Detection of Fundus Lesions Using Classifier Selection

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SUMMARY A system for detecting fundus lesions caused by diabetic retinopathy from fundus images is being developed. The system can screen the images in advance in order to reduce the inspection workload on doctors. One of the difficulties that must be addressed in completing this system is how to remove false positives (which tend to arise near blood vessels) without decreasing the detection rate of lesions in other areas. To overcome this difficulty, we developed classifier selection according to the position of a candidate lesion, and we introduced new features that can distinguish true lesions from false positives. A system incorporating classifier selection and these new features was tested in experiments using 55 fundus images with some lesions and 223 images without lesions. The results of the experiments confirm the effectiveness of the proposed system, namely, degrees of sensitivity and specificity of 98% and 81%, respectively.

key words: fundus, diabetic retinopathy, CAD, image processing, image normalization, classifier

1. Introduction

Though efforts to prevent diabetic retinopathy have been ongoing for more than 20 years, diabetes is still one of the most serious diseases in many countries [1]. Patients are always threatened by the fear of blindness caused by diabetic retinopathy. In Japan, the number of people who take medical examinations in order to keep their health in good condition has been increasing. During the examination of diabetic retinopathy, the doctor examines eye-fundus images taken by special cameras. An eye fundus image is shown in Fig. 1. In addition to normal portions such as blood vessels and optic disc, there are some bright (or yellowish) and dark (or reddish) parts: lesions. The current situation where the number of images is increasing drastically makes the doctor’s workload very heavy. This is the reason why a CAD (computer aided detection) system for automatically detecting diabetic retinopathy is eagerly expected.

The research for analysing blood vessels in digital fundus images began more than 30 years ago [2]. In this decade, the research for a CAD system to detect diabetic retinopathy has been ongoing. Lee et al. examined the CAD system’s reliability by comparing its results to the ones by human specialists [3]. In their research, targets were hemorrhages, microaneurysms, hard exudates, and cotton-wool spots. The agreement rates for both sensitivity and specificity in detecting these targets between the computer and the specialists were over 90%. This means that the CAD system is reliable for practical use, especially for screening.

To diagnose the diabetic retinopathy, it is necessary to consider many features. Zahlmann et al. constructed the knowledge based system to detect diabetic retinopathy [4]. They used the visual acuity, status of the anterior segment (ex. internal ocular pressure, cataract, posterior capsule formation, rubecosis iridis), status of the fundus (ex. lesions, complications of new vessels), and previous ophthalmological therapy. These features are integrated using the fuzzy rule.

When focusing on the diagnosis using only the status of the fundus, one of the important features is the color. Luo et al. used color based processing to detect the lesions of diabetic retinopathy [5]. They classified the lesions into 2 classes using color, which are white or yellowish ones and dark or reddish. The former ones include hard exudate, soft exudate, and cotton wool spot, while the latter ones include microaneurysms and hemorrhages. We call the former ones bright lesions and the latter ones dark lesions. Luo et al. calculated the reference color for bright lesions, dark lesions and background using the 2D histogram in $L^∗ - u^∗$ color space. Then they applied the watershed transform in order to extract the lesion area to the color difference image, whose pixel value indicates the difference from each
to learn that different evaluation method is adopted unless otherwise described. Osareh et al. developed
the system to detect exudates [6]. They evaluated several features and concluded that average of pixel value on green
component image and blue component image in RGB color system, and average of intensity in the lesion had good
detecting accuracy. Li et al. developed the method to detect an optic disc and exudates [7]. For exudate, they used region
growing and edge detection. They achieved 100% for sensitivity and 71% for specificity at the exudate detection ac-
curacy. This means all the test images which have exudates were decided as non-healthy, while 71% of the test images
were decided to be healthy. Hereafter, this evaluation method is adopted unless otherwise described.

The methods mentioned above are based on bottom-up approach which means to use region segmentation to detect
lesions. Zhang et al. proposed a top-down approach for dark lesion (hemorrhage) detection [8]. Their method was based
on window scanning, where the pixel values in a window are used as a feature vector. This approach will be effective
when the target has a specific intensity pattern such as a human face’s one. However, a lesion is featured by its
different characteristic from the background around it. In order to learn that difference, the classifier have to learn the
background as well as the lesion in the same window. For a good generalisation ability, an enormous number of training
samples are necessary to cover enough variations of the combinations of the lesion and the background. Therefore,
we decided to adopt bottom-up approach.

Another problem is which classifier to apply. Niemeijer et al. developed the system for dark lesions [9]. They improved the method using fluorescein angiography images into one using color images. They applied a K-NN classifier with 21 features, and achieved 100% for sensitivity and 87% for specificity. Ege et al. evaluated the system from the point of view of the statistical classifier [10]. They tested a Bayesian, a mahalanobis, and a K-NN classifier. The mahalanobis classifier had the best result; its sensitivities were 69, 83, 99, and 80% for microaneurysms, hemorrhages, ex-
udates, and cotton wool spots, respectively.

There has already been a commercial based product to detect the dark lesions. Larsen et al. evaluated that system and the result was 96.7% for sensitivity and 71.4% for specificity [11].

Usher et al. described the total system to detect the lesions of diabetic retinopathy [12], [13]. The system is for both dark and bright lesions. It is comprised of image normalization (step 1), image analysis for detecting basic portions such as the blood vessels and the optic disc (step 2), detection of candidate lesions (step 3), and discrimination of true lesions from false positives (FPs) (step 4). Here, FPs are not lesions but portions detected as lesions incorrectly. Step 2 excludes the portions of blood vessels and the optic disc from the whole fundus image because these portions usually have no diabetic retinopathy lesions and the color
of the portions is very similar to that of lesions. This step can simplify the discrimination of true lesions (TLs) from
false positives (FPs) in the next step. The detection of candidate lesions is executed by a special segmentation based on
region growing and adaptive binarization. Step 4 uses a neural network that utilizes the intensity and geometrical features detected from the candidate lesions.

In Usher’s system, the positions of candidate lesions are not utilized in the classifier. However our research revealed that the FPs tend to arise near blood vessels. This fact will contribute to decreasing the number of FPs.

This paper firstly describes the grey level adjustment essential for precise detection of lesions and the detection
of basic portions as preprocesses. Secondly, it is shown that the degree of difficulty in lesion detection varies with the
distance between a lesion and its nearest blood vessel. This fact leads to the idea of “classifier selection” for decreasing the number of FPs around blood vessels. Thirdly, actual classification based on some new features from the periphery of candidate lesions is proposed. Finally, a system applying the proposed techniques is evaluated by experiments using actual fundus images.

2. Detection of Lesions

Figure 2 shows the flow diagram of the lesion detection process. The left and the right sides of the figure indicate the
preprocessing parts and the lesion detection parts, respectively. In this process, grey level adjustment and classifier
selection are introduced, and new features that allow the classifier to detect candidate lesions around blood vessels
are also introduced.

2.1 Detection of Basic Portions

The detection of basic portions such as blood vessels and the optic disc from an input image is done by preprocessing. The input image is normalized in advance using Sinthanayothin’s method [14]. Himaga’s method [15] can be
used to extract blood vessels. With this method, first, the input image is transformed into an image in which the blood vessel regions are emphasized by matched filters composed of Gaussian kernels. Directional recursive region growing segmentation (D-RRGS) technique is then applied to the image to extract blood vessel regions. The extraction of the optic disc can be completed by the matching with a standard template of an average image of the optic disc patterns.

2.2 Grey Level Adjustment for Lesion Detection

The aim of grey level adjustment is to regularize the difference of “value” (or brightness, lightness) component in an HSV color system between images because they are essential features for lesion detection. This grey level adjustment consists of two processes: area-dependent grey level adjustment (ADA) and area-independent grey level adjustment. The objective of the ADA is to correct the low brightness of the pixels at the outskirts of a fundus image caused by the lack of lighting intensity and the aberration of the lenses, while the objective of AIA is to remove the difference in the brightness of the individual fundus and that of the lighting environment.

In ADA, first, a window around a target pixel \( r_0 \) to be adjusted is set. And \( R_W(r_0) \) is denoted as the pixel set in the window and \( R_F \) as the pixel set of the whole fundus image except the blood vessels and the optic disc. The difference of ADA from Sinthanayothin’s method [14] is that the average and standard deviation that are used to correct the “value” component at \( r_0 \) are calculated in region \( R_W(r_0) \cap R_F \), because the existence of the blood vessels in \( R_W(r_0) \) affects them. The equations used in ADA are shown from Eqs. (1) to (3).

\[
\bar{v}(r_0) = \frac{v(r_0) - \text{avg}(v(r), r_0)}{\text{stdev}(v(r), r_0)}
\]

\[
\text{avg}(v(r), r_0) = \frac{\sum_{r \in R_W(r_0) \cap R_F} v(r)}{|R_W(r_0) \cap R_F|}
\]

\[
\text{stdev}(v(r), r_0) = \sqrt{\frac{\sum_{r \in R_W(r_0) \cap R_F} (v(r) - \text{avg}(v(r), r_0))^2}{|R_W(r_0) \cap R_F|}}
\]

\( v(r) \): “value” (in HSV) at position \( r \) before grey level adjustment

\( \bar{v}(r) \): “value” at position \( r \) after ADA

\( \hat{v}(r_0) = a_0[\bar{v}(r_0) - \text{avg}(\bar{v}(r))] / \text{stdev}(\bar{v}(r)) + b_0 \) (4)

\( \text{avg}(\hat{v}(r)) = \frac{\sum_{r \in R_F} \hat{v}(r)}{|R_F|} \) (5)

\( \text{stdev}(\hat{v}(r)) = \left\{ \frac{\sum_{r \in R_F} (\hat{v}(r) - \text{avg}(\hat{v}(r)))^2}{|R_F|} \right\}^{1/2} \) (6)

\( \hat{v}(r) \): “value” at \( r \) after AIA

\( a_0 \) and \( b_0 \): constants

\( \text{avg}(\hat{v}(r)) \): average of \( \hat{v}(r) \) in \( R_F \)

\( \text{stdev}(\hat{v}(r)) \): standard deviation of \( \hat{v}(r) \) in \( R_F \)

An example of the grey level adjustment is shown in Fig. 3. In the figure, (a) is the original image and (b) is the adjusted image. It can be seen that the shadow at the outskirts of (a) is corrected in (b). Figure 4 is a magnified image of the white rectangle area in Fig. 3 (b). In Fig. 4, (a) is the result of the conventional method in which blood vessels and optic disc are used to calculate \( \text{avg}(v(r), r_0) \) and \( \text{stdev}(v(r), r_0) \), and (b) is that of the proposed method. In comparing the brightness of the areas between blood vessels, that of Fig. 4 (a) is brighter than that of Fig. 4 (b). This is because that the calculation of \( \text{avg}(v(r), r_0) \) in Eq. (2) includes the low “value” components of blood vessels in the case of the conventional method. Therefore, the adjusted value \( \hat{v}(r_0) \) in Eq. (1) will be high apparently. On the other hand, that kind of problem does not occur in the case of the proposed method.

The idea of ADA is similar to that of so-called “dynamic thresholding” [16], [17], used for getting binarized image of documents under the illumination ununiformity.
2.3 Detection of Candidate Lesions

The segmentation and the adaptive thresholding techniques are utilized to detect candidate lesions [12], [13]. According to [5], it is desirable to apply those techniques to the CIEL* a*b* or CIEL* u*v* color system. However, the problem is that the red component image is often saturated, as described in [18]. This means that the precise conversion from RGB to CIEL* a*b* or CIEL* u*v* is not possible.

Therefore it is more practical to apply those techniques to green component image in the RGB color system. Green component image has also much information in fundus images [6], [18]. The region growing method is used for this segmentation. This method makes groups from pixels with similar values: that is, it can extract one candidate region (i.e., a set of pixels) as one lesion. Next, adaptive thresholding is applied to the green component image with segmented region information. The regions whose average pixel value of green component image is brighter than their peripheries are detected as bright lesions. Such regions are exudates and cotton wool spots. The regions whose average value is darker than their peripheries are detected as dark lesions such as microaneurysms and hemorrhages.

2.4 Classifier Selection

The analysis of detected candidate lesions using 85 fundus images where a doctor attached the ground truth proved that FPs arise more frequently near blood vessels, as shown in Figs. 5 and 6. Here, the positions and areas of blood vessels in this analysis were extracted by Himaga's algorithm [15]. The horizontal axis indicates the chess board distance of a FP from its nearest blood vessel. The low computational cost of chess board distance is useful to use it in the real system. The distance is measured between the nearest two pixels, one is in a candidate lesion and another is in blood vessels. The broken line indicates the number of FPs that are more than the value on the horizontal axis away from their nearest blood vessels. The solid line indicates the ratio of the number of FPs against the number of TLs. According to Figs. 5 and 6, the nearer a candidate lesion is to blood vessels, the higher probability that the candidate is a FP. To increase the reliability of our system, this fact can be made good use of in our approach to reduce the number of FPs. The approach is to introduce a classifier selection and apply a new classifier for lesions near to blood vessels.

The candidate lesions far from blood vessels can be classified by using neural networks [12], [13]. The input features are average intensity, geometric characteristics of the candidate lesion, and so on. On the other hand, the candidate lesions around the blood vessels are classified by a classifier based on rules using several new features. The features include intensity, area, shape of the candidate and relative intensity to its periphery. The latter classifier is described in Sect. 2.5. The classifier for a candidate lesion is selected according to its distance from its nearest blood vessel. A different threshold distance for selecting a classifier has been
determined for each kind of lesion. Because the slope of a solid line of bright lesions (shown in Fig. 5) is not steep, the one-pixel-distance covering the peak is set as the threshold. Candidate lesions whose distance from their nearest blood vessel is within one pixel are input into the new classifier for bright lesions, while the other candidates are input into the neural networks for bright lesions. On the other hand, the solid line of dark lesions (shown in Fig. 6) is dull more than a distance of four pixels; therefore, four pixels is set as the threshold. The procedure of this classifier selection is the same as that in the bright lesion case. (Note that above thresholds are determined under the condition that the image size is 700 × 605 pixels. In the case of a different image size, it is necessary to change the thresholds accordingly.)

We also examine the relation between the number of TLs and its distance from the nearest blood vessel. Figure 7 is of bright lesions and Fig. 8 of dark lesions. Since the number of pixels for each distance from the nearest blood vessel is different, we indicate the number of TLs per pixel as solid lines. The broken lines indicate the number of TLs. The number of bright lesions does not have an explicit tendency. Meanwhile, the number of dark lesions increases by four times from distance 2 to 8, which is considered to be one of the reasons why the probability of FPs increases nearer to the blood vessels.

2.5 New Classifier

As described above, a different classifier is utilized according to the distance from the nearest blood vessel to the candidate lesion. A neural network: 3-layer perceptron, which uses features such as intensity and geometric characteristics [12], [13] is applied to classify the candidate lesions far away from the nearest blood vessel. This neural network was trained with 2,831 TLs and 20,042 FPs extracted from 85 images of diabetic retinopathy patients. The position and area of each lesion is provided by a doctor as a ground truth data.

To design the new classifier for the candidate lesions around the nearest blood vessels, the following two facts must be considered: (i) regions that are bright and lie along the blood vessels tend to be FPs of bright lesions and (ii) partial regions that cannot be extracted as blood vessels tend to be FPs of dark lesions. To discriminate FPs that have those characteristics, shape and color features are appropriate. We proposed new features such as “G-ratio”, “T-degree”, and “G-BV-difference” based on shape and color. In this paper, we considered it will be more important to clarify the effectiveness of these new features. Therefore, a simple thresholding is applied as the new classifier. The detail of the features is described in the following subsections.

2.5.1 Bright Lesion

In this subsection, the classifier that corresponds to Fig. 2 (a) and the new features “G-ratio” and “T-degree” are explained.

Regarding the difference between the features of type (i) FPs and those of true lesions, it is shown that FP’s intensity gives a weak contrast with its periphery and that it has a line-shape along the blood vessel. To obtain the intensity contrast, one new feature is proposed, namely, the ratio of the average of pixel value on green component image in a candidate lesion (Fig. 9 (a)) to the average of pixel value on “value” component image in HSV color system at the periphery (Fig. 9 (d)). Here, green component is an effective color feature to detect lesions [6]. The latter value is calculated only at the periphery of the lesion, and it can be used as a robust standard. Hereafter, we call this feature “G-ratio”.

To obtain the shape feature of a FP, another new feature is proposed. This feature is based on the degree of touching
between the candidate lesion and a peripheral blood vessel. If this value is high, the shape is more like a line along the blood vessel. Hereafter, we call it “T-degree”, which is calculated from Eq. (7)

\[ T_d = \frac{p_{bp}}{l} \]  

(7)

where \( l \) denotes the length of the contour of the candidate lesion, and \( p_{bp} \) denotes the number of pixels of the contour that are in the expanded blood vessel region (Fig. 10).

The classification for the type-(i) bright lesions uses G-ratio, T-degree, and an additional feature to remove the noise, namely, the area of the candidate lesion. The threshold for each feature is determined in advance by analyzing their distribution, which is calculated using the images without any lesions. The candidate lesion whose features exceed all thresholds is regarded as a true bright lesion in this classification.

2.5.2 Dark Lesion

In this subsection, the classifier that corresponds to Fig. 2 (b) and the new feature “G-BV-di\text{ff}erence” are explained. Table 1 lists the characteristics of TLs and FPs among dark lesion candidates.

Most type-(ii) FPs arise under conditions #2 or #4. Further investigation of the type-(ii) FPs suggests green value of the type-(ii) FP tends to be brighter than that of the peripheral blood vessels (Fig. 9 (b)). Therefore, a new feature, called G-BV-di\text{ff}erence, namely, the difference between average green value in candidate lesions (Fig. 9 (a)) and average green value in the peripheral blood vessels (Fig. 9 (b)), is assigned. In the classification of type-(ii) dark lesions, screening according to lesion size and shape is firstly executed. Next, lesions with large T-degree are extracted. Lastly, these lesions are classified by using the G-BV-di\text{ff}erence and G-ratio. G-ratio is a feature used in the bright lesion classifier, and it is also effective for classifying dark lesions. The threshold for each feature is determined in advance by analyzing their distribution, which is calculated using the images without any lesions. The lesion candidate whose features exceed all thresholds is regarded as a true dark lesion in this classification.

3. Experimental Results

The proposed system was evaluated by experiments using 55 fundus images which are of diabetic retinopathy patients and have several lesions in each image, and 223 images without lesions. The images were 700 × 605 pixels in size and 24-bit RGB color. The former images are for calculating the sensitivity: the ratio of the number of images in which at least one lesion is detected to the number of all images with lesions. Namely, the image is categorized as of diabetic retinopathy when the system detects at least one lesion. Meanwhile, the specificity is the ratio of the number of images in which lesions are not detected to the number of images without lesions. This evaluation is also applied in other papers [7], [9]–[11].

Four results are listed in Table 2. #4 is the result of the proposed system: the sensitivity is 98% and specificity is 81%. #1 is the result of the conventional system, which has neither the proposed grey level adjustment nor the proposed classifier. Here, the proposed classifier includes the selection of classifiers and the new classifier. #2 is the one which has the proposed grey level adjustment, #3 is the one which has proposed classifier, and #4 is the one which has both. Comparing result #1 and result #4, the proposed system has an improved specificity of 17 points while the sensitivity stays at 98%. This means the new system can remove FPs without decreasing lesion detection rate. The effectiveness of the selection of classifiers and the new classifier is confirmed by comparing the results between #1 and #3, or #2 and #4.

<table>
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<th>Spec.</th>
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<td>conventional</td>
<td>98%</td>
<td>67%</td>
</tr>
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<td>2</td>
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<td>conventional</td>
<td>98%</td>
<td>65%</td>
</tr>
<tr>
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<td>conventional</td>
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<tr>
<td>4</td>
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<td>proposed</td>
<td>98%</td>
<td>81%</td>
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Fig. 11 Example of FPs.
Notice that the proposed grey level adjustment was effective only when it was used with the classifier selection and the new classifier. This result ought to be the difference of numbers of lesion candidates near blood vessels between the conventional and the proposed grey level adjustment. As indicated in Fig. 4, the "value" near the blood vessels adjusted by the proposed method is darker than that by the conventional method. In that case, a large lesion candidate when using the conventional method may be extracted as plural small lesions when using the proposed method. In spite of its preciseness, the false lesion candidates increases for the proposed grey level adjustment. This will cause more
FPs and somewhat lower specificity when the proposed grey level adjustment is used with the conventional classifier.

Some examples of FPs are shown in Fig. 11. (a)(b) in Fig. 11 are the examples of FPs of bright lesions. Bright areas that have reflection of light are the main cause of FPs of bright lesions. (c)(d)(e) are the FPs of the dark lesions. Blood vessels that are not detected by blood vessel detection are the main cause of FPs of dark lesion. Therefore, this system depends on the accuracy of the blood vessel detector for thin and ambiguous blood vessels. The total results are shown in Fig. 12. The blue circles indicate the positions of bright lesions, and the green circles indicate the positions of dark lesions.

The processing time was 43 second per image (Pentium4 3.2 GHz, 1 GB RAM, Windows XP). There is a difficulty to use this system in the case where the results are necessary in real time. We therefore propose that the outputs from the system could be used at the tele-screening service. There have already been some services where the ophthalmologist read all the retinal fundus images sent from the medical centers or hospitals. This system can help ophthalmologists by screening those images.

4. Conclusion

We developed a system to detect fundus lesions of diabetic retinopathy. The system is characterized by a classifier selection controlled by the positions of candidate lesions and a new classifier with several new features to discriminate true lesions and false positive lesions. The proposed techniques can solve the difficulties in classifying the lesions in the area around the blood vessels. Experimental results show the system has an improved specificity of 81% and the same sensitivity of 98% as a conventional system.

Since this paper was intended to propose the classifier selection and the new features, we constructed the new classifier using simple thresholding. Our future work includes the automation of building up each classifier by AdaBoost or SVM techniques.

The experimental result revealed that the main cause of false positives for bright and dark lesions were the reflection and undetected blood vessels respectively. Developing a reflection detector and confirming the affect of the blood vessel detection performance were other future work.

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