we consider to be applied before executing MA candidate extraction. There may be around 5 methods present in Preprocessing. Candidate extraction is present next to preprocessing. Similar to preprocessing there are 5 techniques or methods present in Candidate extractors.

For a single image, 25 combinations of results are available. Since there are 5 methods available in both preprocessing and candidate extraction, for each method in preprocessing 5 candidate extraction methods are processed. Likewise it repeated for 5 methods in preprocessing. So there are 25 methods proceeded for a single image. Then we should calculate the entropy for all 25 results. Then after calculating the entropy for the 25 methods, we can predict the best technique, considering whose entropy is highest. For ex., If 3rd method's entropy is highest means we determine that 3rd one is the best technique.

Likewise, we should calculate for a set of 10 training images. By following the procedure mentioned above we can determine best techniques for 10 images.

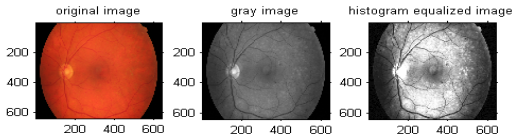
For ex. the best techniques of 10 images are like this format mentioned below:

[3 2 4 3 6 3 8 3 4 3]

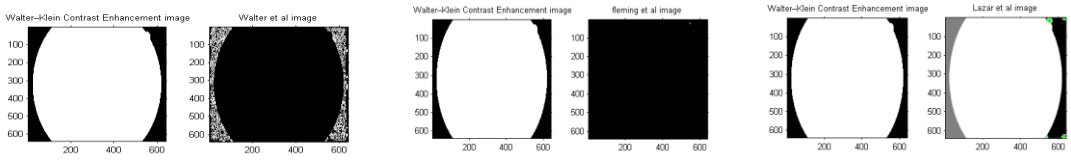
After analyzing the best techniques whose entropies are highest for 10 images, mentioned above, we can see that 3rd technique is repeated many times than other. So we can conclude that the 3rd technique is the best one

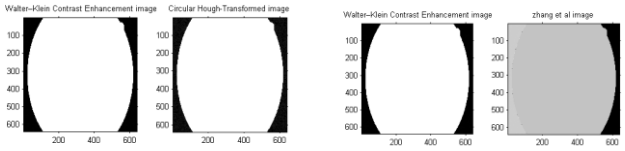
VII. Experimentation And Results

Original color fundus eye image undergoing preprocessing as well as candidate extractor method

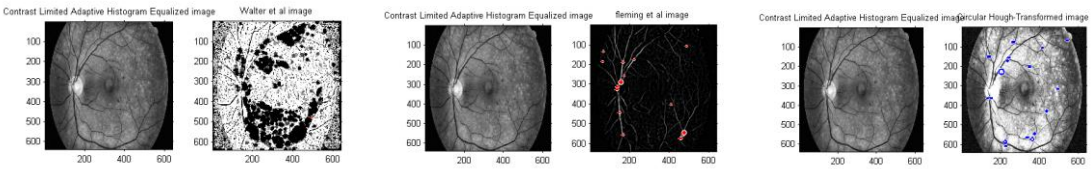


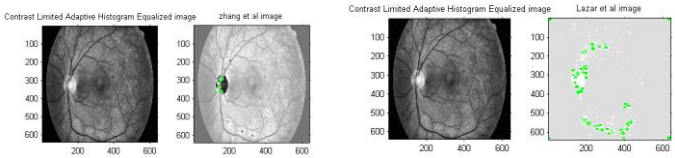
{walter preprocessing,candidate extractor methods}



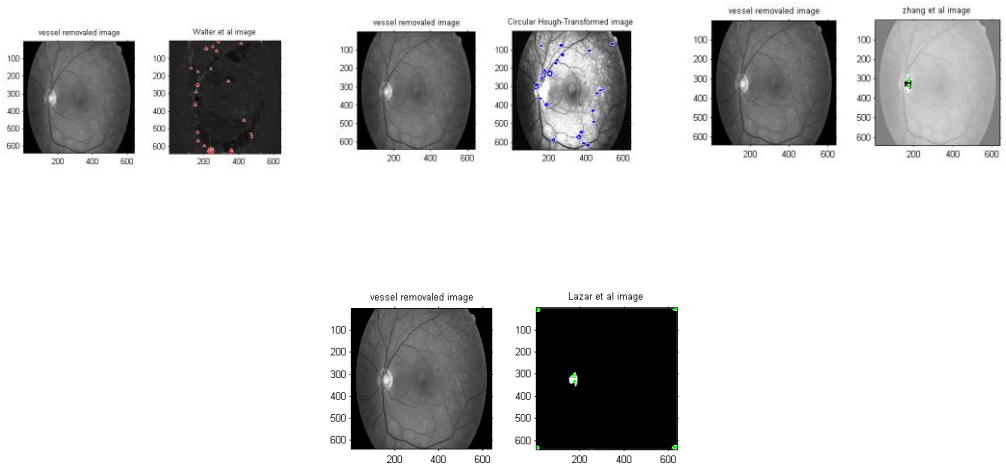


{CLAHE,candidate extractor methods}

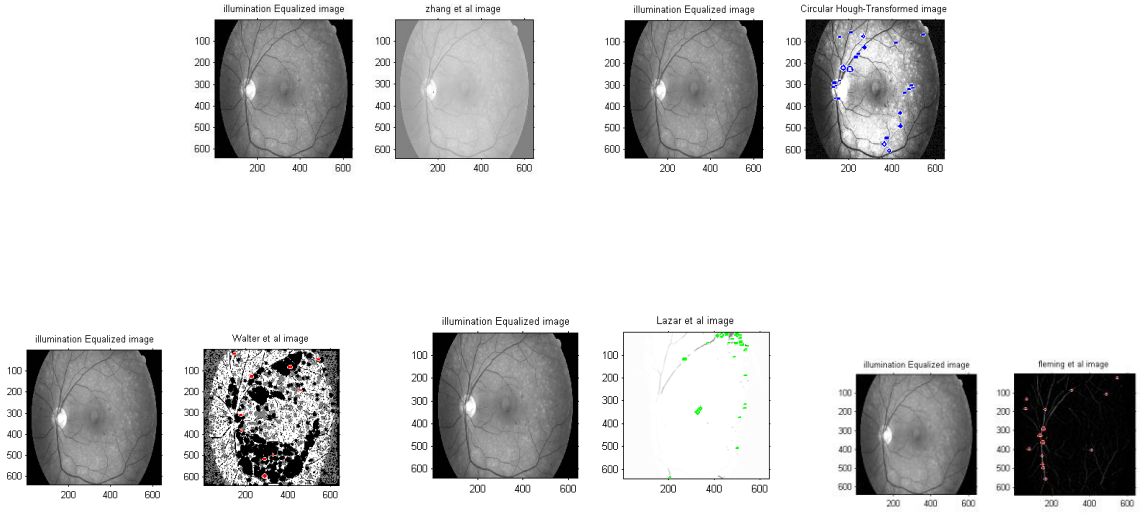




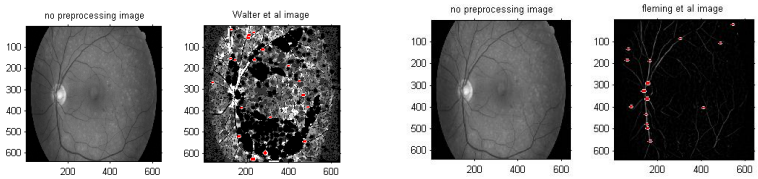
{VESSEL REMOVAL,Candidate extractors}

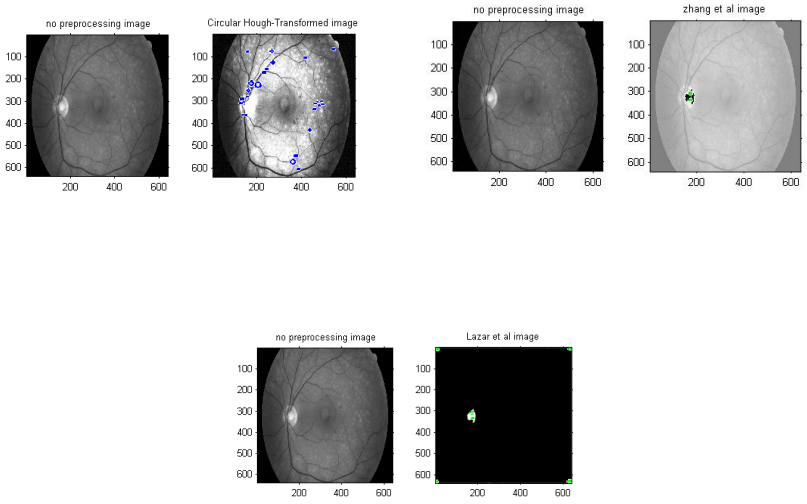


{Illumination equalizatio,candidate extractors}

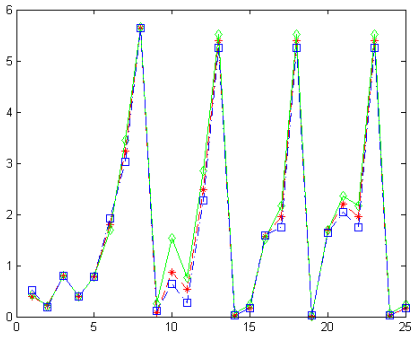


{NO PREPROCESSING METHOD,Candidate extractor}

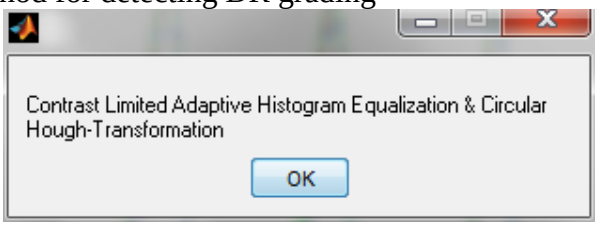




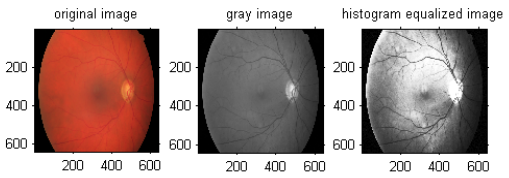
Entropy graph of different amalgamation methods

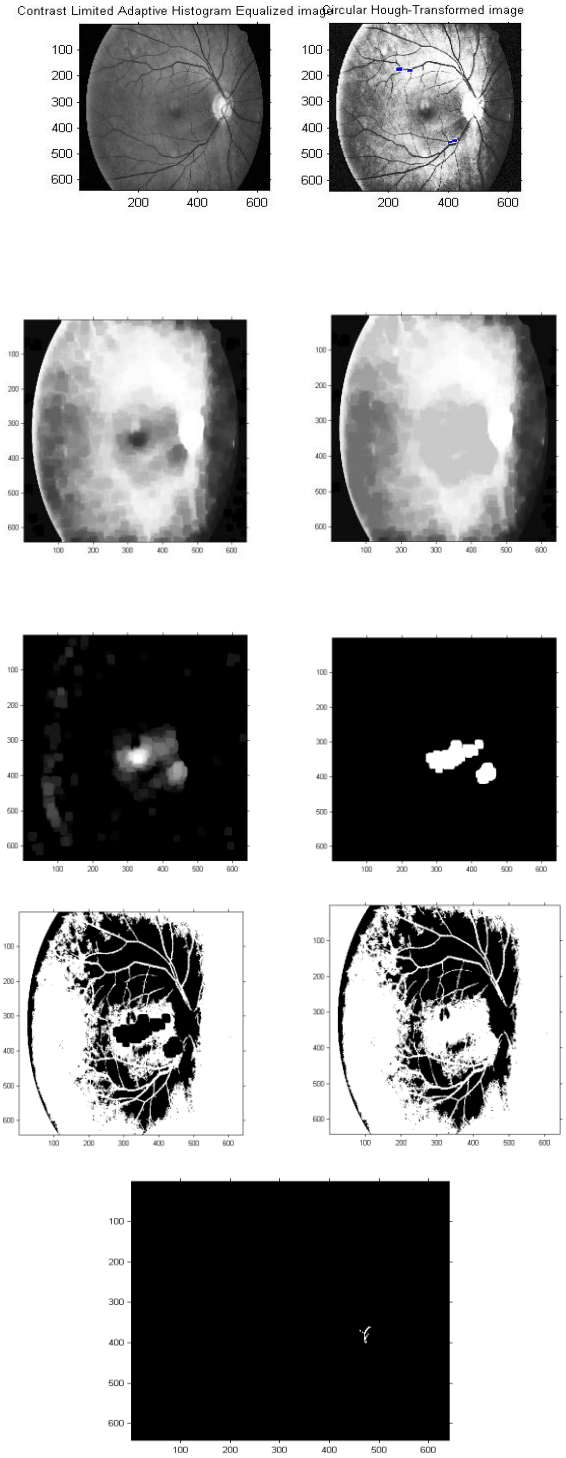


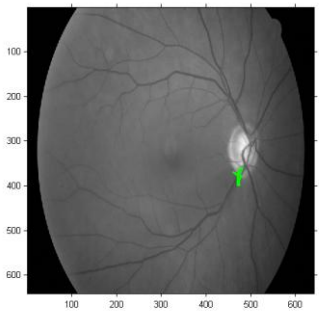
Best amalgamation method for detecting DR grading

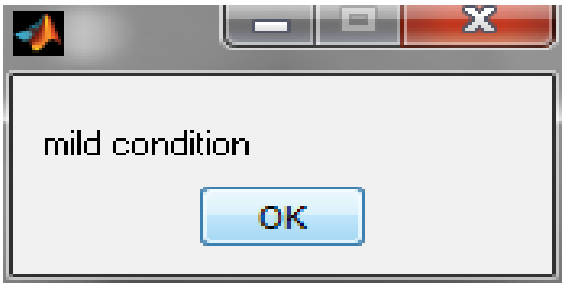


MILD CONDITION
DIAGNOSTIC TEST PERFORMANCE PARAMETERS



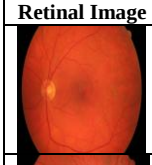
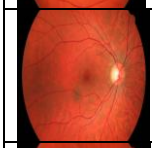
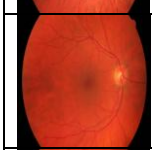
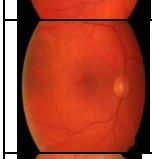
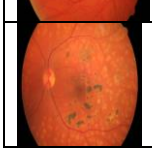

Contrast Limited Adaptive Histogram Equalized image
Circular Hough-Transformed image





In this way we can test number of images under this proposed system and detect Ma as well as Dr grading as given in the result.

And also we can check the performance parameters with the training data set.

Patient's Retinal Image	Diagnosed Condition	Sensitivity	Specificit-y	Accurac-y
	**Mild Condition**	**0.80001**	**0.999**	**0.966**
	**Normal Condition**	**0.3**	**1**	**0.8**
	**Moderate Condition**	**0.8002**	**0.999**	**0.9666**
	**Moderate Condition**	**0.8001**	**0.841**	**0.914**
	**Severe Condition**	**0.801**	**0.997**	**0.96669**

VIII. Conclusion

In this paper, we have proposed an ensemble-based MA detector that has proved its high efficiency in an open online challenge with its first position. Our novel framework relies on a set of $\langle$ preprocessing method, candidate extractor $\rangle$ pairs, from which a search algorithm selects an optimal combination. Since our approach is modular, we can expect further improvements by adding more preprocessing methods and candidate extractors. However, a proper screening system should contain other components, which is expected to increase the performance of this approach, as well.

Acknowledgements

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