NONLINEAR ENHANCEMENT AND SEGMENTATION ALGORITHM FOR THE DETECTION OF AGE-RELATED MACULAR DEGENERATION (AMD) IN HUMAN EYE'S RETINA

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ABSTRACT

Assessment of the risk for the development of Age related Macular Degeneration requires reliable detection of retinal abnormalities that are considered as precursors of the disease. A typical sign for the later are the so-called drusen, which appear as abnormal white-yellow deposits on the retina. This paper presents a novel segmentation algorithm for automatic detection of abnormalities in images of the human eye's retina, acquired from a depth-vision camera. Conventional image processing techniques are sensitive to non-uniform illumination and non-homogeneous background, which obstructs the derivation of reliable results for a large set of different images. Homomorphic filtering and a multilevel variant of histogram equalization are used for non-uniform illumination compensation and enhancement. We develop a novel segmentation technique, the *Histogram-based Adaptive Local Thresholding (HALT)*, to detect drusen in retina images by extracting the useful information without being affected by the presence of other structures. We provide experimental results from the application of our technique to real images, where certain abnormalities (drusen) have slightly different characteristics from the background and are hard to be segmented by other conventional techniques.

1. INTRODUCTION

Age-related macular degeneration (AMD) is a disease that causes progressive damage to the macula, a specialized part of the eye that allows us to see fine details clearly. When the macula malfunctions, blurring or darkness in the center of vision is experienced and tasks such as reading and driving are affected. Some common ways to detect vision loss relate to symptoms that words on a page look blurred, a dark or empty area appears in the center of vision, or straight lines are distorted. AMD is the leading cause of irreversible vision loss in people over 65 in the U.S. Although the cause of AMD is not completely understood, it has been identified that age is the greatest risk factor and there is also a hereditary nature associated with the disease. There are two forms of AMD, namely dry (also called atrophic, non-neovascular, or nonexudative) and wet (also called exudative). Dry AMD is the most common form of the disease and accounts for 90% of all AMD cases. The key identifier for dry AMD is small, round, white-yellow deposits called drusen that build up in the macula. A thorough examination by an ophthalmologist is the best way to determine if one has macular degeneration, or if he/she is at risk of developing the disease. The examination process is tedious for both the examiner and the patient. Depth vision cameras have been developed to capture the retinal images for accurate off-line analysis.

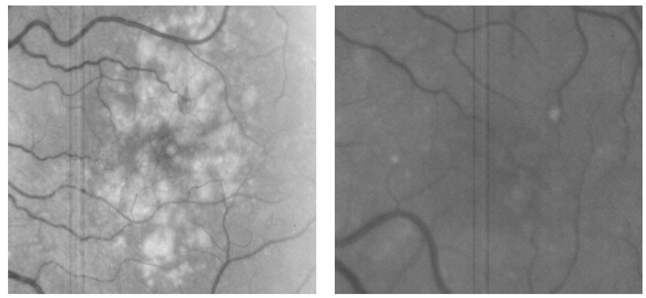


Fig. 1 Examples of acquired images

The goal of our research is the off-line processing of retinal images, like them shown at Fig. 1, so as to detect the presence of drusen and help the examiner meet the right decision. An efficient automated inspection tool would relieve him/her from the examination process and provide a fast and accurate tool for diagnosis of AMD. The purpose of this paper is threefold. First, to obtain a comparison of histogram based techniques for enhancement and segmentation on the problem of AMD. Second, from this integrated consideration to develop a novel segmentation method that overcomes the inefficiencies of other techniques in detecting vaguely defined structures. Third, to propose, analyze and test a complete system for the detection of drusen in human eye's retina.

2. METHODOLOGY FOR DRUSEN DETECTION

Since the correct enhancement and segmentation of retina images provides valuable aid to ophthalmologists, a complete algorithm for automatic segmentation and detection of drusen has been designed and implemented in this paper. The main algorithmic steps are shown at Fig. 2.

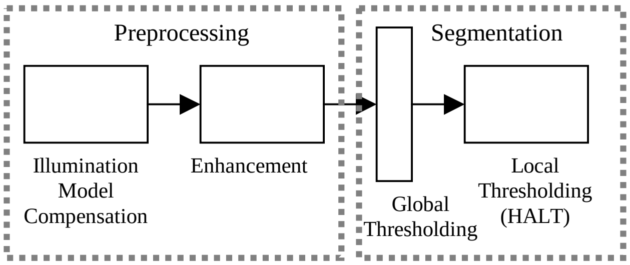


Fig. 2 Algorithm for drusen detection

Both the enhancement and thresholding operators for drusen segmentation are adaptive and based on histogram analysis. In particular, the local thresholding operator is designed from a rigorous analysis of the local histogram, as to exploit the important characteristics of the signal distribution that differentiate drusen from background and overcome the inefficiencies of other histogram based segmentation schemes.

2.1. Preprocessing

The shape irregularity of the retina creates shading across the field of view when illuminated with a bright source, as in the Fundus camera. Non-uniform illumination compensation can be achieved by a commonly used technique, namely the homomorphic filtering. The illumination-reflectance model can be used as the basis for this frequency domain procedure that is useful for improving the appearance of an image by simultaneous brightness-range compression and contrast enhancement. It is particularly effective in cases of large intensity variations of the background, where object differences are diffused within the background changes and objects are hard to be identified.

The next processing step aims at enhancing the contrast of the retina's image. We tested commonly used techniques like the adaptive contrast enhancement filters (ACE) [3], the Wallis statistical differencing [4], the exponential & logarithmic ACE [5] and an iterative local enhancement technique presented in [6]. The main drawback is their complexity in parameter selection that renders them inappropriate for enhancing a large set of retinal images. In order to avoid the selection of parameters for each retina image we process, we develop the M*ultiLevel histogram Equalization (MLE)* technique based on sequential applications of histogram equalization. In fact, it is a multilevel (hierarchical) scheme that progresses from the entire image to smaller regions defined via windows. Due to the expected intensity similarity in small areas, the windows considered are non-overlapping. Compared with a sliding window approach, our scheme results in smaller computational complexity and larger speed of operation, without compromising on the local enhancement ability owing to its multilevel nature. A potential problem could arise using windows that are small enough to fit inside a drusen's region. Similar to any adaptive histogram modification algorithm, it can produce non-desirable misleading contrast variations within a drusen. This problem is only experienced when using small windows. To avoid such effects, we limit the size of windows considered up to the expected size of any drusen in the image. Considering this constraint, the algorithm proceeds as follows: The 1st stage of equalization uses a window equal to images's size (global). The 2^{d} stage splits the image into nine non-overlapping windows and applies the same operation to each part (block) of the previous result. At any stage $\boldsymbol{i}$ a window $\boldsymbol{w^i}$ is further processed by smaller non-overlapping windows if and only if the application involves smaller drusen.

2.2. Segmentation

Segmenting the drusen in the enhanced image is an important prerequisite for measuring and understanding the AMD symptoms. Although non-uniform illumination has been almost compensated and the image has been enhanced, the definition of a single "good" global threshold is hard to achieve. Parts of the drusen are still difficult to distinguish from the background in terms of their intensity because of the brightness similarity; especially when considering drusen near to vessels. The histogram of a local area is more focused and informative with respect to small-included objects. A statistical analysis of the local gray scale distribution facilitates the separation of such objects and the selection of the appropriate local threshold.

In this paper we focus on histogram-based techniques and consider threshold selection techniques in detail. Moreover, the novel proposed method, referred to as *Histogram Adaptive Thresholding (HAL*T), is established and its stochastic background is elucidated. This selection scheme is applied on non-overlapping local regions and also fits well with the region-adaptive approach developed for enhancement.

The analysis of the histogram leads to the appropriate thresholds for effective segmentation in terms of symmetry and tendency (short, medium or long- tailed). Our goal is to separate the drusen, without being affected by intensity variations caused by vessels, noise and uncompensated non-uniform illumination. If we zoom into each local intensity area, we observe different shapes of the histogram for each of them and different relative distributions of the drusen and the background. For each region we first apply location estimators on the distribution of intensity and then derive dispersion measures around this estimator, in order to characterize the distribution. The histogram's mean is a good measure of central tendency for roughly symmetric distributions but can be misleading in skewed distributions, since it is greatly influenced by extreme values [2]. In such cases the median is more effective, since it is an efficient statistic in highly skewed distributions. The mode can be informative, but it can not be used as reliant measure of central tendency, since it is highly susceptible to extreme gray value differences.

In general, the deviation among the mean, median and mode as location estimators of the center of the distribution can provide a measure of symmetry/asymmetry in the distribution, as well as an indication of contamination in the assumed distribution. In background or general homogeneous regions, the gray-scale distribution approaches a normal one and the histogram appears like a Gaussian function. On the contrary, when smaller or larger bright spots (drusen) are present, the histogram is positively skewed denoting a non-symmetric distribution and shifting the mean apart from the mode and median.

Based on the previous analysis, we consider symmetry of a distribution via two quotients, namely the differences $\left|\text{mean} - \text{median}\right|$ and $\left|\text{mean} - \text{mode}\right|$. The $\left|\text{mean} - \text{median}\right|$ difference is a first measure of symmetry based on local statistics, as indicated before. The $\left|\text{mean} - \text{mode}\right|$ difference is chosen as a measure of histogram's main lobe spread. Representative examples of histograms are shown at Fig. 3. Subsequently, the skewness in conjunction with the kurtosis are used as measures of the histogram's tendency. These measures can further increase the confidence with which drusen (outliers on the assumed normal distribution of the background) are detected.

According to our approach, the histogram is checked for general symmetry or asymmetry. The two symmetry quotients are used for this purpose. If both of them are small the distribution under consideration is classified as almost symmetric. In this case, the area under consideration belongs probably to the background. On the contrary, if asymmetry is detected through the shape measures, then Otsu's thresholding scheme [1] is effective in separating the different sub-distributions, so as to segment the drusen area. Otsu's thresholding is suitable for the non-symmetric distribution, since it can effectively detect the transition level from background to drusen. Nevertheless, these are only rough guidelines for the selection of a segmentation scheme that can reveal the presence of drusen in a local area. A symmetric distribution may not always characterize background alone but certain combinations of drusen and background distributions. Similarly, a non-symmetric distribution may not always indicate the presence of drusen. In order to arrive at a decision scheme regarding the presence or absence of drusen, the histogram needs to be analyzed further, in terms of its kurtosis and skewness properties in each local region. More specifically, the HALT operator applies different thresholds at regions of the image

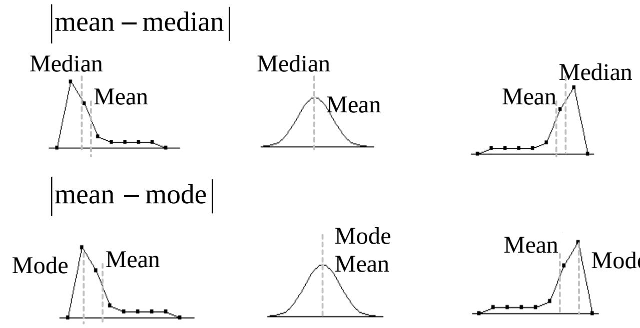


Fig. 3 Three typical cases of histogram shape (negatively skewed, symmetric, positively skewed) and relative positions of corresponding features.

depending on various shape properties of the corresponding histogram.

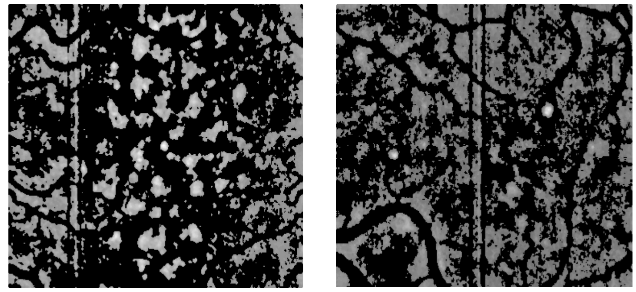
The background is composed of a noise process superimposed on a deterministic smoothly varying terrain. A symmetric Gaussian distribution efficiently characterizes this overall background process. Using the ergodicity assumption, any realization of the stochastic process or any acquired image from this process is also characterized by this Gaussian distribution. The case of a symmetric mesokurtic or leptokurtic histogram is most likely attributed to only a background process. It is expected therefore that by thresholding the distribution at its 90% area and preserving only values above this 90% threshold, we preserve only isolated pixels randomly distributed along the spatial extent of the image. These pixels are easily removed by median filtering. Alternatively, a platykurtic symmetric distribution can be easily generated from two symmetric distributions, one characterizing the background and the other reflecting the drusen intensity variations. In the last case, Otsu's threshold must be applied in order to separate the underlying distributions.

Regarding asymmetric histogram distributions, a positively skewed distribution indicates the presence of drusen influencing the higher part of the intensity distribution. Otsu's threshold ids most appropriate in this case, if there is strong evidence that drusen are the cause of this positive influence. Negatively skewed distributions are most likely to describe areas of background, since drusen abnormalities affect the higher end of the histogram (bias towards bright values). So, by setting 90% as a threshold would also remove such regions. Summarizing, the thresholding procedure is divided into two distinct cases: (a), histogram is totally or almost symmetric, where kurtosis plays a decisive role in selecting the threshold and (b), histogram is totally or almost asymmetric, where skewness determines the appropriate thresholding scheme.

3. RESULTS

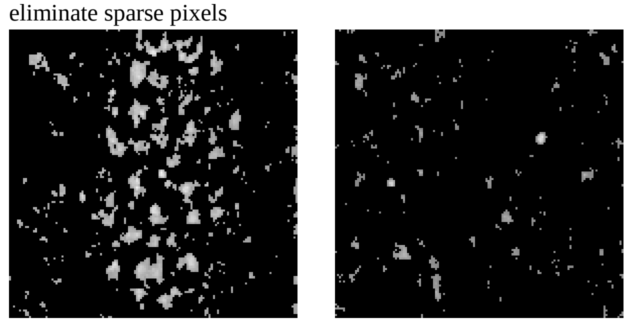
Two representative examples of retinal images are shown at Fig. 1. The first contains large drusen dominating extensive areas and the second one contains few, small and vaguely defined drusen. In order to demonstrate the performance of our algorithm and the efficiency of the HALT operator we proceed in a comparison with Otsu's thresholding scheme over local-region histograms. Both example images are enhanced using multilevel histogram equalization (MLE) and then thresholded using Otsu's and HALT techniques. A median filter is applied afterwards to remove isolated pixels.

Otsu's localized thresholding scheme works fine in regions that are dominated by drusen (brighter areas), since the distinction between them and the background is evident. This is demonstrated at Fig. 4–(a), where drusen at the central part of the image are correctly distinguished from the surrounding areas. However, the algorithm is strongly affected by regions that do not contain any abnormality, like those regions at the sides of the image. Due to remaining effects of non-uniform illumination, parts of these regions are brighter and are misclassified as anomalies. Fig. 4-(b) brings out another disadvantage of this scheme. Vaguely defined drusen, which are either small or located inside bright background regions, are not segmented. The algorithm detects the most obvious drusen (two of them are easily conceived), but fails to detect "hidden" anomalies. On the contrary, the HALT technique removes most of the background in both cases, as shown at Fig. 5. Even the most hard-to-see drusen are segmented without loosing their actual size and shape. Some false negatives generated by the existence of noise can be easily removed at a following detection step.



(a) (b)

Fig. 4 Images after MLE enhancement, local thresholding using Otsu's method at each block and median filtering to eliminate sparse pixels



(a) (b)

Fig. 5 Images after MLE enhancement, local thresholding using HALT method and median filtering to eliminate sparse pixels

4. CONCLUSION

The paper considers histogram- based techniques for the problem of automatic AMD evaluation. The detection of anomalies in human eye's retina is a biomedical problem, appropriate for image processing and automated segmentation, whose solution is intended to help the doctors in their decision making process. Use of the proposed detector may reduce false negatives and give reliable detection accuracy in both position and mass size.

We propose a histogram- based enhancement technique (MLE), which uses histogram equalization as its core operator and a histogram- based segmentation technique (HALT) to segment areas that differ slightly from their background regions. Furthermore, we establish an unsupervised and non-parametric method for drusen extraction and consider its effectiveness through several examples.

The proposed method is able to detect actual drusen in all cases. Even in hard-to-diagnose cases, where many small and vague drusen exist, our method succeeds in isolating them from the background. A significant factor that affects the overall performance of other approaches is the presence of noise, which makes surfaces look rough and renders the segmentation process difficult. Although, it is not a common case, since the presence of noise is rare in such images (only one in our test set), our method provides adequate results even in the case of noise contamination.

5. REFERENCES

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