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AUTOMATIC DIAGNOSIS OF DIABETIC RETINOPATHY USING FUNDUS IMAGES

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ABSTRACT This thesis applies the process and knowledge of digital signal processing and image processing to diagnose diabetic retinopathy from images of retina. The Pre-Processing stage equalizes the uneven illumination associated with fundus images and also removes noise present in the image. Segmentation stage clusters the image into two distinct classes while the Disease Classifier stage was used to distinguish between candidate lesions and other information. Method of diagnosis of red spots, bleeding and detection of vein-artery crossover points were also developed in this work using the color information, shape, size, object length to breadth ration as contained in the digital fundus image in the detection of thisdisease.

In addition to diagnosis of Diabetic Retinopathy (DR), two graphical user interfaces (GUI's) were also developed during this work, this first is for collection of lesion data information and was used by the ophthalmologist in marking images for database while the second GUI is for automatic diagnosing and displaying the diagnosis result in a more friendly user interface and is as shown in chapter three of this report.

The algorithm was tested with a separate set of 25 fundus images. From this, the Receiver Operating Characteristics (ROC) was determined for red spot disease and bleeding, while cross over points were only detected leaving further classification as part of future work needed to complete this global project. Sensitivity (classify abnormal fundus images as abnormal) and specificity (classify normal fundus image as normal) was calculated for the algorithm is given as 98% and 61%.

Keywords: Diabetic Retinopathy, Fundus Image, Digital Image Processing, Segmentation, Retina, Classifier.

INTRODUCTION

In recent times, Sweden and other parts of the world have been faced with an increase in age and society related diseases like diabetes. According to recentsurvey [1], 4% of the country population has been diagnosed of diabetes disease alone and it have been recognize and accepted as one of the main cause of blindness in the country if not properly treated and managed. Early detection and diagnosis have been identified as one of the way to achieve a reduction in the percentage of visual impairment caused by diabetes with more emphasis on routine medical check which the use of special facilities for detection and monitoring of the said disease [1]. The effect of this on the medical personnel need not be over emphasized, it has lead to increase work load on the personnel and the facilities, increase in diabetes screening activities just to mention a few. A lot of approaches have been suggested and identified as means of reducing the stress caused by this constant check up and screening related activities among which is the use medical digital image signal processing for diagnosis of diabetes related disease like diabetic retinopathy using images of the retina. Diabetes is a disorder of metabolism. The energy required by the body is obtained from glucose which is produced as a result of food digestion. Digested food enters the body stream with the aid of a hormone called insulin which is produced by the pancreas, an organ that lies near the stomach. During eating, the pancreas automatically produces the correct amount of insulin needed for allowing glucose absorption from the blood into the cells. In individuals with diabetes, the pancreas either produces too little or no insulin or the cells do not react properly to the insulin that is produced. The build up of glucose in the blood, overflows into the urine and then passes out of

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the body. Therefore, the body loses its main source of fuel even though the blood contains large amounts of glucose [2].

Basically there are three types of diabetes, Type 1 Diabetes, is caused as a result of auto immune problem. The immune system of the body destroys the insulin producing beta cells in the pancreas leading to no or less production of the required insulin by the pancreas. Type 2 Diabetes is a result of malfunctioning of the beta cell itself. This malfunction includes non production of insulin or a situation known as insulin resistance. In insulin resistance, the muscles, fat and other cells do not respond to the insulin produced. Type 3 is known as gestational diabetes and only occurs during pregnancy. During this stage, the body resist the effect of insulin produced.

The effect of diabetes on the eye is called Diabetic Retinopathy (DR). It is known to damage the small blood vessel of the retina and this might lead to loss of vision. The disease is classified into three stages viz: Background Diabetic Retinopathy (BDR), Proliferate Diabetic Retinopathy (PDR) and Severe Diabetic Retinopathy (SDR). In BDR phase, the arteries in the retina become weakened and leak, forming small, dot-like hemorrhages. These leaking vessels often lead to swelling or edema in the retina and decreased vision. In the PDR phase, circulation problems cause areas of the retina to become oxygen-deprived or ischemic. New fragile, vessels develop as the circulatory system attempts to maintain adequate oxygen levels within the retina. This phenomenon is called neovascularisation. Blood may leak into the retina and vitreous, causing spots or floaters, along with decreased vision. In the SDR phase of the disease, there is continued abnormal vessel growth and scar tissue, which may cause serious problems such as retinal detachment and glaucoma and gradual lossof vision.

This research work is one of the method of applying digital image processing to the field of medical diagnosis in order to lessen the time and stress undergone by the ophthalmologist and other members of the team in the screening, diagnosis and treatment of diabetic retinopathy. This work determine the presence of BDR and PDR or otherwise in a patient by applying techniques of digital image processing on fundus images taken by the use of medical image camera by a medical personnel in the hospital.

OBJECTIVE

The primary aim of this project is to develop a system that will be able to identify patients with BDR and PDR from either color image or grey level image obtained from the retina of the patient. These types of images are called fundus images. The different diabetic retinopathy diseases that are of interest include red spots, micro aneurysm and neo vascularisation and they fall between BDR and PDR stages of the disease. While SDR types are expected to be referred to the ophthalmologist.

The secondary aim includes developing a MATLAB based Graphic User Interface (GUI) tool to be used by the ophthalmologist in marking fundus images. The marked images are to be used for the development of DR grading and database system for this present and future work.

Principles and Application of Image Processing

Color Space Conversion

In digital image processing, images are either indexed images or RGB (Red, Green, Blue) images. An RGB image is an M x N x 3 array of color pixels, where each color pixel is a triplet corresponding to red, green and blue components of RGB image at specified special location. The range of value of an RGB is determined byits class. An RGB image of class double, has value in the range of [0 1], while classof uint8 is [0 255], similarly for the range [0 65535] is called class uint16.

There exist other color spaces or models in some applications other than the two models mentioned above, these include NTSC (luminance(Y), hue(I), saturation (Q) color model), HIS

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(luminance(H), hue(I), saturation (S)) color model), YCbCr (luminance(Y), hue(I), saturation (Q)) color model), HSV (hue(H), saturation(S), Value(V)) color model), CMY(cyan(C), Magenta(M), Yellow (Y) color model) and CMYK(cyan(C), Magenta(M), Yellow (Y), black(K)) color model. Image processing toolbox provides conversion functions from RGB to any above listed color spaces except HIS which will be discussed later in this section and is based on Gonzalez etal method [14].

a) NTSC color spacing: NTSC (luminance(Y), hue (I), saturation (Q)) color system is used in television in United States. One of the advantages of this method is that the greyscale information is separate from color data. The percentage of RGB components are given as red 29.9%, green 58.7% and blue 11.4%. The image data consists of three components luminance (Y), Hue (I) and Saturation (Q). The transformation matrix is as given below.

$$\begin{bmatrix} Y \\ I \\ Q \end{bmatrix} = \begin{bmatrix} 0.299 & 0.587 & 0.114 \\ 0.596 & -0.274 & -0.322 \\ 0.211 & -0.523 & 0.312 \end{bmatrix} \begin{bmatrix} R \\ G \\ B \end{bmatrix}$$

The appropriate MATLAB function to use is: rgb2ntsc (RGB IMAGE NAME).

b) The YCbCr color spacing: In YCbCr (luminance(Y), hue (I), saturation (Q)) color spacing, the luminance information is represented by a single component Y while the color information is stored as two color difference components Cb, Cr. The difference between the blue component and reference value component is calledCb while the difference between the red component and reference value is referredto as component Cr [14]. This color model is widely used in digital video.

Convert from RGB to YCbCr uses the transformation matrix below

$$\begin{bmatrix} Y \\ Cb \\ Cr \end{bmatrix} = \begin{bmatrix} 16 \\ 128 \\ 128 \end{bmatrix} + \begin{bmatrix} 65.481 & 128.553 & 24.966 \\ -37.797 & -74.203 & 112.000 \\ 112.000 & -93.786 & -18.214 \end{bmatrix} \begin{bmatrix} R \\ G \\ B \end{bmatrix}$$

Appropriate MATLAB function for converting from RGB to YCbCr is: rgb2ycbcr (RGB IMAGE NAME)

c) The HSV color space: HSV (hue (H), saturation(S), Value (V)) color space is generated by looking at the RGB color cube along the grey axis (the axis joining the black and white vertices) resulting in a hexagonally shaped color palette. This colorsystem is based on the cylindrical coordinates, thereby making conversion from RGB to HSV similar to a mapping RGB coordinate values to cylindrical coordinates function. Appropriate MATLAB function for converting RGB to HSV is: rgb2hsv(RGB IMAGENAME)

d) The CMY and CMYK color spaces: Secondary colors of light are Cyan,magenta, and yellow. Cyan pigment subtracts the red light from reflected white light, which it self is composed of equal amounts of red, blue and green light. The conversion matrix is as below

$$\begin{bmatrix} C \\ M \\ Y \end{bmatrix} = \begin{bmatrix} 1 \\ 1 \\ 1 \end{bmatrix} - \begin{bmatrix} R \\ G \\ B \end{bmatrix}$$

MATLAB function for conversion is: in complement (RGB IMAGE NAME)

e) HSI color space: HSI means hue saturation and intensity. In this color model space, the intensity component is decoupled from color carrying information (hue and saturation) in color image, hence an ideal tool for the development of image processing algorithms. The HSI space consists of a vertical intensity axis and the locus of color points that lie on a plane perpendicular to this axis, as the plan move up and down the intensity axis [14]. The

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important components of HSI color space are the vertical intensity axis and the length of the vector to the color point and the angle this vector makes to the red axis.

$$H = \begin{cases} \theta & if\ K\ B \le G \\ 360 - \theta & if\ K\ B \ge G \end{cases}$$

Where

$$\theta = \cos^{-1}\{\tfrac{1}{2}[(R-G)+(R+B)]/[(R-G)^2 + (R-B)(G-B)]^{1/2}\}$$

The transformation equations used in the conversion of RGB to HSI are

$$S = 1 - [3/(R+G+B)][\min(R, G, B)].$$

Finally, the intensity component is given by

$$I = 1/3\ (R+ G+ B).$$

Histogram Equalization

Histogram equalization is nothing but a finding of cumulative distribution function for agiven probability density function. Modeling of the histogram is usually done by the use of continuous process functions rather than discrete process functions.

Suppose for a given image the intensity levels are continuous quantities and is normalized to the range **[0 1]**. According to Gonzalez and Woods [2002], transformation can be performed on the probability density function of the intensity levels input image $P_r(r)$ is to obtain S as shown below

$$S = T(r) = \int_0^r P_r(\omega) d\omega$$

where ω is the dummy variable of integration.

After the transformation, the image will have an increased dynamic range, high contrast and the probability density function of the output will be uniform, which can be regarded as a Cumulative Distribution Function (CDF).

$$Ps\ (s) = 1 \text{ for } \quad 0 \le s \le 1, \text{ else zero}$$

n digital images, the intensity levels are discrete in nature, so the method above is often referred to as histogram equalization method, though the output image histogram is not uniform due to the discrete nature of the variables. For discrete value data, the summations and equalization methods above become

$$S_k = T(r_k) = \sum_{j=1}^{k} P_r(r_j) = \sum_{j=1}^{k} \frac{n_j}{n}$$

for **j = 1,2,……..L**, where $\mathbf{s}_k$ is the intensity value in the out put (processed) image corresponding to the value $\mathbf{r}_k$ in the input image. Example of this is as shown below

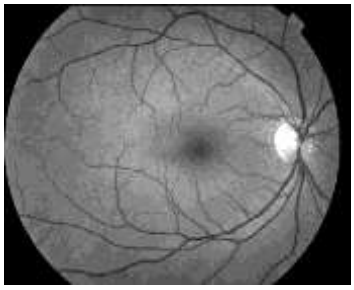
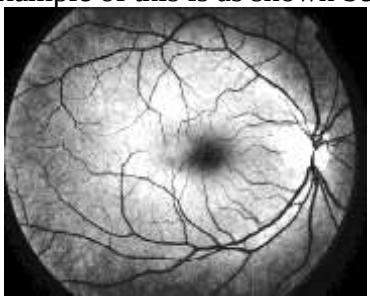


Figure 3-1, Original Image Figure



3-2, Image after Histogram Equalisation

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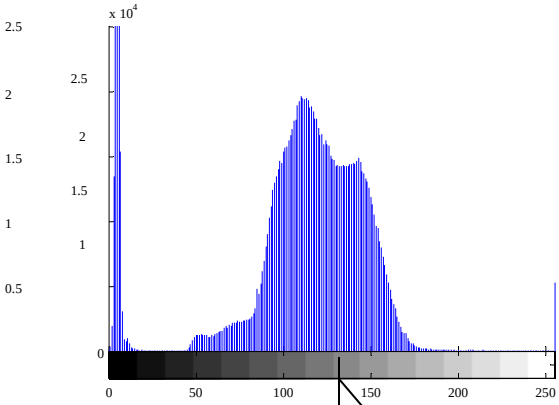


Figure 3-3, Histogram of Original Image

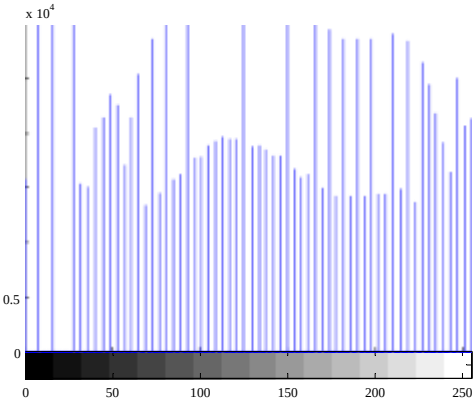


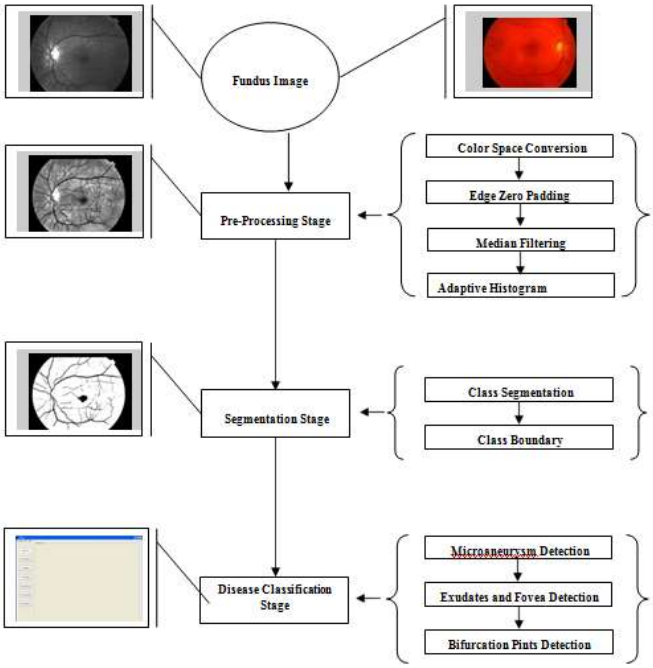
Figure 3-4, histogram of Image after Histogram Equalization

Cleary Figure 3-1, shows an image with low dynamic range which can be seen in histogram Figure 3-3 the most important features like veins intersections and nodes can hardly be seen, most of the image intensity is concentrated in the range around 100 to 150 so it needs an enhancement. Figure 0-2 shows an enhanced image while Figure 0.4, shows the same image with considerable spread of the histogram over theentire intensity scale.

IMPLEMENTATION

In this chapter, the stages involved in the automatic diagnosis of fundus image are discussed. It starts with a brief review of the block diagram of the processes involved in diagnosis of DR and is similar to that contained in Figure 1-1 (Figure 1 is containedin Chapter 1 of this report). This is followed by comprehensive discussion of each of the stages involve with this research work.

Figure 4-1, Block Diagram of Automatic Diagnosis of Diabetic Retinopathy using Fundus Images



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Histogram Equalization

One of the problems associated with fundus images is uneven Illumination. Some areas of the fundus images appear to be brighter than the other. Areas at the centre of the image are always well illuminated, hence appears very bright while the sides atthe edges or far away are poorly illuminated and appears to be very dark. In fact the illumination decreases as distance form the centre of the image increase. Many methods were tried in resolving this problem of un-even illumination, among which are the use of Naka Rushton method and Adaptive Histogram Equalisation Method (AHEM). AHEM gives better performance, higher processing speed and work well for all images of different sizes, hence the reason for it being used as method of correcting un-even illumination. Nevertheless the two methods will be discussed in this sub section.

a) Naka Rushton Method

Bevilacqua [1] in their work titled 'A combined method to detect retinal fundusfeatures' take advantage of the non-Linear filtering effect of the eye in order to correct the impulsive noise created during the acquisition of fundus images and produced an image with uniform intensity. The filtering effect is based on the method called Naka Rushton method and the equation is as given below

$$O(i,j) = \frac{I(i,j)}{I(i,j) + \mu_{window}}$$

where

$O(i,j)$ is the transformation result, $I(i,j)$ is the original image and μ_{window} is the average of the chosen exploration window.

Using this method, a grey level compression of the image was produced with high contrast between the background and the objects information contained there in. Thegrey level represented in the original image was compressed, though it works well forsmall parts of image but doesn't perform well for images with complete size. Aside this, a lot of noise was added to the image using this method and this leads to false and poor segmentation stage. Also in the work done by Bevilacqua et all, it was only of interest to find vascular features and not all the features associated with fundus images so a more robust method, with less noisy output and fast processing speed isneeded for the large images used for this work hence the need for Adaptive Histogram Equalization Method (AHEM).

b) Adaptive Histogram Equalization

The main objective of this method is to define a point transformation within a local fairly large window with the assumption that the intensity value within it is a stoical representation of local distribution of intensity value of the whole image. The local window is assumed to be unaffected by the gradual variation of intensity between the image centers and edges. The point transformation distribution is localized aroundthe mean intensity of the window and it covers the entire intensity range of the image. Consider a running sub image W of N X N pixels centered on a pixel P (i,j) , the image is filtered to produced another sub image P of (N X N) pixels according to the equation below

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$$p_n = 255\left(\frac{[\phi_w(p) - \phi_w(Min)]}{[\phi_w(Max) - \phi_w(Min)]}\right)$$

WHERE

$$\phi_w(p) = \left[1 + \exp\left(\frac{\mu_w - p}{\sigma_w}\right)\right]^{-1}$$

The size of the window chosen for this work is as given in the appendix.
As a result of this adaptive histogram equalization, the dark area in the input image that was badly illuminated has become brighter in the output image while the side that was highly illuminated remain or reduces so that the whole illumination of the image is same. It is worthy of mentioning that this method also used overlap mean in the final build up of the image. The input and output images are shown in Figure 4-7 and Figure 4-8 respectively.

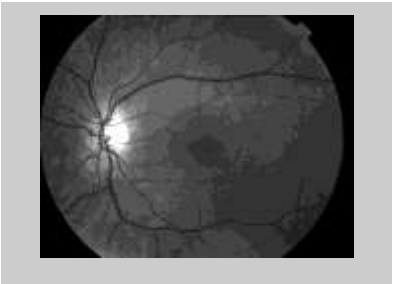

Figure 4-7, Original Grey Image

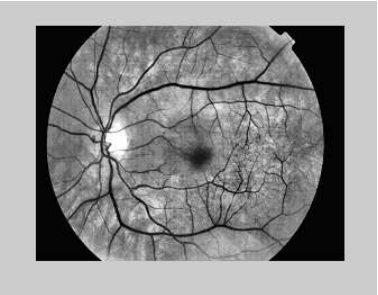

Figure 4-8, Pre-Processed Image

All the aforementioned processes constitute the Pre-Processing sections and the output image of this PPS is as shown in Figure 4-8 above.

Segmentation

The main objective of segmentation is to group the image into regions [14] with same property or characteristics. It plays a major role in image analysis system by facilitating the description of anatomical structures and other regions of interest. Method of image segmentation include: simple thresholding, K-means Algorithm and Fuzzy C-means. Some of these methods were as discussed.In this research, segmentation by K-means with two non-overlapping classes are found to be better than segmentation by simple thresholding. Background and noisy pixels were segmented into one class and the fundus image features which consist of the spots, exudates veins and features of the fundus images were segmented into another class without any pixel belonging into two classes. The non-overlapping of this method made it suitable for this particular research work where it is only of interest to distinguish between the background and the main fundus image features. The algorithm for the segmentation is as shown in table 3.3 *Figure 4-9, Segmented Image*

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The output of the Segmentation stage is as shown in Figure 4-9 above

RESULTS

This chapter starts with presentation of result obtained from diagnosis of twenty five (25) fundus images which were used for detection and diagnosis. For each set of data, the Receiver Operator Characteristics (ROC) curve is also presented and this is shortly followed by the analysis of the result and some of the thresholds used in obtaining the ROC.

Result Obtained

The result obtained from the diagnosis of DR by this research work is as shown in the different ROC. Twenty-five images (10 normal images and 15 abnormal images). Detection for abnormalities is centered on detecting red spot disease and bleeding.

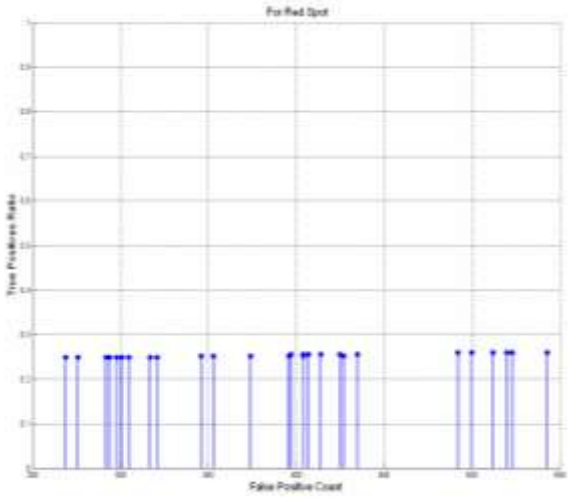

Figure 5-1, Red Spot ROC

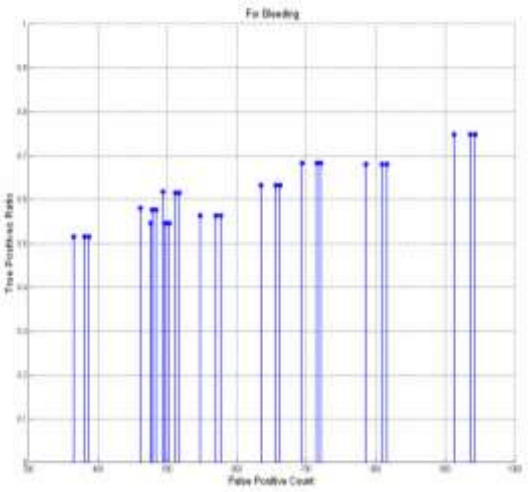

Figure 5-2, Bleeding ROC

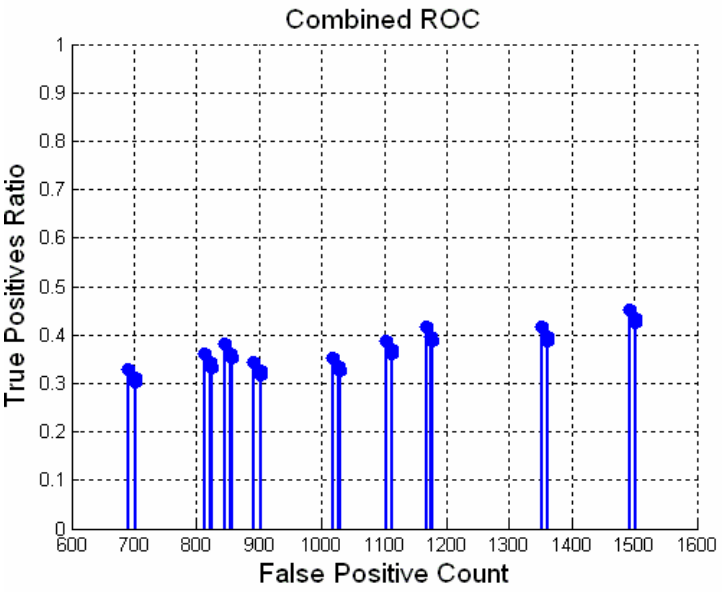

Figure 5-3, Combined ROC

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Analysis

Classifier Performance for Red Spots Detection and Classification.

In this section, red spot detection will be analyzed, the set and values of classifiersused are:

a) Object Ratio
b) Red Spot Compact Ratio
c) Bleeding Compact Ratio

Discussion:

Each of the points in the ROC Figure 5.1 represent a set of classifier values used inthe determining the best threshold value to be used for our algorithm.

Classifier Performance for Bleeding Detection and Classification

In the detection of bleeding from fundus image as carried out during this researchwork, the following are the set of thresholds used for the classifier:

d) Object Ratio
e) Red Spot Compact Ratio
f) Bleeding Compact Ratio

Discussion:

Each of the points in the ROC in Figure 5.2 represent a set of classifier values usedin the determining the best threshold value to be used for our algorithm.

Combined Classifier Performance

In the detection of both red spots and bleeding from fundus image as carried out during this research work, the following are the set of thresholds used for the classifier:

g) Object Ratio
h) Red Spot Compact Ratio
i) Bleeding Compact Ratio

Discussion:

Each of the points in the ROC in Figure 5.3 represent a set of classifier values usedin the determining the best threshold value to be used for our algorithm.

General Classifier Performance:

General classification involves classifying an image as normal or abnormal. This involves the presence or otherwise of any of the disease mentioned in the previous sections above. From this the specificity and sensitivity of the system is determined. Sensitivity refers to the percentage of abnormal fundus image classified as abnormalby the method while specificity can be defined as percentage of normal fundus imageclassify as normal.

Sensitivity for this algorithm is calculated to be 98% while specificity value is 61%

Discussion: In detecting abnormalities or otherwise, the presence of at least, quantity five of the sum of the disease analyzed above, i.e. red spot or/and bleeding points in an image leads to the image being classified as abnormal image. The only exception to this is the crossover points, there are two types of vein artery crossover in fundus images, one is regarded as normal crossover point while the other is regarded as abnormal crossover. The abnormal crossing occurs when and artery crosses a vein and during the high blood pressure it presses the vein and causes a stop of the blood flow in vein. Because of this type of abnormal crossing of vein and artery bleeding can occur from vein at that point. All

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other types of vein-artery crossings are normal. In thiswork, vein artery crossings were detected only but further probing need to be donefor classification.

CONCLUSION

a) Development of a system that will be able to identify patients with BDR and PDR from either color image or grey level fundus image
b) The different diabetic retinopathy diseases that are of interest include red spots and bleeding both falls between BDR and PDR stages of the disease. While SDR types are expected to be referred to the ophthalmologist.
c) Development of a MATLAB based Graphic User Interface (GUI) tool to be used by the ophthalmologist in marking fundus images. The marked images are to be used for the development of DR grading and database system for this present and future work.

In line with the aims and objectives of this research work, this research group is able to develop a MATLAB GUI based system called CVision which is able to detect DR with a specificity of 61% and sensitivity of 98%.Furthermore, two MATLAB based GUI's were developed for this work, the first one was used my ophthalmologist in marking images for database while the second one was used for the DR diagnosis.

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