CHAPTER 3
AN ECONOMIC SYSTEM FOR SCREENING OF DIABETIC RETINOPATHY USING FUNDUS IMAGES

3.1 BACKGROUND

The digital image processing methods can be used in numerous situations to identify/track the changes in the retinal region. The classification of abnormalities within the human eye using these techniques has increased progressively in the recent past [10, 11]. Diabetic retinopathy is notably the major cause of vision loss due to diabetics. This occurs mainly due to the vascular changes in the retinal region, causing swelling of blood capillaries. When it progresses, these can be ruptured and, in due course, which becomes the major cause for extravasations of plasma and constructing regions of fat deposits within the retinal region and known as exudates. In the initial level diagnosis, the ophthalmologists look for microaneurysms which are very small and difficult to detect visually, when it is at an early and premature stage of diabetic retinopathy. Hence, radiological expects search for exudates that generally form clusters which can be distributed across the retinal region and are certainly visible at its mature stage. Conditions where more exudates present within the macula region can lead to vision loss. The early diagnosis and treatment may prevent or decrease the vision loss of the patient.

Hence, the aim of this study is to develop a computer aided diagnostic system (CAD) capable of supporting medical decision, improving diagnosis quality and decreasing the workload of medical professionals within the background of diagnose diabetic retinopathy. The novel framework consists of the following stages: (1) Extract blood vessels, (2) Extract optic disk,(3) Detection of exudates from retinal digital fundus images and (4) Classification.
3.2 STEPS INVOLVED TO DETECT DIABETIC RETINOPATHY

The proposed system is a hybrid technique where exudate was extracted from the image by removing vessel, optic disc and border. The detailed modus operandi involved of the proposed study is outlined in the Figure 3.1. This provides information on about the study design, data collection and description of the steps involved in image processing implementation such as preprocessing, segmentation and novel morphological feature extraction.

3.2.1 Data Description

A free eye screening camp was conducted in a leading eye care hospital, Chennai, India, at the end of the year 2012. This study was performed on 60 Indian subjects whose age ranged from 50-85 years. Prior to the study, a detailed questionnaire was provided to the patients. Answers were provided signed and informed consent obtained forms to the investigation protocol. For all the subjects, digital images of size 640 x 480 were taken with a CARL-ZEISS-FF-450-plus Visupac fundus camera with the illumination, resolution, field of view, magnification and dilation procedures kept constant.

3.2.2 Fundus Image Analysis

The retina is a layered structure with numerous layers of neurons interconnected by synapses and is a light-sensitive tissue lining the internal surface of the eye. The central retinal artery and vein seems available to one another at the nasal side of the middle of the optic disk [61]. Information regarding the structure of blood vessels can help in categorizing the severity of the diseases and together assist as a landmark throughout the segmentation process. Distinct features of the fundus image are displayed in Figure 3.2.

Accumulations of protein and lipid in the retina are called exudates. By Nature, they are white or cream colored, reflective and bright lesions witnessed on the retina. They indicate high permeability in vessels and the related risk of retinal edema or swelling. A vital step within the extraction
framework is removal of distinguished structures of the retina, such as blood vessel tree and optic disc. Detection of exudate candidates and highlighting thereof is done after the removal of these structures.

Figure 3.1 Flow diagram of the proposed diabetic retinopathy detection system
3.2.2.1 Color normalization

The pigmentation in the retinal tissue varies widely among patients. Hence, it is likely that the color of exudates does not appear brighter than the background in some regions of the image. For this reason, normalization of the images was done to a standard reference image chosen from the test data set using a histogram specification technique. As a first step, histogram equalization was done for each sub channel of the RGB image using a global-local adaptive histogram equalization with the help of partially overlapped windows (GLAPOW) method [62]. The next step was intensity normalization. This modified the image values through a histogram transformation operator which maps a given intensity distribution \(L(x, y)\) into a desired distribution \(N(x, y)\) using a histogram equalized image \(M(x, y)\) as an intermediate stage. Independent application of the method was done to each individual sub block of 5 x 5 [63]. Following normalization, a local contrast enhancement method was applied for improvement of both the contrasting attributes of tissue pigments and the overall intensity in the image. The aim was to apply a transformation of the values inside small windows in the image to ensure distribution of all values around the mean exhibiting all possible intensities [63, 64]. Hence, given each pixel in the initial image and a small running window in the image was filtered to produce the new image \((I)\) based on Eq.3.1.

\[
I(x, y) = N \ast \left[ \frac{\Phi_w(p) - \Phi_w(min)}{\Phi_w(max) - \Phi_w(min)} \right]
\]

(3.1)

Where \(N\) is the peak signal, \(p\) is intensity of the pixel, \(\Phi_w\) is sigmoid function and, max, min refers whole image maximum and minimum values respectively. Finally, color normalization was accomplished by merging the normalized R, G, B (Red, Green, and Blue) components and it is shown in the Figure 3.3.
Figure 3.2 A sample fundus image with different features

Figure 3.3 Normalized color image
3.2.2.2 Edge enhancement

In the next phase, Kirsch’s template [61] was adopted for identifying the blood vessels from the normalized color images. For detecting the edges, the operator made use of eight templates, which were successively rotated by 45° as shown in Figure 3.4. The gradient was then computed by convolving the normalized image with eight template impulse response arrays in each and every pixel. Thus, the gradients of different directions were achieved and the final gradient was the summation of the enhanced edges through consideration of all directions for RGB channels than any one specific channel and shown in Figure 3.5.

3.2.2.3 Color space conversion

The next step was conversion of the enhanced RGB color images to HSI (Hue, Saturation, and Intensity) color image using the Eq. (3.2).

\[
H = \begin{cases} 
\theta, \text{if } B \leq G \\
360 - \theta, \text{if } B > G 
\end{cases}
\]

\[
S = 1 - \left( \frac{3}{R+G+B} \right) \min(R, G, B) 
\]

\[
I = \frac{(R+G+B)}{3}
\]

Where

\[
\theta = \cos^{-1} \left( \frac{[(R-G) + (R+B)]}{\left[ (R-G)^2 + (R-B)(G-B) \right]^{1/2}} \right)
\]

Min(R, G, and B) denotes the minimum value among of red, green and blue components of the image [65].
Table 3.4 Templates of Kirsch’s method

<table>
<thead>
<tr>
<th></th>
<th>0°</th>
<th>45°</th>
<th>90°</th>
<th>135°</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>5</td>
<td>-3</td>
<td>-3</td>
<td>-3</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>0</td>
<td>-3</td>
<td>5 0</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>-3</td>
<td>-3</td>
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<td>-3</td>
<td>5</td>
<td>-3</td>
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<tr>
<td>225°</td>
<td>-3</td>
<td>0</td>
<td>5</td>
<td>-3</td>
</tr>
<tr>
<td>270°</td>
<td>-3</td>
<td>-3</td>
<td>5</td>
<td>-3</td>
</tr>
<tr>
<td>315°</td>
<td>-3</td>
<td>-3</td>
<td>5</td>
<td>-3</td>
</tr>
</tbody>
</table>

Figure 3.4 Templates of Kirsch’s method

Figure 3.5 Enhanced image by Kirsch’s method
Extraction of the intensity channel for HSV image alone was then done. This is displayed in Figure 3.6. Here, the intensity level between the blood vessels (foregrounds) shown is seen as comparatively low with other background regions. This indicates selection of an accurate threshold value to segment the objects of interest as a difficult task. This proves the essential nature of the subsequent enhancement of the image for further analysis. Therefore, a spatial averaging filter of size 13 × 13 was applied to the gray scale (i.e. intensity channel) image in the next step. This is shown in Figure 3.7. The obtained image was then equalized by performing histogram equalization for out coming gray levels in the range [0, L−1] and displayed in Figure 3.8.

### 3.2.2.4 Binarisation

In the step that follows, binarisation process was done by setting a heuristic threshold value (T = 0.78). The adopted threshold value was effective and found quite appropriate for the test image data set. This process resulted in two sets of pixels, as exemplified in Eq. (3.4). The resultant image is shown in Figure 3.9.

\[
I_B(x, y) = \begin{cases} 
1(\text{white}), & \text{if } I(x, y) \geq T \\
0(\text{black}), & \text{otherwise}
\end{cases} \quad (3.4)
\]

The morphological closing process is found essential for closing the holes or unfilled area within the blood vessel region [66]. The outcome is shown in Figure 3.10.

### 3.2.2.5 Novel feature extraction

The binary image contains many objects such as blood vessels, optic disc, exudates, etc., in the retinal region. The following steps were carried out for retaining only exudates (smaller objects) in the binary image (IB).
Figure 3.6 Intensity channel image of enhanced edge by Kirsch’s method

Figure 3.7 Spatial averaging filtered image
Figure 3.8 Histogram equalized image

Figure 3.9 Binarised image
(1) The blood vessels contain no information on exudates. Hence, the technique detailed by Badsha et al [67] was used for extraction of blood vessels alone, as shown in Figure 3.7 and removal thereof from the obtained binary image (IB).

(2) Optic disc is the most apparent feature (the brightest area that can be observed as a pale, well-defined round or vertically somewhat oval) in a fundus image, which is the entrance area for blood vessels and optic nerve to the retina. It serves as the locus of most other features. Thus, the methodology prescribed by Valencia et al [68] was utilized for removing the optic disc from the binary image (IB).

(3) Finally, the following equation (Eq. 3.5) was applied [69], [70] for removing the border of the retina from the binary image (IB). The resulting image is shown in Figure 3.11.

\[
I_E(x, y) = \begin{cases} 
I_B(x, y), & (x, y) \in \text{border of } I \\
0, & \text{otherwise} 
\end{cases}
\]  

(3.5)

The following morphological features detailed by Sopharak et al [71], [72] were extracted from the image (IB - IE). It contains only information about small objects:

i. **Area**: The area was calculated based on the total number of white pixels with black pixel as the neighbor in the binary image.

ii. **Number of regions**: The number of regions is nothing but the total number of segments in the binary image.

iii. **Eccentricity**: Eccentricity was estimated based on major and minor axis lengths respectively by using the following equation:

\[
\text{Eccentricity} = \frac{1}{L_1} \sqrt{L_1^2 - L_2^2}
\]

(3.6)
Figure 3.10  Morphological holes filled binary image

Figure 3.11 Extracted blood vessel image
iv. **Extent:**

\[
\text{Extent} = \frac{\text{Area}}{\text{Area of bounding box}}
\]  

(3.7)

v. **Orientation:** Orientation is defined as the angle between the major axis of the segmented object that has the same second moments around the region and the horizontal axis.

vi. **Convex area of the polygon:** Convex polygon area consisting of a segmented region is given by

\[
\text{Convex area} = \frac{1}{2} \begin{vmatrix}
    x_1 & y_1 \\
    \vdots & \vdots \\
    x_n & y_n \\
    x_1 & y_1
\end{vmatrix}
\]

(3.8)

vii. **Solidity:** Solidity could be defined as the ratio of the solid or filled area and convex hull area i.e.

\[
\text{Solidity} = \frac{\text{Filled Area}}{\text{Convex area}}
\]  

(3.9)

### 3.2.3 Classification

A kernel-based SVM has been adopted for checking the enforcement of the present diagnosis system in order to attain high accuracy [73] – [75]. RBF was utilized as the kernel function as it was found to work well on the datasets of the researcher. Optimization of the parameter combination was done by quadratic programming and found to have yielded better categorization outputs at \(\gamma = 1\) and \(C = 1\). Small values were used with the intention of keeping reproducing noise and over-fitting at bay to the data samples that were used in the training procedure. Performance investigation on the training samples enabled the activation of the RBF parameter and
weighting factors. A data analysis scheme written in MATLAB was excavated, which makes use of existing SVM tools for MATLAB that were actualized by Scholkopf [76] to perform classification.

### 3.3 RESULTS

Outcomes of the classifier were compared with the ophthalmologists’ hand-drawn ground-truth images for evaluation of the performance of the technique proposed in this work. Evaluation of the performance of the identification systems is usually done with evaluation of sensitivity, specificity and accuracy. The confusion matrix has been designed, keeping this factor. It considers trade-off between the actual and classifier generated outputs as shown in Table 3.1.

True positive (TP) is defined as the fact wherein the presence of retinopathy in the patient would be predicted when it is the fact. True negative (TN) is the process wherein prediction is done when the condition is normal as the subject has normal health in reality. Similarly, false positive (FP) is the condition of incorrect diabetic retinopathy prediction when the subject would be normal in reality. False negative (FN) is a condition which is normal prediction, when the person has diabetic retinopathy in reality. Sensitivity measures the proportion of actual positives to the total and correctly identified as such (e.g. the percentage of diabetic retinopathy people who are identified as having the diabetic retinopathy).

The sensitivity of the test indicates the probability that it would indicate a TP result when used on an infected subject. The sensitivity of the test could be determined by the formula

\[
\text{Sensitivity} = \frac{TP}{(TP + FN)} \times 100
\]  

(3.10)

The specificity measures the proportion of negatives, which are correctly identified (e.g. the percentage of healthy people who are identified as not having the diabetic retinopathy). A theoretical optimal prediction could achieve 100% sensitivity (i.e. predict all people from the diabetic retinopathy group as diabetic retinopathy) and 100% specificity. The specificity of a test
is the probability that a test would produce a TN result when used on a non-infected population. The specificity of a test could be determined by calculating:

\[
\text{Specificity} = \frac{TN}{(TN + FP)} \times 100
\]  
(3.11)

The accuracy of the test indicates the closeness of the test results to the true value and repeatability of the test. The accuracy of the test could be determined by the formula

\[
\text{Accuracy} = \frac{(TP + TN)}{(TP + TN + FP + FN)} \times 100
\]  
(3.12)

Test was conducted on a set of 60 retinal digital fundus images, including 34 (57%) images with exudates and 26 (43%) images without exudates on an Intel E7500 Core2Duo processor, 2.93 GHz PC using MATLAB. Application was made on the feature extraction techniques detailed in the methodology section (eq 3.6 to eq 3.9) to each of the fundus images and 7 features were extracted and stored. The classification process of the images was performed later based on RBF (Radial basis function) kernel SVM. For the SVM classifier, 32 images were utilized for training the classifier and 28 for testing the classifier in each fold of analysis.

Table 3.2 gives information based on the 5-fold cross validation as regards to the average percentage of 92% sensitivity and 91% specificity of the diagnostic classification based on the predictions of the RBF kernel-SVM within the framework of ground-truth outcomes. Finally, 91% accuracy was seen in the proposed SVM based CAD system in the classification of diabetic retinopathy. The eventual resulting image of the exudate detection of SVM classification method is shown in the following figure (Figure 3.12) and the superimposed image of exudate on the input is shown in Figure 3.13.

3.4 DISCUSSION

Despite the promising characteristic of the prevention from vision loss by premature (early) diagnosis and appropriate management of diabetic
retinopathy, lack of treatment at the initial stage and appropriate healthcare with regard to routine eye examination and additionally poor access to diabetic retinopathy screening programs could leave several diabetic patients, who have developed diabetic retinopathy, to continue with the ignorance of the disease and being untreated. The assessment of the quality of pathology detection is a complex task; human visual grading systems are not always perfect. Consequently, the disagreement of a human grader with a automated detection algorithm could be the result of an error of the human visual grading or of the detection algorithm.

The advantage of the proposed CAD system based on SVM classifier lies in the simplicity of protocol and the wide availability of fundus images. This tool is a step in the screening of diabetic retinopathy subjects, considering its ability to demonstrate 92% of diabetic retinopathy subjects those could be identified properly. Similarly, the findings of Osareh et al also confirm the achievement of the SVM classifier of a high level of diagnostic accuracy in terms of diabetic retinopathy classification over others [77]. Zhang et al have studied an automated algorithm using multi-scale morphological processing which has achieved the sensitivity and predictive value of 84.1% and 89.2% respectively [28]. Fleming et al have studied multiple linear top hats by using multi-scale method and achieving a maximum sensitivity, specificity of 98.6% and 95.5% respectively [78]. The early diagnosis of diabetic retinopathy by means of fundus image features accomplished an accuracy of 91.2% and specificity of 92% by SVM classifier.

### Table 3.1

**Alternative diagnostic test (classifier) results with respect to the ground-truth outcome**

<table>
<thead>
<tr>
<th>Diagnostic tool (classifier) result</th>
<th>Ground-truth result (Ophthalmologists’ hand-drawn)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>Positive (present)</td>
</tr>
<tr>
<td>Negative</td>
<td>False negative (absent)</td>
</tr>
</tbody>
</table>
Table 3.2
Performance of the SVM classifier via 5-fold cross validation

<table>
<thead>
<tr>
<th>Fold #</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Accuracy (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fold #1</td>
<td>94.1</td>
<td>90.9</td>
<td>92.8</td>
</tr>
<tr>
<td>Fold #2</td>
<td>87.5</td>
<td>89.3</td>
<td>85.7</td>
</tr>
<tr>
<td>Fold #3</td>
<td>94.7</td>
<td>88.9</td>
<td>97.7</td>
</tr>
<tr>
<td>Fold #4</td>
<td>92.3</td>
<td>89.6</td>
<td>89.2</td>
</tr>
<tr>
<td>Fold #5</td>
<td>85.7</td>
<td>92.9</td>
<td>89.5</td>
</tr>
<tr>
<td>Average</td>
<td>91.6</td>
<td>90.5</td>
<td>91.2</td>
</tr>
</tbody>
</table>

Figure 3.12 Extracted exudates
This proposed CAD system has an edge over manual assessment (ground-truth) with the capability of automated evaluation. The CAD system, can reduce the measurement errors occurring, through image morphological feature extraction with the conventional (ophthalmologists’ hand-drawn) assessments. Although the results of the proposed study are encouraging, more cases of diabetic retinopathy are needed for further investigation and validation.

3.5  CONCLUSION

The development of the proposed CAD system is in progress. The methods for segmenting anatomical structures such as optic disk, blood vessels and outer border along with exudates have been presented and promising results are shown. The proposed CAD system could identify diabetic retinopathy cases with an average accuracy of more than 91%, a sensitivity of more than 91%, and a specificity of 90.5%. Therefore, with this leading satisfied sensitivity, specificity and accuracy results, the proposed methodology can be prospected to be a useful technique for cataloging the subject with diabetic retinopathy, additionally; it could be supplementary diagnostic methodology that will mask faulty diagnosis.