Diabetic Retinopathy Classification Using Gray Level Textural Contrast and Blood Vessel

Edge Profile Map

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This thesis titled
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ABSTRACT

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Diabetic Retinopathy Classification Using Gray Level Textural Contrast and Blood Vessel Edge Profile Map

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Diabetic retinopathy is an inevitable cause of diabetes that eventually leads to blindness without early detection and treatment. This thesis incorporates classification of an input fundus image into one of the three classes, healthy/normal, Non-Proliferative Diabetic Retinopathy (NPDR) and Proliferative Diabetic Retinopathy (PDR).

In this research, an approach to automate the identification of the presence of diabetic retinopathy from color fundus images of the retina has been proposed. The blood vessel edge profile from these images is obtained using Gaussian kernel as the filtering function. A local entropy based thresholding using fixed as well as adaptive mask has been conducted. Gradient driven second order statistic contrast in four orientations and fractal features quantify the classes. The number of features vary based on the experiment.

Classification has been achieved using two well-known techniques – Artificial Neural Network (ANN) and Support Vector Machines (SVM). The results of this research are compared to those obtained from other approaches developed in the literature.
DEDICATION

“It matters not what someone is born, but what they grow to be.”

– Albus Dumbledore in Harry Potter and the Goblet of Fire by J.K. Rowling

To my family for molding me to the person that I am today.
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CHAPTER 1: INTRODUCTION

Diabetes mellitus or commonly known as diabetes is a disease that affects the pancreatic glands and interferes with the production of insulin. Insulin is a key hormone that regulates the level of blood glucose (sugar) in a human body. Diabetes can be broadly classified into two types – Type 1 or juvenile-onset diabetes and Type 2 or adult-onset diabetes. The former results when there is a destruction of the beta cells producing insulin resulting in insulin deficiency. This form is generally seen in children, adolescents and young adults. Type 2 diabetes is the most common form of diabetes and constitutes 90% of the people affected by diabetes [1]. Type 2 diabetes is usually the result of obesity which results in resistance to the insulin produced causing compensatory hyperinsulinemia at onset but due to increased demands on the pancreas eventually result in beta cell death and insufficient insulin production. According to the 2014 National Diabetes Statistics report by the American Diabetes Association (ADA), 29.1 million people or 9.8% of the United States population have been diagnosed with diabetes [2]. As a result of either form of diabetes, when glucose control is inadequate, multiple long term complications results and affects multiple major organs of the body such as heart, eyes, kidneys and the nervous system [1]. This research focuses on the effect that diabetes has on the eye, in particular, the retina. The effect is termed as diabetic retinopathy. Approaching the research from an electrical engineering background, this work aims to identify healthy patients from those diagnosed with retinopathy. The rest of the chapter is organized as follows. Section 1.1 provides a general description of diabetic retinopathy, Section 1.2 defines the objectives of this research.
1.1 Diabetic retinopathy

Diabetic retinopathy is a common consequence of poorly controlled diabetes that causes damage to the vasculature of the eye. It has been estimated that 5% of the world’s blindness cases can be attributed to diabetic retinopathy [3]. Almost all patients with Type I diabetes after 15 years and more than 60% of patients with Type II diabetes are affected by retinopathy [4]. These statistics provide an alarming trend in the number of people suffering from this disease. In order to understand the disease, it is essential to understand the anatomy of the eye and in particular the retina.

The eye has an asymmetrical spherical shape and consists of five important components – cornea, iris, pupil, lens and retina [5]. Chronic hyperglycemia (high sugar) damages the retinal vasculature that is translated into diabetic retinopathy. The anatomy of the eye and the various layers in the retina is as shown in Figure 1.

![Figure 1. Anatomy of the eye and retina [6].](image)
The retina is a complex, multi layered structure nourished by blood vessels. The photoreceptor cells, rods and cones form a layer at the very end of the retina. The middle layer consists of three types of neurons, namely, bipolar cells, horizontal cells and amacrine cells. The third layer consists of the neuron cell bodies. The cell bodies form a bundle at a region on the retina known as the optic disk. The optic nerve originates from the optic disk and is connected to the central nervous system. The center of the retina, directly behind the lens, is a rod free region consisting only of cones. This region is termed as fovea. The fovea is covered by a pigment known as macula which protects the retina from absorbing ultraviolet (UV) radiation [7]. This disease is characterized by the following symptoms [8]:

- Blurring of vision
- Visibility of floating spots
- Difficulty in night time vision

Diabetic retinopathy can be categorized into two types based on severity: Non-Proliferative Diabetic Retinopathy (NPDR) and Proliferative Diabetic Retinopathy (PDR). NPDR is a mild form of the disease and occurs due to damage of the blood vessels that supply the retina. The damage is expressed as micro aneurysms (MA), cotton wool spots (CWS), hemorrhages (HEM) and exudates. Early detection during this stage can be rectified through surgery [9]. The human body has a tendency to replace damaged cells by growth of new cells. The eye is one of the most highly vascularized and metabolically active organ in the body. The damage which occurs in NPDR results in decreased blood flow to the retina. This triggers the release of multiple growth factors
which the formation of new blood vessels known as neovascularization. Unfortunately, these new blood vessels are abnormal in terms of their structure and very prone to leakage of serum contents into the retina as well as rupture and both of these problems cause irreparable damage to the retina leading to a severe form of diabetic retinopathy called as PDR. A distinction between the two types of retinopathy is shown in Figure 2.

Medical evaluation of retinopathy involves a detailed analysis of the eye by an ophthalmologist. The protocol followed is exhaustive and requires the support of the following tests, namely, visual acuity, measurement of intra ocular pressure (IOP), gonioscopy and slit-lamp biomicroscopy, retinal photography and fluorescein angiography [11]. Fundus images captured by a fundus camera provide the input for an
assessment of the disease diabetic retinopathy. Figure 3 provides a simple ray diagram of the fundus image captured.

![Ray diagram of a retinal fundus image capture](image)

Figure 3. Ray diagram of a retinal fundus image capture [11].

The fundus images are important as it aids in easily identifying the progression of the disease when compared to a direct eye examination [12]. An automated procedure to detect the disease would enable ophthalmologists in quicker diagnosis.

1.2 Objectives of the research

Review of the literature indicates extensive research is underway pertaining to the classification of diabetic retinopathy by employing image processing techniques such as thresholding, mathematical morphology and filtering [12-14, 16-18]. There are numerous approaches suggested for automatic classification of diabetic retinopathy based on segmenting the optic disk and one or several particular features that characterize the
disease [19-25]. However, these methods do not consider all the anomalies that characterize both types of diabetic retinopathy. They also require the user to define the region of interest. Thus, we propose an approach that can automatically classify a fundus image into one of the three categories – normal, NPDR and PDR. The specific objectives of this research is listed below:

- To create an edge profile map of the fundus images that detects the retinal vasculature and various abnormalities characteristic of the type of retinopathy based on an adaptive mask generation procedure.
- To classify the processed images using features which describe the texture and shape via artificial neural network (ANN) and support vector machines (SVM).
- To provide a comparison of our method with recent methods developed by other researchers and reported in the literature.
CHAPTER 2: BACKGROUND

Diabetic retinopathy identification has been a subject of interest for the last couple of decades. Recent advancements in image processing, machine learning and computer vision algorithms has garnered a greater interest in this field. Section 2.1 describes the various algorithms existing in the literature and Section 2.2 briefly analyzes the limitations of the prevailing methods and outlines the scope for this research.

2.1 Literature review

Literature survey reveals that identification of diabetic retinopathy has been achieved using various approaches summarized in [12-25]. A number of methods achieve detection of diabetic retinopathy by segmenting important regions as well as various abnormalities in the retina from the fundus images [12-14, 16-18].

In [12, 13], a type of anomaly known as exudates has been described as an important indication of the disease. Sopharak et al. describe an approach using mathematical morphology to isolate exudates after eliminating the optic disk region. The algorithm achieves a sensitivity and specificity of 80% and 99.5% respectively [12]. Osreh et al. proposed detection of exudates using Fuzzy-C means clustering, Gabor filtering and neural net [13]. They achieve an accuracy of 93.5%. However, both these methods fail to make a distinction between exudates and small blood vessels and do not take into account other anomalies such as CWS, MA and HEM that are expressed in the disease.

Aguirto et al. use the concept of amplitude modulation and frequency modulation in order to extract features from every retinal structure that characterize a normal and
affected retina [14]. The method described in [14] utilizes the cumulative distribution function for classification that provides a unique distinction between the various types of retinopathy however it is variant to rotation, scaling and translation.

Most of the effects of retinopathy are observed in the area around blood vessels and hence blood vessel segmentation has been deemed of higher importance [15]. Soares et al. follow a 2D Morlet wavelet approach and Bayesian classification in order to detect blood vessels in a retinal fundus image [16]. As mentioned in their discussion and conclusion section, this technique disregards any information about the shape and structure of elements present in the image. Budai et al. describe a Gaussian hierarchy method to isolate retinal blood vessels from fundus images [17]. The classification accuracy achieved is about 94%. However, due to downscaling and then subsequent image fusion a lot of finer details are lost that is required to uniquely identify images of NPDR and PDR. A highly efficient method called matched filtering to detect blood vessels has been described by Chaudhuri et al. [18]. However, this technique can be applied only to stationary processes (process wherein the joint probability distribution function does not vary when shifted in time).

The use of first order statistical features such as area, perimeter, mean, etc. have been used extensively as features for classification [19, 20]. Verma et al. detect blood vessels and hemorrhages and utilize global features, area and perimeter, for classification via neural net [19]. Lee at al. individually isolate hemorrhages, MA and CWS from 430 images. The area of these abnormalities act as input to a neural net for classification. A classification accuracy of 82.6% for normal and NPDR and 88.3% for PDR is
demonstrated [20]. These use of first order statistic features makes the system less robust as they provide no spatial information and are hence unreliable for the problem at hand. Nayak et al. demonstrate that the use of a second order statistic such as contrast in conjunction with first order features provide a higher classification accuracy (93%) which leads us to establish that second order features are more robust in handling rotation, translation and scaling of the input images [21].

With advances in computer vision techniques, content based image retrieval (CBIR) has been used extensively for diabetic retinopathy screening applications [22-24]. In [22], Quellec et al. proposed a multiple instance learning (MIL) based algorithm that detects the diabetic retinopathy lesions without manual segmentation by clinicians. In a similar approach, [23] define the Point of Interest (PoI) in an image and extract features from around this using an algorithm termed as Speeded-Up Robust Features (SURF). A modified color auto-correlogram based feature extraction approach is used in conjunction with the MIL has been utilized in [24]. Although these techniques work well when obtaining the ground truth on extremely large datasets (greater than 100,000 samples) is difficult, they are computationally complex and have a large dependency on reference datasets or “dictionary”. Mookiah et al. have incorporated the use of Probabilistic Neural Network (PNN) for a three class classification achieving an accuracy of 96.15% [25]. However, it has been established that PNNs are extremely slow and require large memory space. This implies that a real-time effective diagnostic tool would be difficult to implement. Also, the training set need to be an accurate representation of the data for the classifier to work as expected.
2.2 Limitations of existing methods and scope of this research

The literature survey dictates various algorithms for automatic detection of diabetic retinopathy [12-25]. However, limitations such as insufficient classification accuracy, limited robustness and unsuitability for hardware implementation define the scope for this research. This research aims to classify the presence of diabetic retinopathy (mild and severe cases) from fundus images by segmenting blood vessels using an adaptive mask generation procedure. It also utilizes two classifiers - ANN and SVM to provide a comparative study. The research has been implemented on a set of images taken from two publically available databases DIARETDB1 [26] and DRIVE [27].
3. METHODOLOGY

This research is aimed to classify an input fundus image into one of the three classes – normal, NPDR and PDR. The images used in this research have been collected from [26, 27]. Section 3.1 describes, in general, the approach of the work carried out in this research. Section 3.2 outlines the approach in Experiment 1 while Section 3.3 outlines the approach utilized in Experiment 2.

3.1 General description of the approach

The entire approach used in this research involved three major computational areas – segmentation of retinal vasculature, feature extraction and classification. Figure 4 illustrates the flowchart outlining the general approach taken in this research.
3.1.1 Segmentation of retinal vasculature

The blood vessels in a fundus image have lower reflectance compared to the other retinal surfaces. Hence, they appear darker than the background. Blood vessels have a tapering structure towards the edges [28]. It is assumed that this change in blood vessels is gradual and a uniform width is considered. Gaussian distributions utilized in matched filter techniques effectively depict the grayscale profile of blood vessels [15 - 17]. The
intensity profile generated from a grayscale retinal image in this research is illustrated in Figure 5.

![Intensity profile of an input fundus image](image)

Figure 5. Intensity profile of an input fundus image.

The intensity profile is instrumental in modelling the kernel function for filtering. Based on the information from Figure 5, a Gaussian kernel is chosen as a smoothing function. The kernel aids in segregating the vessel edge from its background.

In the most general form, an N-dimensional kernel can be represented in the \( \vec{X} = [x_1, x_2, \ldots, x_N]^T \) - Cartesian coordinate system [29] as

\[
G(x_1, x_2, \ldots, x_N) = \frac{1}{(2\pi)^{N/2} |\Sigma|^{1/2}} e^{-\frac{1}{2} (\vec{x} - \vec{\mu})^T \Sigma^{-1} (\vec{x} - \vec{\mu})}
\]

(1)

where \( \vec{\mu} = [\mu_1, \mu_2, \ldots, \mu_N]^T \) is the mean vector, \( \Sigma \) is the positive definite N×N covariance matrix of the form
\[ \Sigma = \begin{bmatrix} \sigma_1^2 & \sigma_{12} & \cdots & \sigma_{1N} \\ \sigma_{21} & \sigma_2^2 & \cdots & \sigma_{2N} \\ \vdots & \vdots & \ddots & \vdots \\ \sigma_{N1} & \sigma_{N2} & \cdots & \sigma_N^2 \end{bmatrix}, \quad |\Sigma| \text{ is the determinant of positive definite } N \times N \text{ covariance matrix and } T \text{ represents matrix transposition. In this work, a two-dimensional normal distribution in the } (n_1, n_2) \text{ image plane is considered. It is given by} \\
\]
\[ X(n_1, n_2) = \frac{1}{(2\pi)^{N/2} |\Sigma|^{1/2}} e^{-\frac{1}{2}(\bar{x} - \bar{\mu})^T \Sigma^{-1} (\bar{x} - \bar{\mu})} \] 
\[ (2) \]

If the coordinate axes are uncorrelated, a two-dimensional Gaussian kernel can be defined as a product of two one-dimensional kernels [29] defined by
\[ G(n_1, n_2) = -\frac{1}{\sqrt{2\pi}\sigma_1} e^{-\frac{n_1^2}{2\sigma_1^2}} \cdot \frac{1}{\sqrt{2\pi}\sigma_2} e^{-\frac{n_2^2}{2\sigma_2^2}} \] 
\[ (3) \]
where \( \sigma_1 = \sigma_2 = \sigma \) is the spread of the intensity profile. If the length of a blood vessel segment \( L \) is assumed to be along the \( n_2 \) axis, then eqn. 3 can be rewritten as
\[ G(n_1, n_2) = -\frac{1}{2\pi\sigma^2} e^{-\frac{n_1^2}{2\sigma^2}}, \quad |n_2| \leq \frac{L}{2} \] 
\[ (4) \]

Since blood vessels are oriented arbitrarily, the kernel must be rotated in all possible directions. The angular resolution \( \theta \) determines the number of kernels \( N \) required, which is given by
\[ N = \frac{360}{\theta} \] 
\[ (5) \]

\( N \) number of kernels are convolved with the original image \( I(n_1, n_2) \) of size \( N_1 \times N_2 \), and at each pixel \( (n_1, n_2) \) only the maximum response is elicited. The resulting grayscale image \( I_g(n_1, n_2) \) is subjected to a local thresholding scheme based on entropy [30].
Entropy based thresholding provides a more accurate method of thresholding compared to Otsu’s thresholding [31] since it takes into account the spatial distribution of pixels. The first step in this thresholding approach is to calculate Haralick’s matrix or gray level co-occurrence matrix [32, 33] defined in eqn. 6.

\[ c_{m,n,\theta} = \sum_{n_1} \sum_{n_2} P\{ l'(n_1, n_2) = m \& l'(n_1 \pm d\theta_0, n_2 \mp d\theta_1) = n \} \]  

(6)

where \( d \) is the distance between the pixels, \( \theta \) is the orientation and

\[ P\{ \} = \begin{cases} 1, & \text{if argument is true} \\ 0, & \text{otherwise} \end{cases} \]

The size of \( C_{m,n,\theta} \) is the same as that of the image \( I_g(n_1, n_2) \) which is specified to be \( N_1 \times N_2 \). Table 1 indicates the possible values of \( \theta_0 \) and \( \theta_1 \) for different orientations and for \( d = 3 \).

Table 1: Values Of \( \theta_0 \) And \( \theta_1 \) For Various \( \theta \).

<table>
<thead>
<tr>
<th>( \theta )</th>
<th>( \theta_0 )</th>
<th>( \theta_1 )</th>
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<tbody>
<tr>
<td>0°</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>45°</td>
<td>-3</td>
<td>3</td>
</tr>
<tr>
<td>90°</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>135°</td>
<td>3</td>
<td>-3</td>
</tr>
</tbody>
</table>

If \( R \) denotes the number of pixel pairs possible for a particular orientation, then the probability of co-occurrence is given as

\[ P(m,n) = \frac{c_{m,n,\theta}}{R} \]  

(7)
In this type of thresholding, the foreground and the background pixels are considered as different sources. If \(0 \leq T \leq N-1\), then entropy for foreground pixels expressed in terms of the probability of co-occurrence is

\[
H_f^{(2)} = \sum_{i=0}^{T} \sum_{j=0}^{T} P(i,j) \log_2 \left( \frac{1}{P(i,j)} \right)
\]  

(8)

Similarly, the entropy for background pixels is

\[
H_b^{(2)} = \sum_{i=T+1}^{N-1} \sum_{j=T+1}^{N-1} P(i,j) \log_2 \left( \frac{1}{P(i,j)} \right)
\]  

(9)

where the superscript indicates that the measure of entropy is a second order statistic. The optimum threshold \(T_{opt}\) is formulated as

\[
T_{opt} = \text{argmax}[H_f^{(2)} + H_b^{(2)}]
\]  

(10)

3.1.2 Feature extraction

Feature extraction is performed on the image obtained after thresholding, \(I_{(n_1, n_2)}\). The three features extracted are second order statistic contrast in four orientations, fractal dimension and two values of lacunarity.

a) Contrast

The co-occurrence matrix is calculated for \(I_{(n_1, n_2)}\) as described by eqns. 6 and 7. For an orientation \(\Theta = \{0^\circ, 45^\circ, 90^\circ\text{ and } 135^\circ\}\), the contrast [33] is calculated as

\[
CON_\Theta = \sum_i \sum_j P(i,j)(i-j)^2
\]  

(11)

b) Fractal dimension

Objects that have integer dimensions conform to traditional Euclidean geometry. Those objects that possess the property of self-similarity are known as fractals. The fractal dimension of a subset of fractals, known as wild fractals, is calculated using box
count method [34, 36]. The image $I_{l(n_1, n_2)}$ is put onto a grid with mesh size $s$. The number of grid boxes that contain a portion of the structure is described by the power law [35]

$$B(s) = \frac{1}{s^D}$$  \hspace{1cm} (12)

where $D$ is the fractal dimension and is given as

$$D = \frac{\log_{10} B(s)}{\log_{10}(\frac{1}{s})}$$  \hspace{1cm} (13)

The box count algorithm for a blood vessel edge profile map has been pictorially represented in Figure 6.

Figure 6. Diagrammatic representation of box count method [37].
c) **Lacunarity**

Lacunarity provides the distribution of gaps or holes in an image. It is considered as textural representation of a fractal [36]. The idea is to map the image \( I_t: \left[N_1, N_2\right] \rightarrow \mathbb{R} \) onto a surface \( S \) in the following way

\[
S = \{i, j, f(i, j) / (i, j) \in [1: N_1] \times [1: N_2]\}
\]  

(14)

where \( f(i, j) = \{(1, 2, \ldots, I_{t_{\text{max}}}) | f = I_t(i, j)\} \), with \( I_{t_{\text{max}}} \) being the maximum gray level intensity present in the image. The probability distribution function can be expressed as

\[
Q(s, r) = \frac{b(s, r)}{B(r)}
\]  

(15)

\( b(s, r) \) is the number of boxes with side \( r \) containing \( s \) points of the surface representing the object whose lacunarity must be established and \( B(r) \) is the total number of boxes with side \( r \). The first and second moments are calculated as

\[
Z_1(r) = \sum_{s=1}^{s_{\text{max}}} s \cdot Q(s, r)
\]  

(16)

\[
Z_2(r) = \sum_{s=1}^{s_{\text{max}}} s^2 \cdot Q(s, r)
\]  

(17)

The ratio of the moments defined in eqns. 16 and 17 is formulated as

\[
\Lambda(r) = \frac{Z_1(r)}{Z_2(r)}
\]  

(18)

Lacunarity is defined by

\[
\lambda = \frac{d\Lambda(r)}{dr}
\]  

(19)

The lacunarity is calculated for foreground pixels as well as for foreground pixels plus background pixels. Figure 7 shows a plot of lacunarity versus box size on a logarithmic scale.
3.1.3 Classification

A classifier such as neural network or support vector machines (SVM) that is linear or has piecewise linear approximation capabilities with known implementation is particularly attractive since it provides an efficient means of hardware realization. In this research, ANN as well as SVM is utilized for classification.

A three layer, feed-forward artificial neural network has been chosen to implement classification using the backpropagation training algorithm [38]. The first layer is the input layer and the number of neurons depends on the number of features. The second layer is the hidden layer and the number of neurons in this layer is determined empirically. The output layer consists of three neurons, each pertaining to a class – normal, NPDR and PDR.

A well-developed technique known as SVM has been incorporated in this research for classification to provide a perspective from another paradigm [39]. In this work, a multiclass, one-against-one training is employed to provide the best hyperplane for separation of the three classes [40]. The main objective is to minimize the function
\[ f(w, b, \xi) = \frac{1}{2} w^T \cdot w + C \sum_i \xi_i \]  
subject to the condition
\[ y(w^T \cdot x_i + b) \geq 1 - \xi_i, \xi_i \geq 0 \text{ (for all } x_i) \]

where \( x_i, i = 1, 2, 3, \ldots, N \) is the feature vector, \( w \) is the weight vector, \( C \) is a penalty parameter that compensates for misclassification and \( \xi_i \) are known as slack variables. The quadratic optimization technique involves solving Lagrangian multipliers and Karush-Kuhn-Tucker (KKT) conditions [40]. The output, defined by the three classes: Normal, NPDR and PDR, is given as
\[ y = \sum_{i=1}^{nsv}(\alpha_i, \alpha_i^*)K(x, x_i) + b \]

where \( \alpha_i, \alpha_i^*, i = 1, 2, \ldots, N \) are Lagrangian multipliers, \( K(x, x_i) \) is the inner product kernel that satisfies Mercer’s condition [41] and \( nsv \) refers to the data corresponding to non-zero \( \alpha_i, \alpha_i^* \) pairs.

In this work, the entire dataset was divided into training and testing sets using a two-fold cross-validation by varying the holdout parameter from 0.1 to 0.9 in steps of 0.1. The results reported is the average classification accuracy.

### 3.2 Experiment 1

This experiment was conducted on a set of 69 images from [26] and [27]. There were 19 images belonging to the Normal class, 33 NPDR images and 17 images from the PDR class. A detailed block diagram depicting various stages in this experiment is as shown in Figure 8.
Figure 8. Detailed block diagram of experiment 1.

The experiment follows the steps outlined in Section 3.1. The blood vessel edge profile is generated using a fixed mask prior to thresholding. This implies that a single value of standard deviation is used for every input image in the Gaussian kernel function given in eqn. 4. The following step involved extracting all the seven features as described in Section 3.1.2. Classification using the ANN involved seven neurons in the input layer. The outline of ANN for this experiment is indicated in Figure 9.
Figure 9. Schematic diagram of ANN for experiment 1.

Figure 10 illustrates the outline of the SVM structure analogous to the neural net.

Figure 10. Schematic diagram of SVM for experiment 1.
This research has a number of control parameters or variables out of which the edge detection modelling, number of samples and feature space has been deemed the most crucial based on the outcome of experiment 1. Based on the design of experiment theory [42], a further enhancement of experiment 1 depending on the aforementioned control variables, experiment 2 was formulated. The adaptive mask generation procedure to segment the retinal vasculature was utilized as an improvement of fixed mask approach in experiment 1. The number of samples was increased from 69 to 106. The seven dimensional feature space was represented as a subset of three dimensional feature spaces. This segregated the complex feature space into a more manageable form. All these factors led to development of experiment 2.

3.3 Experiment 2

In this experiment, the sample set from experiment 1 was increased to 106 images from the same databases [26, 27]. A major step in this experiment was to include the concept of adaptive processing for mask generation prior to thresholding. A general adaptive image processing system involves the use of information from the input image along with apriori information in order to produce a more reliable output [43]. A simple block diagram illustrating the concept is shown in Figure 11.
The system impulse response \( h(n_1, n_2) \) is input driven and it is defined by the Gaussian kernel.

\[
h(n_1, n_2) = G(n_1, n_2) = -\frac{1}{2\pi\sigma^2} e^{-\frac{n_1^2}{2\sigma^2}}, |n_2| \leq \frac{L}{2}
\]  

(23)

where \( \sigma \) and \( L \) have been defined as in eqn. 4.

This implies that the standard deviation utilized in the kernel function is based on the input fundus image. The mask generated is a linear convolution between the system impulse response and the input grayscale image. It is given as

\[
M(n_1, n_2) = h(n_1, n_2) \ast I(n_1, n_2)
\]

(24)

The remaining steps in the procedure to segment the retinal vasculature is as described by eqn. 6 through eqn. 10. During the feature extraction phase, three features, namely, contrast in 0° and 90° and lacunarity considering foreground pixels only are utilized. The outline of the classifiers for this experiment is illustrated in Figures 12 and 13.
Figure 12. Structural representation of ANN for experiment 2.

Figure 13. Framework of SVM classifier for experiment 2

A block diagram explaining the various steps for experiment 2 has been elucidated in Figure 14.
Figure 14. Detailed block diagram for experiment 2.
CHAPTER 4: RESULTS AND DISCUSSION

The entire approach in this research has been tested on the DIARETDB1 [26] and DRIVE [27] databases. The hardware utilized is an Intel Core i5_3210M CPU at 2.50 GHz. The algorithms have been implemented on MATLAB R2009b and ImageJ.

Section 4.1 discusses the results from experiment 1 while Section 4.2 evaluates experiment 2. Section 4.3 provides analysis of our approach in comparison with well-known methods in the literature for three-class classification of diabetic retinopathy.

4.1 Results of experiment 1

The original color fundus images from the DIARETDB1 database were of size 1500×1152 and those from the DRIVE database were of size 565×584. Figures 15(a), 15(b) and 15(c) illustrate the original images from Normal, NPDR and PDR classes.

Figure 15(a). Original color fundus image for class normal.
Figure 15(b). Input color fundus image from NPDR class.

Figure 15(c). Retinal fundus image from the PDR class.
The segmentation of retinal vasculature yields a blood vessel edge profile map which is essential to isolate the healthy blood vessels and various disease anomalies. This map overlaid on the original images has been depicted in Figure 16 for all the three classes.

Figure 16(a). Blood vessel edge profile map of a healthy retina.
Figure 16(b). Blood vessel edge profile of a retina from NPDR class.

Figure 16(c). Retinal blood vessel edge profile map of a patient diagnosed with PDR.
Based on the flowchart illustrated in Figure 4, it is essential to describe the attributes that are unique to each class. The seven features extracted in this experiment provide a unique description about the individual classes. The spatial inter-relationship between the pixels are provided by the contrast in four directions. The fractal features uniquely characterize the presence of anomalies. The scatter plots for all the features are shown in Figure 17 through Figure 19.

![Contrast(0 degrees)](image)

![Contrast(45 degrees)](image)

*Figure 17. GLCM based contrast in 0° and 45° direction.*
Figure 18. Textural contrast in 90° and 135° orientation.

Figure 19. Scatter plot of the fractal features.

The seven individual features have also been represented in two dimensional bar graphs as indicated in Figures 20-23.
Figure 20. Bar graph representation of GLCM based contrast in $0^\circ$ and $45^\circ$.

Figure 21. Haralick’s co-occurrence matrix based contrast in $90^\circ$ and $135^\circ$. 
It can be seen from the scatter as well as the bar graph plots that the NPDR class has characteristics that are similar to the other two classes. In the above plots, the NPDR
class lies between the normal and PDR classes and hence it is the most difficult to
classify. The results of classification using ANN and SVM are indicated below in Table
2.

Table 2: Classification accuracy and sensitivity for experiment 1.

<table>
<thead>
<tr>
<th>Type of Classifier</th>
<th>Classification Accuracy (In %)</th>
<th>Sensitivity (In %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANN</td>
<td>91.7</td>
<td>93</td>
</tr>
<tr>
<td>SVM</td>
<td>93</td>
<td>97</td>
</tr>
</tbody>
</table>

The seven dimensional feature space was represented as a subset of three
dimensional spaces. As a result of which 35 plots were generated. The plots with features
only from texture features and plots containing only fractal features are shown along with
plots that contain a combination of the above in Figure 24. The remaining plots are
illustrated in Appendix II.
Figure 24(a). Contrast in 0°, 45° and 135°.

Figure 24(b). Contrast in 0°, contrast in 45° and fractal dimension.
Figure 24(c). Contrast in $0^\circ$, lacunarity considering foreground pixels and lacunarity considering foreground pixels and empty spaces.

Figure 24(d). Contrast in $0^\circ$, $90^\circ$ and lacunarity considering foreground pixels.
It can be seen that a combination of contrast in 0°, contrast in 90° and lacunarity considering foreground pixels only provide a good separation between the three classes. This established the motivation to utilize only three features in experiment 2.

4.2 Results of experiment 2

As mentioned earlier, this experiment was conducted on a sample size of 106 images. The adaptive mask generation procedure improved the detection of the blood vessels and anomalies in the color fundus images. Figure 25 illustrates the blood vessel edge profile map overlayed on the original color fundus images for normal, NPDR and PDR cases. Figure 26 illustrates more examples and rest of the images are provided in Appendix III.

Figure 25(a). Blood vessel edge profile map of a healthy retina.
Figure 25(b). Blood vessel edge profile of a retina from NPDR class.

Figure 25(c). Retinal blood vessel edge profile map of a patient diagnosed with PDR.
Figure 26. Additional fundus images and processing results.
The use of adaptive processing for mask generation and three features, namely, contrast in $0^\circ$, contrast in $90^\circ$ and lacunarity considering foreground pixels, resulted in a classification accuracy of 97.2% using ANN and 98.1% with SVM. The results of classification for experiment 2 has been indicated in Table 3.

<table>
<thead>
<tr>
<th>Type of Classifier</th>
<th>Classification Accuracy (In %)</th>
<th>Sensitivity (In %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANN</td>
<td>97.2</td>
<td>97</td>
</tr>
<tr>
<td>SVM</td>
<td>98.1</td>
<td>99</td>
</tr>
</tbody>
</table>

4.3 Analysis of the algorithm

Modelling the input color fundus image by a Gaussian model based on the intensity profile provides a reliable method of segmenting the retinal vasculature. The first order features do not provide reliable data for classification of diabetic retinopathy. Due to the nature of processed images, textural features give the necessary description that aids in robust classification. The shape features emphasized the severity of the disease.

The complexity of the research arises due to the fact that it is a three class classification problem instead of a simple binary classification. This implies that the
problem at hand is highly stochastic in nature. Also, there is a tradeoff in including additional samples to the existing feature space. The progression of the disease from the normal or healthy stage to the NPDR stage and further into the PDR stage is represented by a complex feature space that poses a problem of misclassification. The progression of the retinopathy in association with the three dimensional feature space has been depicted in Figure 27.

Figure 27. Different classes of retinopathy in conjunction with a feature space.

Experiment 1 utilized a combination of these features that provided a classification accuracy of 93% using SVM. This is an improvement compared to [20,
Lee et al. [20] demonstrate a classification accuracy of 82.6% for normal and NPDR and 88.3% for PDR. In [21], Nayak et al. have achieved an accuracy of 93% with sensitivity of 90% and specificity of 100%.

Delving into the adaptive mask generation approach provided segmentation of blood vessels on an input-driven basis. It ensured that the vessels were detected right up to the edge of the input fundus image. This adaptive processing enabled selection of the standard deviation of the Gaussian kernel according to the color fundus image. Based on the results of the feature ranking by class separability criteria, three features – contrast in 0°, contrast in 90° and lacunarity considering foreground pixels are ranked higher compared to the other features. The approach utilized in experiment 2 results in a classification accuracy of 98.1% using the SVM. Figure 28 illustrates the linear SVM classifier maximizes the margin of the decision boundary in the given feature space.

![Figure 28. 3-D feature subspace indicating support vectors and decision boundary.](image)
This is higher than the results obtained by Mookiah et al. [25]. Table 4 summarizes the comparison of results [44] from our approach to those developed in [20-21, 25].

Table 4: Comparative study of diabetic retinopathy detection algorithms for three class classification problem.

<table>
<thead>
<tr>
<th>Authors</th>
<th>Features</th>
<th>Methods</th>
<th>Salient feature</th>
<th>Performance measure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lee et al. [20]</td>
<td>HEM, MA, exudates and CWS</td>
<td>NN</td>
<td>High reproducibility</td>
<td>Normal-82.60%, NPDR-82.60%, PDR-88.30%</td>
</tr>
<tr>
<td>Nayak et al. [21]</td>
<td>Exudates, area of blood vessel and contrast</td>
<td>NN</td>
<td>Texture and morphological features</td>
<td>Sensitivity-90%, Specificity-100% Accuracy-93%</td>
</tr>
<tr>
<td>Mookiah et al. [25]</td>
<td>Blood vessels and exudates area, bifurcation points, global texture and entropies</td>
<td>GA optimized PNN classifier</td>
<td>PNN tuning by GA and Particle Swarm Optimization (PSO)</td>
<td>Sensitivity-96.27%, Specificity-96.08%, Accuracy-96.15%</td>
</tr>
<tr>
<td>Our method: Experiment 1</td>
<td>Textural contrast in four orientations, fractal dimension and two values of lacunarity</td>
<td>NN and SVM</td>
<td>All anomalies considered – MA, CWS, hemorrhages, exudates and neovascularization With a fixed mask</td>
<td><strong>NN:</strong> Sensitivity – 93% Accuracy – 91.7% <strong>SVM:</strong> Sensitivity – 97% Accuracy – 93%</td>
</tr>
</tbody>
</table>
Table 4: continued

| Our method: Experiment 2 | Contrast in 0° and 90° and lacunarity considering foreground pixels only | NN and SVM | All anomalies considered Adaptive mask generation procedure utilized | NN: Sensitivity – 97% Accuracy – 97.2% SVM: Sensitivity – 99% Accuracy – 98.1% |
CHAPTER 5. CONCLUSION AND FUTURE WORK

As mentioned in Section 1.2, this research aimed to automate the detection of diabetic retinopathy from color fundus images. This work has been implemented on the basis that retinopathy is a vascular disease and the major anomalies are a manifestation of either rupturing of the blood vessels or growth of excess vessels. The textural contrast features provide a description of how pixels are spatially interrelated in different directions. Fractal features describe the shape of the profile. It also characterizes the presence of different lesions or spots in the image.

Experiment 1 utilizes the entire set of seven features whereas experiment 2 uses the essential features based on feature ranking technique. In both cases, it is demonstrated that a combination of the two sets of features is required for robust classification that is rotation invariant, translation invariant and scaling invariant. The concept of adaptive mask generation for local entropy thresholding makes the system flexible to any retinal fundus image. The research provides a comprehensive approach in terms of machine learning by conducting classification using two well-known supervised learning techniques. Also, the classification accuracy attained using both ANN and SVM are comparable to and better than the results of other methods implemented in the literature.

Recommendations for future work involve building a hardware prototype using microcontrollers and digital image processors. This could be used in designing a model for e-health system that can aid ophthalmologists as an effective diagnostic tool. It could also be used as the principle screening method in less advanced countries allowing sophisticated diagnosis being made available via digital photographs taken in remote
areas to identify those at risk. This research could be extended to identify early vessel changes before they could be detected by the human eye. In addition, this research could form the basis for a multi-sensory data fusion model in order to monitor diabetes. This research could be extended to identify only the abnormalities in the fundus image based homomorphic filtering techniques. Another major outcome of the research includes incorporating sub-types of NPDR (mild and moderate NPDR) for classification. The research could be carried forward to check the correlation of blood glucose level with the progression of diabetic retinopathy.
REFERENCES


APPENDIX I: PSUDO CODE

Segmentation of retinal vasculature

1. Start

2. Read color fundus image and convert to grayscale

3. Determine size of image

4. Call to function that performs Gaussian filtering
   a. For i = 1 to row_number
      i. For j = 1 to column_number
         1. Calculate impulse response for length, L = 9
         2. Convolve impulse response with input
         3. Elicit maximum response and store
         4. Rotate image
      ii. End
   b. End
   c. Store result as output_stage1

5. Call to function that performs local entropy thresholding
   a. Calculate GLCM for output_stage1
   b. Compute probability of co-occurrence
   c. Divide output_stage1 into foreground and background
   d. Calculate entropies Hf and Hb
   e. Compute optimum threshold

6. Call to function that generates mask
a. Fixed mask for experiment 1 or

b. Calculate standard deviation for input image and based on standard deviation value determine mask

7. Based on mask and threshold value, convert image to binary using *imbw*

8. Blood vessel edge profile image J obtained

9. Stop

Feature Extraction

1. Start

2. Read blood vessel edge profile

3. Calculate GLCM for 0°, 45°, 90° and 135°

4. Calculate respective probabilities of co-occurrences

5. Calculate contrast for 0°, 45°, 90° and 135°

6. Calculate fractal dimension by box-count method and two values of lacunarity using FracLac toolbox in ImageJ

7. Store features as a matrix

8. Stop

Classification

1. Start

2. Initialize dataset to be features

3. Label dataset into respective classes

4. For i = 0.1 to 0.9
a. Divide dataset into training and testing by cross-validation using hold-out parameter i.

b. Classify using ANN and SVM

c. Obtain classification accuracy

d. End

5. Average classification accuracy

6. Stop
APPENDIX II: RESULTS EXTENDED: 3-D FEATURE SPACE
Three feature space - Lacunarity, Lacunarity-foreground and background and Fractal Dimension
APPENDIX III: RESULTS EXTENDED: BLOOD VESSEL EDGE PROFILE MAP

FOR EXPERIMENT 2