DETECTION OF MICRO ANEURYSMS USING MULTIPLE CLASSIFIERS AND HIDDEN MARKOV MODELS

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Abstract: Diabetic retinopathy is a complication of diabetes and early detection is essential for effective treatment. In this paper, a novel technique for the detection of micro aneurysms is presented. Various features are extracted using image processing techniques and then fed through multiple classifiers for initial classification of candidate micro aneurysms. Hidden Markov models are then used to perform contextual analysis to recognise true micro aneurysms.

1 INTRODUCTION

Diabetic retinopathy (DR) is an eye disease that has been one of the major causes of blindness in the world (W.H.O, 2005) and early detection of the disease through screening can prevent blindness and allow for maintenance of good vision. A typical screening process involves the acquisition of patients' retinal images followed by a manual examination of each individual image by medical experts in order to identify any signs of deterioration. This process is known to be inefficient, time consuming and expensive.

Micro aneurysms are one of the first visible signs of DR and it is known that quantities of this clinical sign can help diagnose the progression of the disease. Micro aneurysms are swelling of the capillaries that are caused by the weakening of the vessel walls due to high sugar levels in diabetes and eventually leak to produce exudates. In retina images, micro aneurysms appear as small reddish dots with similar intensity as haemorrhages and blood vessels. This particular sign is an important early indicator of the disease and can contribute to helping ophthalmologists identify effective treatment for the patient at an early stage. The motivation of this work is to develop a technique that is able to detect micro aneurysms as part of a diagnosis system, so that medical experts are able to diagnose the stage of the disease with ease, saving screening time, manpower and cost.

In order to detect micro aneurysms, the technique employed must also be tolerant to the appearance of fine blood vessels that appear on or near the vicinity of the main blood vessels. Furthermore, the technique must also be scalable over a large volume of images. In the literature, a few image processing techniques have been applied in Walter & Klein (2000), Cree et al. (1996), Niemeijer et al. (2005), Sinthanayothin et al. (2002) to detect micro aneurysms. However, some of these techniques (Walter & Klein, 2000; Cree et al., 1996) require the blood vessels to be removed prior to micro aneurysm detection. This results in true micro aneurysms that are near or on the blood vessels to be removed as well. Furthermore, these techniques use only a set of rules to identify true micro aneurysms, which have not been proved to be tolerant to errors over a large data set.

Classification algorithms have been utilised in Niemeijer et al. (2005), Sinthanayothin et al. (2002) to detect micro aneurysms. Image processing techniques are first applied to extract features followed by recognition through a classifier, but the single classifier used is unable to ensure consistent accuracy over a large volume of diverse images.

In our work, an algorithm has been developed to detect micro aneurysms. The first stage of the algorithm aims to divide the image into smaller sub images, followed by image processing techniques prior to feature extraction. Due to uneven

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illumination, the image is firstly partitioned into 32x32 pixel sub images to minimise this effect. In the second stage, multiple classifiers are used to classify the candidate micro aneurysms. Contextual analysis is then performed using *Hidden Markov Models* (HMM) to further analyse the regions. This algorithm has been evaluated over a large-scale database taken from various sources.

This paper is organised as follows. In Section II, we present the techniques used in the proposed algorithm. Experimental results are given in Section III. Finally, we summarise our work in Section IV.

2 PROPOSED FRAMEWORK

In this section, we describe the proposed framework to detect micro aneurysms. One of the main obstacles is the variability in the retina image, such as the degree of pigmentation of epithelium and choroid in the eye, size of the pupil, illumination, disease, image settings (which varies even with the same equipment), patients' ethnic origin, and other variants. Another challenge is to identify micro aneurysms that are near other anatomical structures. For example, there may be instances where micro aneurysms appear near blood vessels suggesting that recognising of such features using classification and contextual analysis cannot be treated in isolation. Therefore, an integral approach has been proposed as illustrated in Figure 1. Detailed explanations of each component are given in the following sections.

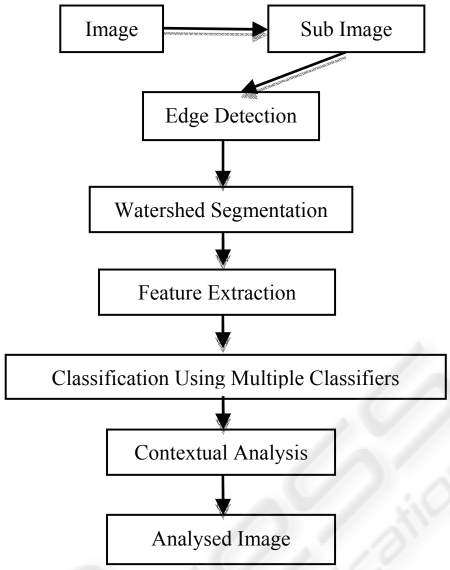

Figure 1: Proposed Framework.

2.1 Image Segmentation

As micro aneurysms appear with low contrast in retina images, a contrast enhancement algorithm (Sagar et al, 2007) is first carried out as a pre-processing stage to enhance the overall contrast. This is applied to the green component of the image as blood vessels and other dark lesions appear more distinct in the green component of a RGB image. Due to the variability among images, it is impossible to use a global image segmentation technique to detect candidate micro aneurysms region while maintaining consistent accuracy. Also, as micro aneurysms may appear near or on the blood vessels, we chose to preserve the structure of the blood vessels during initial image segmentation.

In order to obtain as many candidate micro aneurysms regions as possible, we choose to use a sliding window technique where canny edge detection is applied to each 32x32 pixel sub image to detect all closed boundaries. Furthermore, to ensure candidate regions locating on the boundaries between two sub images are detected as well, the edge detection is carried out on overlapping sub images with 16 pixels width intervals.

Using this technique, all candidate regions are detected and reduced to seeds for the watershed segmentation algorithm. Previous work by Spencer et al., (1996) used region grow algorithm to grow the candidate regions to their actual size. However, through experimentations, we found that there is no definite method to define the stopping criteria, hence resulting in overgrown regions. This is especially so when the micro aneurysms are near haemorrhages or blood vessels, thus, giving erroneous results.

However, the watershed algorithm can overcome this problem as it performs especially well where two objects are touching and there exists few gray levels between the two objects. This technique is particular useful in our application as it allows micro aneurysms that are close to blood vessels, close to haemorrhages or even close to another micro aneurysm to be segmented accurately. Once the candidate micro aneurysms have been segmented, features are extracted from these regions.

2.2 Multiple Classifiers

Traditionally, to find the best classifier for a single problem, a few classification schemes will be developed using different sets of features, training algorithms, etc. followed by experiments and evaluation of the application to determine the best classifier. However, while each of these classifiers may be successful to a certain extent, neither of them would be a perfect solution to a given problem. It has been reported by Kittler et al. (1998) that although the best classifier would give the best performance, samples that are misclassified by the best classifier would not necessarily be misclassified by the rest of the classifiers. The combination of different classifiers may potentially offer information that can be used to improve the performance of the best classifier.

In our work, various features are used to represent the same pattern and a hierarchical structure has been developed as the classification strategy as shown in figure 2.

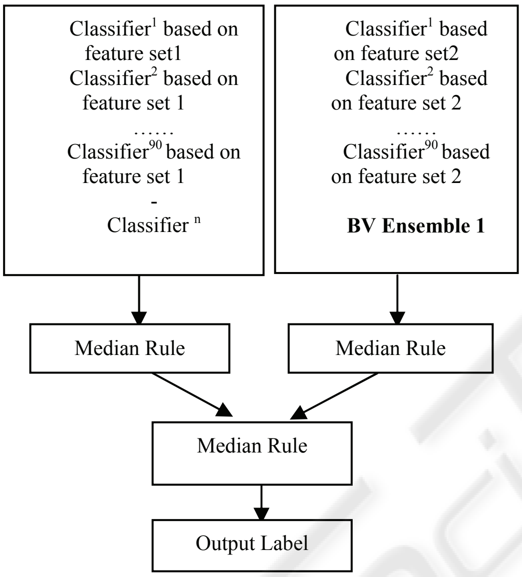

Figure 2: Classification Strategy.

2.2.1 Ensembles of Neural Network

Ensembles of *Multiple Layer Perceptron* networks are trained using the model in developed in our group (Yu & Browne, 2007). Each ensemble is trained using different training algorithms (*Scaled Conjugate Gradient algorithm, Quasi Newton algorithm and the Conjugate algorithm)*, various hidden units (*multiples of 2 ranging from 2 to 20*) and different initial weights are randomly generated from different ranges (*-0.0 to 0.01, -0.001 to 0.001 and -0.0001 to 0.0001*) resulting in a total of 90 classifiers for each ensemble. The results from each of the individual classifiers are combined using the median rule as the output of the ensemble. The median rule is then used again to combine the output of the two ensembles.

2.3 Feature Extraction

Many features could be used to represent micro aneurysms. However, combining all these features into a single classifier may cause a high dimension problem and cause the classifier to hold redundant information. Therefore, in our work, we separate these features and represent micro aneurysms using two different sets of features.

2.3.1 Feature Set 1: Shape and Colour Features

The first set consisted of 8 different features. The features can be separated into two groups, shape features and colour features. The shape features are used to restrict the shapes to circular objects in order to eliminate elongated structures such as blood vessels. The list of features for the first set is listed in table 1.

Table 1: List of Features.

1.	Area of the region
2.	Perimeter of the region
3.	Circularity, $c = p^2/4\pi*Area$
4.	Bounding box, the size of the smallest rectangle containing the object.
5.	Extent, scalar that specifies the proportion of the pixels in the bounding box that are also in the region
6.	Mean of region using pixels from contrast enhanced image
7.	Total energy level of region from contrast enhanced image
8.	Total energy level of background pixels from contrast enhanced image

2.3.2 Feature Set 2: Intensity Distribution Feature

The second set of features is based on the 3-D shape of micro aneurysms. The micro aneurysms is projected onto a three dimensional space using the intensity values of the 10 by 10 region centred on the micro aneurysm. As micro aneurysms are lower in intensity values as compared to the background area, it is necessary to inverse the values of the region in such a way that it displays a 'mole hill' as demonstrated in figure 3.

The angles from all locations of the region are then calculated against the centroid of the region to determine the steepness of the hill and the angle of each location is stored in a 10 by 10 array. This feature is useful in eliminating noise as the

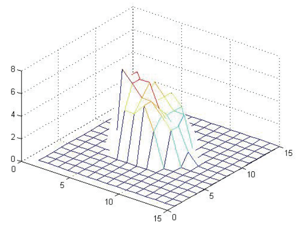

Figure 3: 3D plot of Micro Aneurysms.

region would be small and their angles would be really steep. On the other hand, there is also a distinct discrimination against blood vessels as the angles would be rather constant throughout all locations in the region.

Since the dimension of the input vector is 10 by 10 and is generally too large to train a neural network with good generalisation, Principal Component Analysis (PCA) is applied to reduce the dimensions of the input space to the top 10 components, hence allowing for good generalisation accuracy.

2.4 Hidden Markov Models

While using multiple classifiers can effectively deal with diversity, the hierarchical multiple classifier combination strategy also provides excellent tolerance to classification errors. However, misclassifications still occur due to either visually similar symptoms or structures of the retina, therefore, requiring a form of contextual analysis for further analysis of these candidate regions. In our work, we propose a stochastic modelling process as a post processing step to perform this analysis.

Hidden Markov Models has been widely used in speech recognition (Rabiner, 1989), hand writing recognition (Parui et al., 2008) and in DNA sequence analysis (Won et al., 2008). We apply a similar idea of modelling the data and recognition to detection micro aneurysms. In our work, we use it as a means of contextual analysis by taking into consideration the surroundings of the micro aneurysms.

The idea is to train a few Hidden Markov Models based on different kinds of sub images with different context followed by sequence recognition.

2.4.1 Feature Extraction for HMM

Before development of the models, the outputs from the multiple classifiers are analysed and based upon the observations, the relevant models are then created and listed in table 1.

Table 2: List of Models Created.

Observation	*Model*
Micro aneurysms only	MA
Micro aneurysms and Blood vessels	MABV
Background	BG

Various kinds of sub images are cropped into 15 by 15 sub images pixels from the image after the contrast enhancement procedure. Following this, each sub image is again divided into 9 5x5 pixel smaller sub images as seen in figure 4 to be used as observation sequences for the HMM.

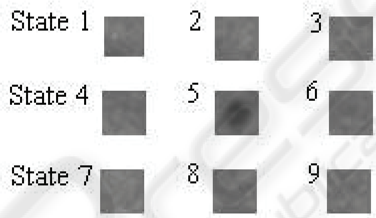

Figure 4: States of Sub Image.

The *Discrete Cosine Transform* (DCT) is then performed to obtain the features for each of the 5x5 pixel sub image. The DCT is used as it can represent an image in terms of sum of sinusoids of varying magnitude and frequencies, thus obtaining the most important information in just a few coefficients. Once the DCT has been applied for each observation, the result from the DCT process for each state is reshaped into a 25x1 column and used as part of a sequence for inputting into the HMM.

2.4.2 Creation of Hidden Markov Model

In our models, each HMM has 9 states excluding the start and end states which are common to each of the models that are created using the HTK toolkit.

In order to train the various models, a large number of training samples are obtained from retina images that exhibit micro aneurysms to estimate the model parameters. The feature vectors of each 5 by 5 pixel sub image are converted into a state so that a state sequence is obtained for each 15 by 15 pixel sub image and the models are created using a left to right topology. The initial state distribution, state transition probabilities, initial probabilities are then estimated using the package from the HTK toolkit.

Subsequently, for recognition, each new sequence will be input into the different HMMs and the model which best match the sequence would be used as the output.

3 EXPERIMENTAL RESULTS

3.1 Data Set

The training samples used to train the multiple classifiers and Hidden Markov Models are obtained from 100 retina images of various sources including the Optimal Detection and Decision-Support Diagnosis of Diabetic Retinopathy database.

3.2 Experiment Set Up

1000 training samples are obtained from these 100 retina images and used to train the two multiple classifiers. 700 background sub images, 1000 micro aneurysms sub images and 500 micro aneurysms and blood vessel sub images are used to train the different HMMs.

In order to determine the effectiveness of our proposed technique, a further 220 retina images with micro aneurysms are used to test the system. By using the data from various sources, this ensures that the data are more diverse, hence, testing the method to its full potential.

3.3 Results

The performance of this technique is evaluated by first labelling the ground truth of the micro aneurysms followed by a comparison with both the initial output of the ensemble and the final output of the HMM. Ideally, the sensitivity and specificity of the technique should be determined. However, in certain images, the number of true positives out weights the number of true negatives resulting in high sensitivity and low specificity. Hence, in order to determine the accuracy in detecting the micro aneurysms, the *Precision* [Equation 1] which is defined as the proportion of true positives against true positives and false positives is calculated.

$$\text{Precision} = \frac{TruePositives}{TruePositives + FalsePositives} \quad (1)$$

Using the ensembles, the method is able to detect a substantial amount of micro aneurysms. However, due to the high *False Positives Rate* at 1.31, the *Precision* using the ensembles is only 0.50. Further analysis showed that the main cause of the false positives is largely due to background and fine background vessels that are being misclassified by the ensembles.

On performing contextual analysis using Hidden Markov Models, the *Precision* is increased to 0.80 and the *False Positive Rate* is greatly reduced to 0.27. Observations from the output of the HMM shows that the false positives are usually caused by fine blood vessels which have not yet been modelled and by background sub images which are nearer the vicinity of the Optic Disc. Figure 5 illustrates the technique's ability to detect micro aneurysms while figure 6 shows the technique's ability to detect micro aneurysms along the blood vessel using watershed segmentation. To present the detected micro aneurysms clearly, true positives are represented by a white box, while true negatives are represented by a black box.

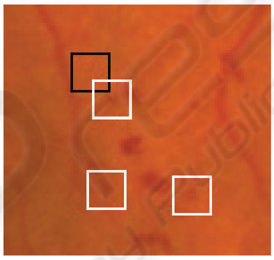

Figure 5a: Detected Micro aneurysms.

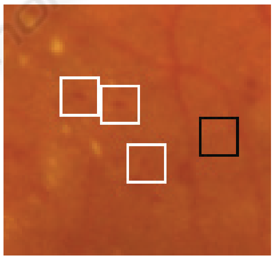

Figure 5b: Detected Micro aneurysms.

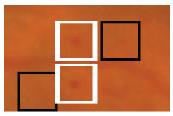

Figure 5c: Detected Micro aneurysms.

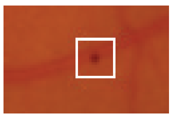

Figure 6: Detected Micro aneurysms on blood vessel.

4 CONCLUSIONS

In summary, a novel way to detect micro aneurysms using multiple classifiers and Hidden Markov

Models has been demonstrated. The experimental results have shown that by using Hidden Markov Models as a contextual analysis model, overall performance can be greatly improved, demonstrating its excellent potentials for further development. While the precision of this technique is only 0.80 with a false positive rate of 0.27, this technique is evaluated over 220 retina images obtained from various source, thus demonstrating the ability to overcome diversity usually found in a large-scale database.

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