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Detection and Classification of Exudates using K-Means Clusters in Color Retinal Images

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Abstract:
Diabetes mellitus is a major cause of visual impairment and blindness. Twenty years after the onset of diabetes, almost all patients with type 1 diabetes and over 60% of patients with type 2 diabetes will have some degree of retinopathy. Prolonged diabetes retinopathy leads to maculopathy, which impairs the normal vision depending on the severity of damage of the macula. This paper presents a computer-based intelligent system for the identification of clinically significant maculopathy, non-clinically significant maculopathy and normal fundus eye images. Features are extracted from these raw fundus images which are then fed to the classifier. Our protocol uses feed-forward architecture in an artificial neural network classifier for classification of different stages. Three different kinds of eye disease conditions were tested in 350 subjects. We demonstrated a sensitivityof more than 95% for these classifiers with a specificity of 100%, and results are verypromising. Our systems are ready to run clinically on large amounts of datasets.

I. Introduction:

Medical image analysis is a research area that has recently attracted intense interest among scientists and physicians. It consists of the study of digital images with the objective of providing computational tools that help quantify and visualize interesting pathologies and anatomical structures. The progress achieved in this area over recent years has significantly improved the type of medical care that is available to patients. Physicians can now examine inside the human body to diagnose, treat, monitor changes and plan different treatments more successfully than previously. The physician can thus obtain decision support, be reassured of repetitive tasks, and consistently receive valuable measurements. However, this is a multidisciplinary task and requires comprehensive knowledge in many disciplines, such as image processing and computer vision, machine learning, pattern recognition and expert systems. The severe progression of diabetes is one of the greatest immediate challenges to the current health care. The number of people afflicted continues to grow at an alarming rate. The World Health Organization expects the number of diabetics to increase from 130 million to 350 million over the next 25 years [1]. However, only half of the patients are aware of the disease. Diabetes leads to severe late complications including macro and micro vascular changes resulting in heart disease and retinopathy. Diabetic retinopathy (DR) is a common complication of diabetes and the leading cause of blindness in the working population of western countries. It is a silent disease and may only be recognized by the patient when the changes in the retina have progressed to a level where treatment is complicated and nearly impossible. The prevalence of retinopathy varies with the age of onset of diabetes and the duration of the disease in younger patients (below 30 years of age) is minimal during the first 5 years but increases to greater than 95% after 15 years of diabetes [2]. In contrast, in patients whose onset of diabetes occur after the age of30, up to 20% may have signs of retinopathy on presentation with the prevalence in this group rising more slowly to approach 60% after 15 years of diabetes [2].

1.1. Structure of the normal human eye:

The eye works like a camera. Light rays reflected by objectsenter the eye through the cornea, which acts

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like a window in the white of the eye and provides the focusing power[3,4]. The cornea is the principal lens of the eye and is thesite where refractive surgery is conducted.Light travels through the pupil or black circle of the iris(the coloured part of the eye). The main function of the irisis to control the quantity of light entering the eye by eitherbecoming smaller in size in bright light or larger in dimlight. Light then travels through the lens. The function ofthe lens is to adjust the focus for near vision. The retina actsas the film in the camera; it is a membrane that covers theback of the eye. The images that we see are focused andthen the information is carried by the optic nerve to thebrain. The brain, upon reception of these signals interpretsthe images and objects seen by the eye. Figure 1(a) shows across section of the human eye.

The macula is the most sensitive part of the retina and isresponsible for vision. It is located near the optic nervedirectly at the back of the eye (on the inside). This area isalso responsible for colour vision. The optic disc (or opticnerve head) is the entry and exit site of blood vessels andoptic nerve fibres from the retina to the optic nerve. Theoptic nerve transmits electrical impulses from the retina tothe brain. It is a brighter region than the rest of the ocularfundus and its shape is usually round. The optic disc is approximately 3 mm nasal to the fovea, and measuresabout 1.5 – 2 mm in diameter. The optic disc contains acentral depression called the optic cup and its depth varies from individual to individual. Figure 1(b) illustrates atypical normal fundus image with highlighted regions ofmacula, fovea and optic disc components. The macula orcentral area has the following components from the centreto the periphery: foveola, fovea, parafovea and perifovea,as shown in figure 2. Figure 3(a) shows a fundus image ofthe normal eye.

Diabetes can affect the eye in a number of ways. Themost serious eye condition associated with diabetes,diabetic retinopathy, involves the retina, and, morespecifically, the network of blood vessels lying within it. Diabetic retinopathy is usually graded according to itsseverity. This condition is very common in people who havehad diabetes for a long time. The vision may be normalwith no threat to the sight.At this stage the blood vessels in the retina are only verymildly affected and they may bulge slightly (microaneurysm)and may leak blood (haemorrhages) or fluid(exudates). The macula area of the retina mentioned earlierremains unaffected.With time, if the background diabetic retinopathybecomes more severe, the macula area may becomeinvolved. This is called maculopathy. In diabetic maculopathy,fluid rich in fat and cholesterol leaks out of damagedvessels. If the fluid accumulates near the centre of the retina(the macula), there will be distortion of central vision. Iftoo much fluid and cholesterol accumulates in the macula,it can cause permanent loss of central vision. Non-clinicallsignificant maculopathy and clinically significant maculopathyare the two types of the maculopathy eye disease.

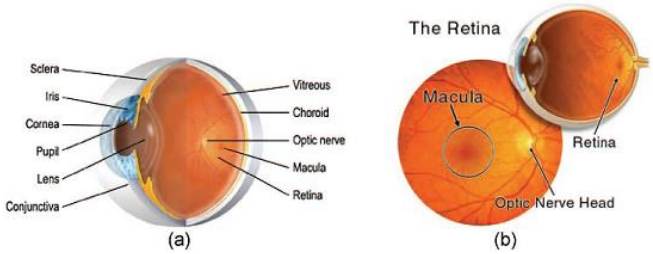

Figure 1.Structure of (a) the human eye and (b) the human retina.

1.2. Non-clinically significant maculopathy (non-CSME):

Figure 3(b) shows a non-CSME fundus image, where thereare no visible symptoms, so patients may not realize they areaffected. Exudates start to leak out from the damaged vesselswhich result from diabetes and areas of leakage develop inthe retina. This results in the retina becoming spongy, but thepatient's vision is not seriously affected because the locationsof the exudates are far away from the fovea.

1.3. Clinically significant maculopathy (CSME):

In this stage, most of the retinal blood vessels are damagedand the leakage area becomes bigger. The exudates leak outand deposit very close to the fovea.

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Hence, the visibility isgreatly affected since images cannot properly be focused onthe macula.

Figure 3(c) shows the CSME fundus image.Most studies about diabetic maculopathy and associatedrisk factors are hospital-based cohort studies [5 – 8]. Thereis only one population-based [9] cohort study which wasextended to a longitudinal study [10]. Recent data haveshown that better glycaemic and blood pressure control arebeneficial in reducing the incidence of macular edema [8].The quantification of diabetic maculopathy and detectionof exudates on fundus images were studied [11 – 14]. Globaland local thresholding values were used to segment exudatelesions from the red-free images. Before thresholding can bedone, the digitized colour photographs were pre-processedto eliminate photographic non-uniformities (shade correction),and the contrast of the exudates was then enhanced.The lesion-based sensitivity of exudates identificationtechnique was reported to be between 61% and 100%(mean 87%) [12,14,15].

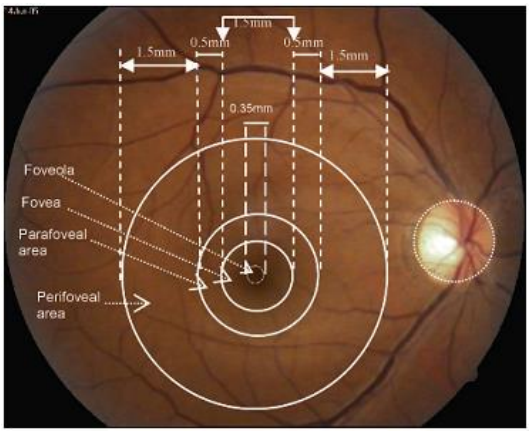

Figure 2.Normal fundus image showing the major vascular arcade.

The various levels or stages of diabetic eye diseases arereflected in the fundus images. Verification of this requires askilled ophthalmologist, who can detect various features bylooking at the fundus image. Fully automated methods todetect the severity of maculopathy can greatly help doctorsin diagnosing diabetic eye diseases. Computerized detectionis highly useful in areas where experienced ophthalmologistsare rarely available.

Many investigations have been carriedout on computer assisted analysis [11,16 – 18] Automaticdetection of microaneurysms, hard exudates, cotton woolspots and haemorrhages for pathology detection wasstudied [18 – 23]. Feature detection is necessary for identificationand classification of the pathologies. There aremany algorithms and techniques proposed to extract thefeatures from fundus images [24 – 26].

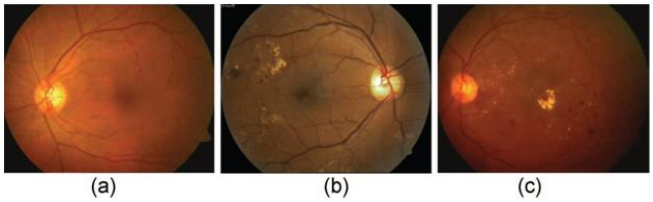

Figure 3. Fundus images: (a) normal, (b) non-clinically significant maculopathy and (c) clinically significant maculopathy

II. Data acquisition and processing:

In this work, about 124 retinal photographs of normal, clinically non-significant and clinically significant diabetic maculopathy were studied. These patient data wereprovided by the Kasturba Medical Hospital, Manipal, India. The number and details of photographs in eachgroup is shown in table 1. Images were stored in 24-bitJPEG format with an image size of 5766720 pixels. Duringthe image acquisition process, a patient's chin is positionedon the chin rest and the patient is asked to look into thecamera. The photographer aligns the digital system withthe centre of the patient's papillary axis. Figure 3 shows the fundus images of normal, non-clinically significant and clinically significant diabetic maculopathy.

2.2. Local contrast enhancement:

The contrast of the fundus images tends to diminish as thedistance of a pixel from the centre of the image increased.The objective of preprocessing was to reduce this effect andto normalize the mean intensity. The intensities of thethree colour bands were transformed to an intensity-huesaturationrepresentation [32]. This

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allowed the intensity tobe processed without affecting the perceived relative colourvalues of the pixels.
The contrast of the intensity was enhanced by a locally adaptive transformation. Consider sub-image, W(i, j), of size M6M pixels, centred on a pixellocated at (i, j). Denote the mean and standard deviation ofthe intensity within W(i, j) by hfiW and sW respectively.Suppose that fmax and fmin are the maximum and minimumintensities of the whole image. The adaptive local contrastenhancement transformation is defined by equations (1)and (2). Let the intensity, f, of the picture elements(pixels) of an N6N digital image be indexed by (i, j) 15 i,j5N. A sub-image of size M6M centred on (i, j) withM¼49 is taken in this work. Denote the mean and standarddeviation of the intensity within W by hfiw and sw(f)respectively. The objective is to define a point transformationdependent on W such that the distribution is localizedaround the mean of the intensity and covers the entireintensity range. The implicit assumption is that W is largeenough to contain a statistically representative distributionof the local variation of grey levels, yet small enough to beunaffected by the gradual change of contrast between thecentre and the periphery of the fundus image. The adaptivecontrast enhancement transformation is defined by:

$$g(i,j) = 255\frac{[\Psi_w(f) - \Psi_w(f_{\min})]}{[\Psi_w(f_{\max}) - \Psi_w(f_{\min})]} \quad (1)$$

where the sigmoid function is given by:

$$\psi_w(f) = \left[1 + \exp\left(\frac{\langle f\rangle_w - f}{\sigma_w}\right)\right]^{-1} \quad (2)$$

Where fmax and fmin are the maximum and minimum valuesof intensity within the whole image

$$\langle f\rangle_w = \frac{1}{M^2}\sum_{k,l\in W(i,j)} f(k,l) \text{ and}$$

$$\sigma_W^2(f) = \frac{1}{M^2}\sum_{k,l\in W(i,j)}[f(k,l) - \langle f\rangle_W]^2 \quad (3)$$

The local contrast enhancement function provides largecontrast enhancement for an initially small s (poor contrast)and little contrast enhancement for an initially large s (highcontrast). As a result of local contrast enhancement, thedark area is brighter and clearer showing more detail.However, the technique of local contrast enhancement notonly adjusts the contrast of the image but also increases thenoise. Hence, a 2D Gaussian smoothing filter or medianfilter has been applied in order to reduce the noise before thelocal contrast enhancement process.

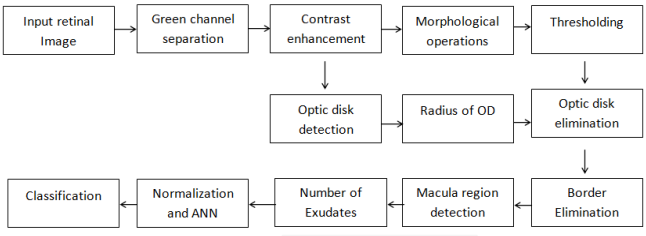

Figure 4. Proposed system for the identification of diabetic maculopathy stages

III. Detection of optic disc:

The optic disc appears in the fundus image as a yellowishregion. It usually occupies approximately one seventh ofthe entire image, 80680 pixels. The appearance was characterizedby a relatively rapid variation in intensity becausethe 'dark' blood vessels are beside the 'bright' nerve fibres.The variance of intensity of adjacent pixels was used forrecognition of the optic disc. Consider a sub-image W(i, j)of dimensions M6Mcentred on pixel (i, j). Let h f iw(i, j) asdefined by equation (A3)

$$\langle f\rangle_{w(i,j)} = \frac{1}{M^2}\sum_{k,I\in w(i,j)} f(k,l)$$

be the mean intensity within W(i, j). (If W(i, j) extends beyond the image, then undefined intensities are set to zero and the normalization factor is correspondingly reduced.) A variance image was formed by the transformation $g(i,j) \to p(i,j) = \langle f^2\rangle_w - (\langle f\rangle_w)^2$, where the sub-image was 80X80 pixels. An image of the average variance within sub images was then obtained as $p(i,j) \to q(i,j) = \langle p\rangle W(i,j)$.The

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location of the maximum of this image was taken a thecentre of the optic disc, (id, jd).

IV. Detection of fovea:

The centre of the fovea was usually located at a distance of approximately 2.5 times the diameter of the optic disc, from the centre of the optic disc. It was the darkest area of the fundus image, with approximately the same intensity as the blood vessels. The fovea was first correlated to a template of intensities.

2.5. Detection of exudates:

The exudates are well contrasted compared to the background surrounding them and appear to be a bright pattern. They have irregular shapes and borders [33,34]. Detection of exudates is a challenging job as other features in the image such as optic disc and blood vessels have higher grey level variation and brightness patterns than the exudates. The exudates appear with more contrast in the green channel [33]. Morphological image processing techniques are used for the detection of exudates. Dilation and erosion are two basic operations in morphological image processing [32]. Closing and opening operations are applied extensively for detecting the exudates. Exudates contribute to the defects in a diabetic maculopathy retina, and all stages of diabetic maculopathy have them. Therefore it is important to distinguish them from the noisy background of the retina image for visual diabetic retinopathy classification purposes. The algorithm developed uses a morphological operation to smooth the background, allowing exudates to be seen clearly. Two structuring elements (SE) are used:

(i) octagon SE to remove the vessels from the image; and
(ii) disc-shaped SE to identify the exudates.

V. Artificial neural network classification

An artificial neural network (ANN) is an information processing paradigm that is inspired by the way biological nervous systems, such as the brain, process information. The key element of this paradigm is the novel structure of the information processing system. It is composed of a large number of highly interconnected processing elements (neurons) working in unison to solve specific problems. Data enters at the inputs and passes through the network, layer by layer, until it arrives at the outputs. During normal operation, i.e. when it acts as a classifier, there is no feedback between layers. Hence, it is termed a feed-forward neural network. If the nature of the classification is more complex, a three-layer feed-forward neural network with sigmoid activation function is more suitable [35]. This sigmoid transfer function is a prerequisite for the use of the powerful backpropogation learning algorithm. In the present case, the nature of boundary between different classes is not clearly known, and therefore the three-layer network with sigmoid activation function is chosen as the classifier. Figure 11 shows the three-layer feed-forward neural network used for the classification. During the training phase, the connection weights of the last two layers are modified according to the 'delta rule' of the backpropagation algorithm [36]. There are four input neurons, one hidden layer with five neurons and three output neurons. The output neuron will classify three classes as '100' for normal, '010' for CSME and '001' for non-CSME. The network is trained with given set of training data and later tested with remaining testing samples.

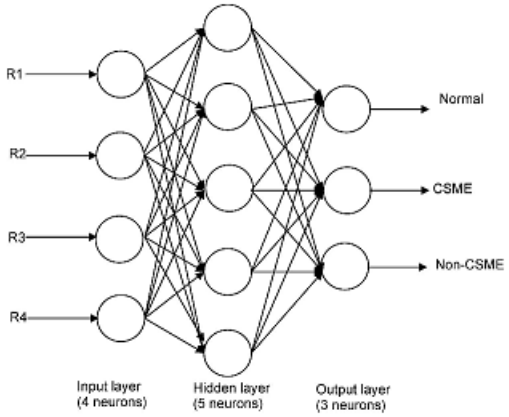

Figure 11. ANN structure for the classification

VI. Edge Detection Techniques:

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Edges are local changes in the image intensity. Edges typically occur on the boundary between two regions. The main features can be extracted from the edges of an image. Edge detection has major feature for image analysis. These features are used by advanced computer vision algorithms. Edge detection is used for object detection which serves various applications like medical image processing, biometrics etc. Edge detection is an active area of research as it facilitates higher level image analysis. There are three different types of discontinuities in the grey level like point, line and edges. Spatial masks can be used to detect all the three types of discontinuities in an image. There are many edge detection techniques in the literature for image segmentation. The most commonly used discontinuity based edge detection techniques are reviewed in this section. Those techniques are Roberts edge detection, Sobel Edge Detection, Kirsh edge detection, LoG edge detection and Canny Edge Detection.

Roberts Edge Detection:

The Roberts edge detection is introduced by Lawrence Roberts (1965). It performs a simple, quick to compute, 2-D spatial gradient measurement on an image. This method emphasizes regions of high spatial frequency which often correspond to edges. The input to the operator is a grayscale image the same as to the output is the most common usage for this technique. Pixel values in every point in the output represent the estimated complete magnitude of the spatial gradient of the input image at that point.

Sobel Edge Detection:

The Sobel edge detection method is introduced by Sobel in 1970 (Rafael C.Gonzalez (2004)). The Sobel method of edge detection for image segmentation finds edges using the Sobel approximation to the derivative. It precedes the edges at those points where the gradient is highest. The Sobel technique performs a 2-D spatial gradient quantity on an image and so highlights regions of high spatial frequency that correspond to edges. In general it is used to find the estimated absolute gradient magnitude at each point in n input grayscale image. In conjecture at least the operator consists of a pair of 3x3 complication kernels as given away in under table. One kernel is simply the other rotated by 90^0 . This is very alike to the Roberts Cross operator.

Kirsch Edge detection:

Kirsch edge detection is introduced by Kirsch (1971). The masks of this Kirsch technique are defined by considering a single mask and rotating it to eight main compass directions: North, Northwest, West, Southwest, South, Southeast, East and Northeast. The masks are distinct as follows:

$$E = \overset{k_0}{\begin{bmatrix} -3 & -3 & 5 \\ -3 & 0 & 5 \\ -3 & -3 & 5 \end{bmatrix}} \quad NE = \overset{k_1}{\begin{bmatrix} -3 & 5 & 5 \\ -3 & 0 & 5 \\ -3 & -3 & -3 \end{bmatrix}} \quad N = \overset{k_2}{\begin{bmatrix} 5 & 5 & 5 \\ -3 & 0 & -3 \\ -3 & -3 & -3 \end{bmatrix}} \quad NW = \overset{k_3}{\begin{bmatrix} 5 & 5 & -3 \\ 5 & 0 & -3 \\ -3 & -3 & -3 \end{bmatrix}}$$

$$W = \overset{k_4}{\begin{bmatrix} 5 & -3 & -3 \\ 5 & 0 & -3 \\ 5 & -3 & -3 \end{bmatrix}} \quad SW = \overset{k_5}{\begin{bmatrix} -3 & -3 & -3 \\ 5 & 0 & -3 \\ 5 & 5 & -3 \end{bmatrix}} \quad S = \overset{k_6}{\begin{bmatrix} -3 & -3 & -3 \\ -3 & 0 & -3 \\ 5 & 5 & 5 \end{bmatrix}} \quad SE = \overset{k_7}{\begin{bmatrix} -3 & -3 & 5 \\ -3 & 0 & 5 \\ -3 & 5 & 5 \end{bmatrix}}$$

The edge magnitude is defined as the maximum value found by convolution of each mask with the image. The direction is defined by mask that produces the maximum magnitude. Example, mask k_0 corresponds to a vertical edge, while mask k_5 corresponds to a diagonal edge. Notice that the last four masks are actually the same as the first four, but flipped about a central axis.

LoG edge detection:

The Laplacian of Gaussian (LoG) was proposed by Marr(1982). The LoG of an image f(x,y) is a second order derivative defined as

$$\nabla^2 f = \frac{d^2 f}{dx^2} + \frac{d^2 f}{dy^2}$$

It has two effects, it smoothes the image and it computes the Laplacian, whch yields a doubleedge image. Locating edges then consists of finding the zero crossings between the double edges. The Laplacian is generally used to found whether a pixel is on the dark or light side of an edge.

Canny Edge Detection:

In industry, the Canny edge detection technique is one of the standard edge detection techniques. It was first created by John Canny for his Master's thesis at MIT

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in 1983, and still outperforms many of the newer algorithms that have been developed.

To find edges by separating noise from the image before find edges of image the Canny is a very important method. Canny method is a better method without disturbing the features of the edges in the image afterwards it applying the tendency to find the edges and the serious value for threshold. The algorithmic steps are as follows:

- Convolve image f(r, c) with a Gaussian function to get smooth image f^(r, c).
  f^(r, c)=f(r,c)*G(r,c,6)
- Apply first difference gradient operator to compute edge strength then edge magnitude and direction are obtain as before.
- Apply non-maximal or critical suppression to the gradient magnitude.
- Apply threshold to the non-maximal suppression image.

Unlike Roberts and Sobel, the Canny operation is not very susceptible to noise. If the Canny detector worked well it would be superior.

VII. Results and discussion:

The area covered by the exudates in the four regions (R1, R2, R3 and R4, as discussed in section 2.5) are considered as parameters for identifying the severity in the maculopathyimages. The output of the feature detection is shown in figures 8 and 10. The total number of white pixels, which indicate the exudates in each region, is the input data for the artificial neural network. Table 2 shows the ranges of thethree parameters used to feed as input to the ANN. Thesefeatures are subjected to the ANOVA (analysis of variance between groups) test to obtain the p-value. ANOVA uses variances to decide whether the means are different. This test uses the variation (variance) within the groups and translates into variation (i.e. differences) between the groups, taking into account how many subjects there are in the groups. If the observed differences are high then it is considered to be statistical significant. In our work, we have obtained p-values of less than 0.005, indicating that it is clinically significant.

For the purpose of training and testing the classifier, a database of 350 patient samples is divided into two sets—a training set of 205 arbitrarily chosen samples and a test set of 145 samples (table 3). The training consisted of 5000 iterations.

VIII.Conclusion:

Diabetic maculopathy is a complication of diabetes and a leading cause of blindness. It occurs when diabetes damages the tiny blood vessels inside the retina, the light-sensitive tissue at the back of the eye. An automatic system for identification of normal, non-CSME, and CSME retinal fundus image is proposed. The features are extracted from the raw images using image processing techniques and fed to a feed-forward neural network classifier for classification. We demonstrated an accuracy of more than 95% of correct classification, sensitivity of more than 95% and specificity of 100% for the classifier.

The accuracy of the system can further be improved using proper input features (number of microaneurysms and haemorrhaged areas), by using diverse quality of images for training and by increasing the size of the training dataset.classification. We demonstrated an accuracy of more than 95% of correct classification, sensitivity of more than 95% and specificity of 100% for the classifier. The accuracy of the system can further be improved using proper input features (number of microaneurysms and haemorrhaged areas), by using diverse quality of images for training and by increasing the size of the training dataset.

To review the edge detection techniques which are based on discontinuity intensity levels. The relative performance of various edge detection techniques is carried out with an image by using MATLAB software. It is observed from the results LoG and Canny edge detectors produce almost same edge map. Canny result is superior one when compared to all for

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a selected image since different edge detections work better under different conditions.

Even though, so many edge detection techniques are available in the literature, since it is a challenging task to the research communities to detect the exact image without noise from the original image.Further scope can be done by using Support Vector as Classifier for detecting and classify the Exudates.

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