Automated Screening System for Diabetic Retinopathy

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Abstract

Purpose: The purpose is to develop an automatic computerized screening system to recognize automatically the main components of the retina, an important features of background diabetic retinopathy and classify the normal, abnormal and unknown retinal image.

Methods: This paper has presented 4 main methods to succeed of retinal diagnosis. Firstly, the retinal images are pre-processed via adaptive, local, contrast enhancement. Secondly, the main features of a retinal image were defined as the optic disc, and blood vessels. The optic discs were located by identifying the area with the highest variation in intensity of adjacent pixels. Blood vessels were identified by means of a multilayer perceptron neural network, for which the inputs were derived from a principal component analysis of the image and edge detection of the intensity. Next, the background diabetic retinopathy features are identified. Recursive region growing segmentation algorithms were applied to detect the hard exudates. The haemorrhages and microaneurysms were recognised by detecting all feature similar to the blood vessels and removed the vessels out. Finally, all information is accumulated and diagnosed for diabetic retinopathy or a normal retina.

Result: The diabetic retinopathy screening technique has been applied to the 484 normal retina images and 283 images with diabetic retinopathy. The sensitivity and specificity for the computerized screening program to classify the images were corrected 80.21% and 70.66% respectively.

Conclusion: The computerized screening system has been developed to classify the normal and abnormalities of retinal images. The development of getting higher performance is in progress.

1. Introduction

The digital fundus camera in ophthalmology provides us with digitized data, which could be exploited for computerised detection of disease. An example is the care of diabetic retinopathy, which requires the screening of large numbers of patients. Screening of diabetic retinopathy may reduce blindness in these patients by 50% and can provide cost savings to public health systems [1,2]. However, most methods require identification of retinopathy by specifically trained personnel [3-6]. This produces a large number of retinal images for the medical doctors to review. If a fully automated method was employed, the management of certain diseases would be greatly facilitated [7]. A completely automated approach involving fundus image analysis by computer could provide an immediate classification of retinopathy without the need for specialist opinions. Once a diabetic retinal image is found to be abnormal, the system would highlight it to the ophthalmologist for review. This indicates that the system can potentially reduce the number of retinal images that the clinician needs to review by more than 60% [8].

The fully automated system to detect microaneurysms in fluorescein angiograms has been developed [9,10]. Although, fluorescein angiogram images are good for observing some pathologies such as microaneurysms, but this method is not an ideal solution for an automatic screening system since it requires an injection of fluorescein into the body. This disadvantage makes the use of colour fundus images more suitable for automatic screening since it does not require fluorescence injection.

The detection of blood vessels using a method called 2D matched filters has been presented [11]. The large size of the convolution filters consumes heavy computational cost. An alternative method to recognise blood vessels was developed by Akita and Kuga [12]. However, this work does not include automatic diagnosis of diseases, because it was performed from the viewpoint of digital image processing and artificial intelligence. Sinthanayothin et.al had proposed the algorithms of blood vessels, fovea and optic disc recognition but all techniques are based on TRACEE and running on Linux operating system [13]. Most researches in this area were focused on the recognition of some features of fundus images; the completely
The techniques describe in the paper is following the work of Sinthanayothin and apply on a large number of images and finally give the decision for screening result and compare to the clinical situation. This work is also developed under Window operating system as a stand-alone program.

Therefore, this paper presents the process for achieving the screening system as follows. The first step, the retinal images are pre-processed via adaptive, local, contrast enhancement. The second step is to be able to automatically locate the main regions of the fundus—that is, the optic disc and the blood vessels. The data from these regions can then be analysed for features of sight threatening disease of diabetic retinopathy. Finally, all information is accumulated and diagnosed for diabetic retinopathy or a normal retina.

2. Methods

The screening system can be seen in figure 1, which the retinal images were captured in dimensions of 768×576 pixels from the Topcon camera at Siriraj hospital, Thailand and sent to the screening program for classify of abnormality.

![Figure 1: An Automated Computerised Screening System for Diabetic Retinopathy.](image)

2.1 Pre-processing of Colour Retinal Images

To present the full colour techniques for image enhancement in detail, we are interested in the HSI (Hue-Intensity-Satulation) model. Firstly, the RGB model has been converted to IHS model. Then applying the local contrast enhancement technique [15] to the intensity component and converting the result to RGB for display will not affect the colour content of the image.

For the local contrast enhancement technique, let the intensity, \( f \), of the picture elements (pixels) of an \( N \times N \) digital image be indexed by \((i,j) \) \( 1 \leq i, j \leq N \). Consider a subimage of size \( M \times M \) centred on \((i, j)\) in this paper \( M=49 \). Denote the mean and standard deviation of the intensity within \( W \) by \( \Psi_{W}(f) \) and \( \sigma_{W}(f) \) respectively.

The objectivity for this method is to define a point transformation dependent on \( W \) such that the distribution is localised around the mean of the intensity and covers the entire intensity range. The implicit assumption is that \( W \) is large enough to contain a statistically representative distribution of the local variation of grey levels, yet small enough to be unaffected by the gradual change of contrast between the centre and the periphery of the fundus image. The adaptive contrast enhancement transformation is defined by

\[
\begin{align*}
    f(i,j) &\rightarrow g(i,j) \\
    &= 255 \left[ \frac{\Psi_{W}(f) - \Psi_{W}(f_{\min})}{\Psi_{W}(f_{\max}) - \Psi_{W}(f_{\min})} \right] \\
    \text{Where the sigmoidal function was} & \\
    \Psi_{W}(f) &= \left[ 1 + \exp \left( \frac{f_{W} - f}{\sigma_{W}^{2}} \right) \right]^{-1} \\
    \text{While} f_{\max} \text{ and } f_{\min} &\text{ are the maximum and minimum} \\
    &\text{values of intensity within the whole image with} \\
    f_{W}(k,l) &= \frac{1}{M^2} \sum_{(k,j) \in W(i,j)} f(k,l) \\
    \sigma_{W}^{2}(f) &= \frac{1}{M^2} \sum_{(k,j) \not\in W(i,j)} (f(k,l) - f_{W}(k,l))^{2}
\end{align*}
\]

The result of local contrast enhancement technique can be seen in figure 2.

![Figure 2: Fundus image before and after applied local contrast enhancement technique.](image)
The optic-disc appeared in the fundus image as a yellowish region. It typically occupied approximately one seventh of the entire image, 80x80 pixels. The variance of intensity of adjacent pixels was used for recognition of the optic disc.

Consider a sub-image \( W(i, j) \) of dimensions \( M \times M \) centred on pixel \((i, j)\). Let \( <f>_{W(i,j)} \) as defined by equation 3 be the mean intensity within \( W(i, j) \).

A variance image was formed by the transformation

\[
g(i, j) \rightarrow p(i, j) = \left( \frac{1}{M} \sum_{W(i,j)} f^2 \right) - \left( \frac{1}{M} \sum_{W(i,j)} f \right)^2,
\]

(5)

Where the sub-image was 80x80 pixels. An image of the average variance within sub-images was then obtained as

\[
p(i, j) \rightarrow q(i, j) = \left( <p>_{W(i,j)} \right)
\]

(6)

The location of the maximum of this image was taken as the centre of the optic-disc, \((i_d, j_d)\). The examples of optic-disc recognition have shown in the first column of figure 4.

\[
(i_d, j_d) = \arg \max_{W(i,j)} p(i, j)
\]

(7)

2.2.2 Recognition of Blood-Vessels

A multilayer perceptron NN was used to classify each pixel of the image. Pre-processing of the image was necessary before presentation to the input layer of the NN. Pattern classifiers are most effective when acting on linearly separable data in a small number of dimensions. Previously [13], 200 input data was used to train and validate for the pixel belong to the blood vessel. In this paper, these 200 input data has been reduced to 6 input data as figure 3. (First 3 data derived from 1st component of PCA and another 3 data derived from edge gradient.) At the pixel being classify, the data can be calculated from:

**Edge Gradient**: intensity, mean and variance of intensities of the sub-image size 10x10 pixels localized on the pixel being classified.

**Neural Network Algorithm**

Each pixel of a fundus image was classified as vessel or non-vessel. The data input to the NN were 6 values described in the previous paragraph. The net was a three-layer perceptron having 6 input nodes, 30 hidden nodes and two output nodes. A training/validation data set of 25,094 examples, comprising 8,718 vessel and 16,376 non-vessel, was formed by hand and checked by a clinician. The back propagation algorithm with early stopping was applied, using 5/6 of the data for training and 1/6 for validation.

**Postprocessing**

The performance of the classifier was enhanced by the inclusion of contextual (semantic) conditions. Small isolated regions of pixels those were misclassified as blood vessels were removed as can be seen in figure 4.

2.3 Recognition of Diabetic features

2.3.1 Recognition of Hard Exudates

Exudates are yellow lesions of various shapes and size with relatively distinct margins. A recursive region growing segmentation (RRGS) algorithm was used for exudate detection. The basis of RRGS is the identification of similar pixels within region to determine the location of boundary. To establish if two adjacent pixels are similar, they must satisfy some criteria such as grey level, colour or texture. In RRGS,
adjacent pixels within the same region are considered to have fairly homogeneous grey scale properties. Consider each pixels of the image in raster order. A pixel \( p \), at co-ordinates \((x, y)\) has four neighboring pixels orientated above, below, left and right with co-ordinates \((x, y+1)\), \((x, y-1)\), \((x-1, y)\) and \((x+1, y)\) respectively. Consider an adjacent pixel \( p_i \), where \( i \) is the vertical or horizontal co-ordinate relative to \( p \). The first step of the algorithm was to calculate the difference in intensity between \( p \) and \( p_i \). If the difference was less than or equal to a threshold value of 10, then \( p_i \) was added to the region and set to \( p \). The process was repeated until all pixels considered for merging and the original pixel comprised a region. The median intensity of the region was calculated and replaced the original intensity of the merged pixels. The cycle was repeated until the whole image was segmented. The median intensity of the ‘background’ (defined as the region with the most pixels) was set as the threshold value for classification of the image. Segmented regions above and below this threshold were classified as exudate and non-exudate regions respectively. As the optic disc was similar colour to that of exudates with a well-defined boundary, it was extracted from the image using the optic-disc recognition algorithm (as described previously) to avoid classification with the exudates. Finally, the exude mask (with the exudates depicted as blue regions) was overlaid onto the original image as shown in Figure 5.

2.3.2 Recognition of Haemorrhages and Microaneurysms

This part is in progress to recognise haemorrhages and microaneurysms (HMA). Microaneurysms are the first clinically detectable lesions of diabetic retinopathy. They appear as small, round, red dots whilst haemorrhages can have ‘dot’, ‘blot’ or ‘frame’ configurations. The lesions are the same colour as blood vessels and very similar in colour to the fundus background. Firstly, the matching correlation is applied to sharpen the edges of the red lesions against the red-orange background. Secondly, thresholding was used to classify the image for HMA and non-HMA regions. Due to similarities in colour, the blood vessels were classified into the same group as HMA. To overcome this problem, a neural network (NN) technique was used to identify the blood vessels and extract them from the image. However, the result has not been satisfied and needed more development.

2.4 Validation for Normal/Abnormal/Unknown Retinal Image

In this work, the diabetic retinal features have not completely identified yet (Haemorrhages and Microaneurysms recognition are not well identified which cause incorrect decision of system). Therefore, we have taken an account of exudate recognition to be prior criterion to classify between normal and abnormal retinal image. Optic disc recognition has been used as the criteria for unknown data; in the case of unable to locate an optic-disc, it was defined to be an unknown image because of the image might not clear enough. However, the feature recognition results from describing above had to verify in terms of accuracy such as the regions near the vessels (the fibre lied along the vessels) sometime were misclassify as exudates as figure 6. Hence, some misclassified regions had to determined, not lied along the vessels. In this paper, watershed technique (Similar to FloodFill or RRGS algorithm) has been applied to remove the artefact regions by growing from the vessels position, which is recognised by the NN algorithm, described previously.

Figure 5: Exudates recognition result and expanded images before and after labeling exudates regions.

2.3.2 Recognition of Haemorrhages and Microaneurysms

2.4 Validation for Normal/Abnormal/Unknown Retinal Image

The whole procedure for an automatic screening of Diabetic Retinopathy has been shown in figure 7.
3. Results

Figure 8: The example results for screening of Diabetic Retinopathy as Normal, Abnormal and Unknown.

The algorithms for screening of Diabetic Retinopathy were applied 771 retinal images of which 283 contained background diabetic retinopathy and 484 were normal fundus images. Another 4 images, which were not clear, were recognized as unknown. The results can be seen as in figure 8. The sensitivity and specificity for screening of diabetic retinopathy were 80.21% and 70.66% respectively as in Table 1.

<table>
<thead>
<tr>
<th>Data</th>
<th>Results</th>
<th>Screening procedure Classified as Abnormal</th>
<th>Screening Procedure Classified as Normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abnormal</td>
<td>227 (80.21%)</td>
<td>56</td>
<td>6</td>
</tr>
<tr>
<td>Normal</td>
<td>142</td>
<td>342 (70.66%)</td>
<td>342</td>
</tr>
<tr>
<td>Not Clear</td>
<td>4 images classified as Unknown</td>
<td>4 images classified as Unknown</td>
<td>4 images classified as Unknown</td>
</tr>
</tbody>
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4. Discussions and Conclusion

In this study, computer-based algorithms were used to pre-process retinal digital images, localize the major retinal landmarks and recognize diabetic pathologies without any intervention from an operator. A previous paper has described the variety of techniques employed in image pre-processing and identification of optic disc, fovea and retinal blood vessels based on Tracee running on Linux operating system. This study has added and accumulated all techniques re-written in Window system as a stand-alone program, which can be connected to the digital fundus camera for the real screening system. The computerized screening system has been developed to classify the normal and an abnormality of retinal images with the sensitivity 80.21% and specificity 70.66% respectively.

The reasons for false negative (misclassify abnormal to the normal images) for 56 images are as follows: 38 retinal images have only Microaneurysms and Haemorrhages, which has not yet count to the validation process. 11 images have very little exudates or faint exudates. Another 7 images are too dark to recognize. The example of abnormal images that misclassified can be seen in figure 9.

The reasons for false positive (misclassify the normal to diabetic retinopathy images) for 142 images are as follows: most incorrectly classified images were because of the artifacts near the vessels, the artifacts that similar to exudates, misclassified of the optic-disc in prior procedure and the artifact from the light pointer. The example of normal data that screen incorrectly has shown in figure 10.

British Diabetic Association guidelines recommend a minimum standard of 80% sensitivity and 95% specificity of detection of sight-threatening diabetic retinopathy by any method [16]. The result from this research has shown that we have reached the minimum standard of sensitivity. Although, the specificity still need to improve but it does not cause much danger in the screening population. Javitt et al. also suggested that a sensitivity of 60% or greater maximized cost-effectiveness in screening for diabetic retinopathy [17]. The development of getting higher screening performance is in progress by adding the development of Haemorrhages and microaneurysms recognition. Therefore, further work will be required to
improve the detection accuracy of these red-colored lesions, which may be confused with segmented of small blood vessels.

Figure 9: Abnormal images that the screening system classified as a normal data. The 1st image contains only haemorrhages and microaneurysms. The 2nd image has only faint exudates. The 3rd image is too dark to recognized abnormalities.

Figure 10: Normal images that screening system defined as Abnormal. The 1st image has the artifact near vessels. The 2nd image has the shadow near the disc. The 3rd image has some features like exudates. The 4th image has the artifact from the light pointer.

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References