Automatic detection of diabetic retinopathy exudates from non-dilated retinal images using mathematical morphology methods

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Abstract

Diabetic retinopathy is a complication of diabetes that is caused by changes in the blood vessels of the retina. The symptoms can blur or distort the patient’s vision and are a main cause of blindness. Exudates are one of the primary signs of diabetic retinopathy. Detection of exudates by ophthalmologists normally requires pupil dilation using a chemical solution which takes time and affects patients. This paper investigates and proposes a set of optimally adjusted morphological operators to be used for exudate detection on diabetic retinopathy patients’ non-dilated pupil and low-contrast images. These automatically detected exudates are validated by comparing with expert ophthalmologists’ hand-drawn ground-truths. The results are successful and the sensitivity and specificity for our exudate detection is 80% and 99.5%, respectively.

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1. Introduction

Diabetes is the commonest cause of blindness in the working age group in the developed world. Patient’s sight can be affected by diabetes which causes cataracts, glaucoma, and most importantly, damage to blood vessels inside the eye, a condition known as “diabetic retinopathy”. Diabetic retinopathy is a critical eye disease which can be regarded as manifestation of diabetes on the retina. The screening of diabetic patients for the development of diabetic retinopathy can potentially reduce the risk of blindness in these patients by 50% [1–3].

Diabetic retinopathy is characterized by the development of retinal microaneurysms, haemorrhages and exudates. Microaneurysms are focal dilatations of retinal capillaries and appear as small round dark red dots. Haemorrhages occur when blood leaks from the retinal vessels. Exudates occur when lipid or fat leaks from abnormal blood vessel or aneurysms. The number of microaneurysms, haemorrhages and exudates increases as the degree of disease [4]. A number of techniques for microaneurysm and haemorrhage detection have been proposed. Sinthanayothin et al. [5] applied recursive region growing segmentation (RRGS) technique to segment vessels, microaneurysms and haemorrhages. The vessels were detected using a neural network. The remaining objects after vessels had been removed were labelled as microaneurysms and haemorrhages. Niemeijer et al. [6] proposed a method to detect candidate red lesions (microaneurysms and haemorrhages) using a pixel classification technique. Then the detected red lesion candidates were classified using a neural network. The remaining objects after vessels had been removed were labelled as microaneurysms and haemorrhages. Usher et al. [7] used an RRGS, adaptive intensity thresholding and edge enhancement operator to extract the candidate red lesions. Candidate red lesions were classified using a neural network. However, in this paper we concentrate on exudate detection as a visible sign of diabetic retinopathy and a marker for the presence of coexistent retinal edema. If the exudates extend into the macular area, vision loss can occur.

Fluorescein angiogram images provide important information on pathologies. The most effective and accurate ways to
observe and diagnose diabetic macular edema are to investigate a fluorescein angiography. In practical terms, the decision whether to laser treat the retina does not depend significantly on the images from fluorescein angiography, it is mostly done without this investigation. The fluorescein angiograms are not suitable for an automatic screening system because there are side-effects associated with giving a patient fluorescein. The use of colour fundus images is more suitable for an automatic screening system. An automatic exudate detection system would be useful in order to detect and treat diabetic retinopathy in an early stage.

From visual inspection, exudates appear differently in a yellowish or white colour with varying sizes, shape and locations. They are often seen in either individual streaks or clusters or in large circinate structures surrounding clusters of microaneurysms. At the same time, some of them are seen in varying sizes, shape and locations as shown in Fig. 1(a) and (b).

Many techniques have been employed to the exudate detection. Gardner et al. [8] proposed an automatic detection of diabetic retinopathy using an artificial neural network. The exudates are identified from grey level images. The fundus image was analyzed using a back propagation neural network. The technique did not work well on low contrast images. The thresholding and RRGS technique were widely used. Sinthanayothin et al. [5] reported the result of an automated detection of diabetic retinopathy on digital fundus images by RRGS algorithm where the performance was measured on 10x10 patches rather on the whole image. Usher et al. [7] detected the candidate exudates region by using a combination of RRGS and adaptive intensity thresholding. The candidate regions were extracted and used as input to a neural network. Poor quality images affected the separation result of bright and dark lesions using thresholding and exudate feature extraction using RRGS algorithm. Zheng et al. [9] detected exudates using thresholding and a region growing algorithm. The fundus photographs were taken with a non-mydriatic fundus camera and were then scanned by a flat-bed scanner.

Colour normalization and local contrast enhancement followed by fuzzy C-means clustering and neural networks were used by Osareh et al. [10]. The system works well only on Luv colour space but in the case of non-uniform illumination the detection accuracy is low. Mitra et al. [11] applied naïve Bayes classifier for diagnosis of diseases from retinal image. A system can provide a good decision support to ophthalmologist.

Much work has been performed for exudate detection based on variety of techniques. Most techniques mentioned earlier worked on dilated pupils in which the exudates and other retinal features are clearly visible. Based on experimental work reported in previous work, good quality images with larger fields are required. The retinal image of the patient must be clear enough to show retinal detail. Low quality images (non-uniform illumination, low contrast, blur or faint image) do not perform well even when enhancement processes were included. The examination time and effect on the patient could be reduced if the system can succeed on non-dilated pupils. Furthermore, many techniques required intensive computing power for training and classification.

This paper proposes an exudate detection techniques based on mathematical morphology on retinal images of non-dilated pupils that are low quality images. We based our work on this technique because it is very fast and requires lower computing power. So that the final system can be used even on a very poor computer system, such as those that may be available in rural area in developing countries where both expert ophthalmologists and high performance computers are rarely available. In addition, the location of exudates based on macular position is important information for an ophthalmologist [12,13]. They show the severity of disease, where exudates that appear closer to the macular indicate an increased severity of disease. A grid circle centred on the macular was added to provide improved diagnosis to the ophthalmologist.

2. Methods

All digital retinal images were taken from patients with non-dilated pupils using a KOWA-7 non-mydriatic retinal camera with a 45° field of view and taken at Thammasat University Hospital. The images were stored in JPEG image format files (.jpg) with lowest compression rates. The image size is 752x500 pixels at 24 bits per pixel. The overall procedure of exudate detection is demonstrated in Fig. 2.

2.1. Preprocessing

The red, green and blue (RGB) space of the original image was transformed to Hue, saturation and intensity (HSI) space because HSI colour space is more appropriate since it allows the intensity component to be separated from the other two
colour components. A median filtering operation was then applied on I band to reduce noise before a contrast-limited adaptive histogram equalization (CLAHE) was applied for contrast enhancement [14]. CLAHE operates on small regions in the image. The contrast of each small region is enhanced with histogram equalization. After performing the equalizations, the neighbouring small regions were then combined by using bilinear interpolation.

Exudate lesions and optic disc regions normally show high intensity values in this channel and thus the contrast enhancement technique assigns them the highest intensity values [10,15].

2.2. Optic disc elimination

Exudate detection is our main purpose; however we have to remove the optic disc prior to the process because it appears with similar intensity, colour and contrast to other features on the retinal image [15–18]. The optic disc is characterized by the largest high contrast among circular shape areas. While vessels also appear with high contrast, the size of the area is much smaller. Applying a grayscale closing operator (\(\phi\)) on the intensity channel (\(f_I\)) will help eliminate the vessels which may remain in the optic disc region. A flat disc-shaped structuring element with a fixed radius of eight (\(B_1\)) was used. Fig. 3(a) shows a result after closing operator (Eq. (1)) was applied.

\[
O_{p1} = \phi(B_1)(f_I) \tag{1}
\]

where \(B_1\) is the morphological structuring element.

The resulting image was binarized by thresholding (\(\alpha_1\)), shown in Fig. 3(b) and the thresholded image was then used as a mask. All the pixels in the mask were inverted before they were overlaid on the original image to remove candidate bright regions. The result, \(O_{p2}\), is shown in Fig. 3(c). The morphological reconstruction by dilation, \(R\), was then applied on the previous overlaid image.

\[
O_{p3}(x) = R_{f_I}(O_{p2}) \tag{2}
\]

The dilations of marker image (\(O_{p2}\)) under mask image (\(f_I\)) were repeated until the contour of marker image fits under the mask image. The reconstructed image is shown in Fig. 3(d). The difference between the original image and the reconstructed image was thresholded at grey level \(\alpha_2\) using the following equation. The value of \(\alpha_2\) is different from image to image depending on automated selection using the Otsu algorithm.

\[
O_{p4} = T_{\alpha_2}(f_I - O_{p3}) \tag{3}
\]
As a result, high intensities are reconstructed while the rest is removed, as shown in Fig. 3(e).

Normally, the optic disc can be easily identified as the largest area. However, in some cases such as the appearance of huge exudates in the image, there might be some areas in the image which are larger than the optic disc. Because the shape of optic disc is round, therefore the optic disc region selection process needs to be made specific to the largest one among the regions whose shapes are circular. Cirularity of the shape of the region is defined by the value of compactness, \( M \), as defined using the following equation:

\[
M = 4\pi \frac{\text{area}}{\text{perimeter}^2}
\]

where area is the number of pixels in the region and perimeter is the total number of pixels around the boundary of each region.

The selected result (largest among circular shapes), \( OP_5 \), was dilated with a binary dilation operator (\( \delta \)) in Eq. (5) to ensure that all pixels in the optic disc area are covered. This step, a flat disc-shaped structuring element with a fixed radius of six (\( B_2 \)) is used.

\[
OP_{seg} = \delta^{(B_2)}(OP_5)
\]

All optic disc area in the original image was masked out using the previous output. The result is shown in Fig. 3(f).

2.3. Exudate detection

Similar to the previous steps, high contrast vessels can be eliminated first by a closing operator and it is represented by \( E_1 \) in our Eq. (6). A local variation operator, Eq. (6), was then applied to the previous result to get a standard deviation image which shows the main characterization of the closely distributed cluster of exudates. The resulting image, \( E_2 \), is shown in Fig. 4(a).

\[
E_2(x) = \frac{1}{N-1} \sum_{i \in W(x)} (E_1(i) - \mu_{E_1(x)})^2
\]

where \( x \) is a set of all pixels in a sub-window \( W(x) \), \( N \) is a number of pixels in \( W(x) \), \( \mu_{E_1(x)} \) is the mean value of \( E_1(i) \) and \( i \in W(x) \). A window size of \( 7 \times 7 \) was used in this step.

In this step, the resulting image was thresholded at automatically selected grey levels \( \alpha_3 \), using the Otsu algorithm, to get rid of all regions with low local variation. To ensure that all the neighbouring pixels of the thresholded result were also included in the candidate region, a binary dilation operator was also applied with a flat disc-shaped structuring element with a fixed radius of six (\( B_3 \)), as indicated in Eq. (7). The result is shown in Fig. 4(b).

\[
E_3 = \delta^{(B_3)}(T_{\alpha_3}(E_2))
\]
The candidate region to represent exudates should not be only their borders, therefore the enclosed area was flood-filled. The image is represented by $E_4$, and the result is shown in Fig. 4(e). The previously detected optic disc region was dilated before it was used to remove the optic disc from the above resulting flood-filled image ($E_4$), Eq. (8), the result, $E_5$, is shown in Fig. 4(d). To implement this step, a binary dilation operator with a flat disc-shaped structuring element with a fixed radius of 10 ($B_4$) is applied.

$$E_5 = E_4 - \delta (B_4) (\text{OP}_{\text{seg}})$$  \hspace{1cm} (8)

The result from Eq. (8) was used as a mask, showing all possible candidate regions of exudates, to create a marker image ($E_6$), as shown in Fig. 4(e). It was later morphologically reconstructed using a dilation operator upon the original intensity image similar to the step performed with the detection of the optic disc. The result is displayed in Fig. 4(f).

Using Eq. (9), the final result is obtained by applying a threshold operation at selected grey level $\alpha_4$ to the difference between the original image ($f_4$) and the reconstructed image ($E_7$). The resulting image is shown in Fig. 4(g).

$$E_{\text{seg}} = T_{\alpha_4} (f_1 - E_7)$$  \hspace{1cm} (9)

The result from this step will be sent for validation. Fig. 4(h) displays the thresholded result superimposed on the original image.

There are many parameters used in this experiment. They are, namely, the size of structuring element ($B_1$, $B_2$, $B_3$ and $B_4$) used for the dilation operation, window size in local variation operator, threshold values ($\alpha_1$, $\alpha_2$, $\alpha_3$ and $\alpha_4$). $\alpha_2$ and $\alpha_3$ were calculated automatically using the Otsu algorithm. $B_1$, $B_2$, $B_3$, $B_4$, window size, $\alpha_1$ and $\alpha_4$ were varied and tested in order to assess the algorithm performance in a previous experiment. Each parameter was varied as follows:

- $B_1 \in \{6, 7, 8, 9, 10\}$
- $B_2 \in \{4, 5, 6, 7, 8\}$
- $B_3 \in \{4, 5, 6, 7, 8\}$
- $B_4 \in \{8, 9, 10, 11, 12\}$
- window size $\in \{5, 7, 9\}$
- $\alpha_1 \in \{0.5, 0.6, 0.7, 0.8, 0.9\}$
- $\alpha_4 \in \{0.01, 0.02, 0.03, 0.04, 0.05\}$

From the experiment with different parameter settings, we found that changing the structuring element size and threshold values did not significantly affect the performance of the system. All parameters in this proposed methods are set using the values that gave highest sensitivity and specificity in the previous experiment.

### 2.4. Macular detection

The macular is detected from the intensity image by the darkest region on the retinal image; it is not always the case due to high illumination. The typical characteristics of the macular (for example, it is within the neighbourhood of the optic disc) is also used to detect the macular more accurately.

The high contrast vessels were eliminated first by a closing operator. The resulting image was binarized by thresholding. Then the darkest area in the neighbourhood of the optic disc (approximately 2.5 times the diameter of the optic disc from the centre of optic disc) was considered as a macular. A Macular grid was drawn according to the ETDRS report [12] with a radius of one third of the optic disc diameter, one optic disc diameter and two optic disc diameters, respectively.

### 3. Results

Sixty images were tested on an AMD Athlon 1.25GHz PC using MATLAB. Each image took approximately 3 min to process included the optic disc removal step which took around 1 min. The result of the exudates detection was superimposed on the original image. The previously unclear exudate regions were visibly highlighted and the exudates can be visibly observed after the process. This type of presentation will enable clinicians to identify pathology more quickly. The optic disc was also detected well and removed. Usually there are no exudate pixels around the optic disc so the removal of the optic disc did not affect the exudate detection. An example of the detection results are shown in Fig. 5.

The performance of our technique was evaluated quantitatively by comparing the resulting extractions with ophthalmologists’ hand-drawn ground-truth images pixel by pixel. In order to facilitate the experts to produce a ground-truth image, a first draft of ground-truth image was created by us. We marked the very obvious exudate pixels which are normally bright and yellowish areas, pixel by pixel, using a photo manipulation program with one colour. Then, this first draft image was shown to two expert ophthalmologists together with the original image. The ophthalmologists then made some changes by adding some missing exudate pixels and/or removing some misunderstood non-exudate pixels until it was agreed by both experts.

Sensitivity and specificity were chosen as our measurement of accuracy of the algorithms at the pixel level. Not only does this evaluation mechanism show how accurate our detection was, it also shows how inaccurate our detector can be. This pixel-based evaluation considers four values, namely true positive (TP), a number of exudates pixels correctly detected, false positive (FP), a number of non-exudate pixels which are detected wrongly as exudate pixels, false negative (FN), a number of exudate pixels that were not detected and true negative (TN), a number of non-exudates pixels which were correctly identified as non-exudate pixels. From these quantities, the sensitivity and specificity were computed using Eqs. (10) and (11). The misclassified proportion was computed using Eq. (12).

$$\text{sensitivity} = \frac{TP}{TP + FN}$$  \hspace{1cm} (10)

$$\text{specificity} = \frac{TN}{TN + FP}$$  \hspace{1cm} (11)
Fig. 5. Exudates detection on low contrast images. (a) Original images of a normal eye, (b) detected structures (exudate-like) of (a), (c) detected structures superimposed on contrast enhanced images, (d) original images of a diseased eye, (e) detected exudates of (d), and (f) detected exudates superimposed on contrast enhanced images.

\[
\text{misclassified proportion} = \frac{FP}{TP + FP + FN + TN} \tag{12}
\]

After all the 40 retinal images with exudates and 20 normal retinal images without exudates were processed, they were compared with the hand-drawn ground-truth images. Table 1 shows the quantitative result of TP, FP, FN, TN, sensitivity, specificity and misclassified proportion from the images of diseased eyes. For our data set with diabetic retinopathy exudates, the sensitivity and specificity of the exudate detection are 80% and 99.5%, respectively. For normal retinal image detection, the specificity and misclassified proportion are 99.9% and 7.2%, respectively. The sensitivity cannot be calculated in which TP and FN values are all zero due to no exudates in ground-truth images.

Our algorithm has very high specificity which showed that the algorithm does not recognize a non-exudate pixel as an exudate pixel. However, the sensitivity, a relatively lower value, also showed that the low intensity exudates pixels are still too elusive to be detected by this algorithm.

The system also detects the macular region in order to provide the ophthalmologists with the distance information between the detected exudates and the macular. The exudates within the inner circle will affect the vision of patients more than the ones outside it. As shown in Fig. 6(a), exudates are present nearer to the macular than exudates in Fig. 6(b). This indicates that the exudates in Fig. 6(a) will be more harmful to vision than those in Fig. 6(b).

4. Discussion

In this work we have investigated and proposed a set of optimally adjusted morphological steps to automatically detect optic disc and exudates from diabetic retinopathy patient’s non-dilated pupil digital images in an attempt to detect the pathologies earlier. The optic disc was detected and removed prior to the exudate detection because the intensity features of both areas are similar.

From 20 normal patients, the misclassified proportion value of seven people is over the average misclassified proportion and might need a further diagnosis. It means that this system can reduce the ophthalmologist’s workload especially in developing countries where the number of ophthalmologists is not sufficient to deal with the large number of diabetic retinopathy patients.

This system intends to help the ophthalmologists in the diabetic retinopathy screening process for detecting the symptoms faster and more easily. The results demonstrated here indicate that automated diagnosis of diabetic retinopathy based on intensity retinal image analysis can be very successful in detecting exudates. It is not a final result application but it can be a preliminary diagnosis tool or decision support system for oph-

Fig. 6. (a) and (b) Macular grid centred on the macular, superimposed on the exudate detection result.
Table 1

<table>
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<th>24-Bit images</th>
<th>Ground-truth exudates numbers</th>
<th>Detected exudates numbers</th>
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<th>FP</th>
<th>FN</th>
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The results also provide ophthalmologists with distance information between the detected exudates and the macular. The retinal vessel detection could also be added in order to facilitate ophthalmologist decisions on laser treatment. The results of this work can be developed to produce an automated system to detect exudates. Microaneurysm and haemorrhage detection could be added to the system in order to increase its ability to verify the degree of diabetic retinopathy. It will be useful to extend this work by developing a system to detect them.

Future work will address an issue of improving the sensitivity by improving the results of other tasks, such as the detection of the optic disc and blood vessels, and also try to localize faint and small exudates. In future, in work to expand the detection system to recognize microaneurysms and haemorrhages, there may be a problem in separating the pathologies from small vessels. We can detect vessels prior to the detection of pathologies and subtract them from the image. If small vessels are missed during this step and are confused with microaneurysms or haemorrhages it may be possible to combine more than one detection technique [5] to make a final decision on the likelihood of the detected area being either a vessel or microaneurysm or a haemorrhage. At the moment our algorithm is not able to detect differences between hard and soft exudates. However, hard and soft exudates can be distinguished by their colour and the sharpness of their border so this could be detected by tuning the edge filter and feature selection. It is intended that these features will be used in future detection algorithms.

Additionally, ground-truth creation may also be done solely by expert ophthalmologists in order to reduce authors’ bias and the results from that test set may be used to compare with the current one.

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References


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