A Study and Comparison of Automated Techniques for Exudate Detection Using Digital Fundus Images of Human Eye: A Review for Early Identification of Diabetic Retinopathy

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Abstract Exudates are a visible sign of diabetic retinopathy which is the major cause of blindness in patients with diabetes. If the exudates extend into the macular area, vision loss can occur. Automated early detection of the presence of exudates can assist ophthalmologists to prevent the spread of the disease more efficiently. Hence, detection of exudates is an important diagnostic task. Exudates are found using their high grey level variation. The detection of the optic disc is indispensable in the exudates detection process since they both are similar in terms of color, contrast, etc. Here a study of various techniques like morphological approach, region growing approach, fuzzy c-means clustering technique, k-means clustering techniques is made to suggest a technique for automatic early identification of diabetic retinopathy. These four techniques are implemented and their performances are evaluated based on various metrics like sensitivity, specificity, etc. These algorithms are tested on a small image data base and their accuracies are analyzed with respect to expert ophthalmologist's hand-drawn ground-truths.

Keywords: Exudates, Diabetic Retinopathy, Fuzzy C-Mean, K-Mean, Ground Truth

1. Introduction

Diabetes is a metabolic disorder where in human body does not produce or properly uses insulin, a hormone that is required to convert sugar, starches, and other food into energy. Diabetes mellitus is characterized by constant high levels of blood glucose (sugar). Human body has to maintain the blood glucose level at a very narrow range, which is done with insulin and glucagon. The function of glucagon is causing the liver to release glucose from its cells into the blood, for the production of energy.

Diabetes prevalence has increased steadily in the last half of this century and India accounts for the largest number of people 50.8 million suffering from diabetes in the world, followed by China (43.2 million) and the United States (26.8 million), reveal new figures (Figure 1) released by the International Diabetes Federation (IDF). India continues to be the “diabetes capital” of the world, and by 2030, nearly 9 per cent of the country’s population is likely to be affected from the disease. “This trend will continue till the next 20 years unless significant efforts are made to curb this disease.

Diabetic Retinopathy is retinopathy (damage to the retina) caused by complications of diabetes mellitus, which can eventually lead to blindness. Diabetics can cause weakening in the body’s blood vessels. The blood vessels in the retina are very susceptible to this weakening and can go through a series of changes. These changes may be leakage or closure from the tiny blood vessels (known as capillaries) or the growth of weak, new capillaries that bleed very easily. Small bulges (known as microaneurysms) can develop in the walls of capillaries that leak fluid. The fluid causes the retina to swell (edema) as well as leave behind metabolic waste products known as Exudates.

Exudates are the primary sign of Diabetic Retinopathy (Figure 2(b)). If this swell develops near the centre part of your vision (macula), the central vision may be reduced. If the small retinal vessels close off (capillary closure or capillary drop out) the retina will become oxygen starved (ischemic). When this happens, white patches of oxygen starved retina (cotton wool spots) may remain. This can lead to the growth of new blood vessels (neovascularization) which bleed and leak fluid easily. These vessels can form scar tissue, which the vitreous can pull. This can cause bleeding into the vitreous and/or detach the retina.

Diabetic retinopathy is of two types namely Non-Proliferative Diabetic Retinopathy and Proliferative Retinopathy.
1.1 Motivation

The motivation behind to put this paper is that exudates are the primary visible sign of DR disease and are directly related to retinal edema and visual loss, and also one among the most important retina lesion detectable in retinal images. And also to recommend a technique for automated diabetic retinopathy mass screening system which offload the work of ophthalmologists and also decreases the waiting time of the patients at the hospital to some extent.

1.2 Overview of the paper

Here a detailed study of each exudate techniques listed above is studied and their performances are tested against various performance metrics.

2. Related Works

There have been an increase in the use of digital image processing techniques for the screening of DR after it was recommended as one of the
method for screening DR at the conference on DR held in Liverpool UK in 2005 [1]. Most of the available work done can generally be categorized into screening of Background Diabetic Retinopathy (BDR) and Proliferative Diabetic Retinopathy (PDR) while diagnosis of Severe Diabetic Retinopathy (SDR) has been left for the ophthalmologist. However only few works have really been done in the detection of optic disc, microaneurysms and exudates, while most work done are in vascular abnormalities detection using color fundus images.

Exudates detection and identification was investigated by Phillips et al. [2], [3]. Global and local thresholding values were used to segment exudate lesions and reported a sensitivity of 61% and 100% [3] based on 14 images. Ege et al. [4] located exudates and cotton wool spots in 38 color images. Here initially a combination of template matching, region growing, and thresholding techniques; and finally a Bayesian classifier was used to classify the exudates and cotton wool spots. 62% for exudates and 52% for the cotton wool spots was obtained. Wang et al. [5] addressed the same problem by using a minimum-distance discriminant classifier to identify the retinal bright lesions such as exudates and cotton wool spots. The spherical color space was chosen to represent the color features. Because in this study, the objective was to identify bright lesions, cotton wool spots, were also incorrectly classified as exudates. The image-based diagnostic accuracy of this approach was reported as 100% sensitivity and 70% specificity based on a dataset of 150 images.

Neural Networks (NNs) have also been used to classify the retinal exudates. After median smoothing, the green channels of the images were fed directly into a very large NN (using 20X20 patches, with 400 inputs) in [6]. The NN was trained for five days and the lesion-based sensitivity of the exudate detection method was 93.1%. This performance was the result of classifying the whole 20×20 pixel patches rather than a pixel resolution classification. In [7], also NN based exudate detection was conducted. Here the NN was trained to distinguish exudates from drusen based on 16×16 pixel patches. The authors introduced a hierarchical feature selection method, based on sensitivity analysis to distinguish the most relevant features. The final NN architecture had 11 input variables and achieved 91% lesion-based (patch resolution) performance using 15 retinal images. The reported performance was based on whether each 16×16 pixel patch contains exudates, and no image-based and pixel-level validation was reported. Sinthanayothin [8] applied a recursive region growing technique using selected threshold values in gray-level images. Her paper supposed that the processed retinal images are only including exudates, and other bright lesions were not considered. Here 88.5% sensitivity and 99.7% specificity for the detection of exudates against a small dataset comprising 21 abnormal and 9 normal retinal images was reported. Walter et al. [9] identified exudates from green channel of the retinal images according to their gray-level variation. Here exudates contours were determined using mathematical morphology techniques. Here three parameters namely the size of the local window, which was used for calculation of the pixel local variation, and two other threshold values were used. This technique achieved a pixel resolution accuracy including 92.8% mean sensitivity and 92.4% mean predictivity against a set of 15 abnormal retinal images. In [10] marker controlled watershed transform is used for localization of exudates.

Figure 3: A Sample Fundus Photograph obtained using a Fundus Camera

3. Retinal Image Acquisition Techniques

Retinal Imaging has evolved through many years. However, there are certain sentinel landmarks which have changed the way we view and understand the retina forever. The earliest of these occurred in 400 B.C. when Democritus first proposed the construction of the eye as a hollow tube connected to the brain.

3.1 Overview of Retinal Fundus Photography

There are various imaging systems/techniques available for analysis optic nerves and retina. One such imaging technique is called as “Retinal Photography” or “Fundus Imaging”. This technique is used to take photographs of the retinal area for
diagnostic purposes. Fundus Cameras are used for this purposes and the retinal photographs obtained using them are called as ‘Fundus Images or Fundus Photographs’ (Figure 3).

Retinal Photography is becoming a must in optometric practices. It is not only a tremendous practice builder, but essential in the management of various eye diseases especially glaucoma’s. Photographic documentation of diabetic retinopathy patients helps the ophthalmologists to keep a database of the progression of the disease, its ongoing management and control.

3.2 Fundus Camera

A fundus camera or retinal camera (Figure 4) is a specialized low power microscope with an attached camera designed to photograph the interior surface of the eye, including the retina, optic disc, macula, and posterior pole (i.e. the fundus). Fundus cameras are used by optometrists, ophthalmologists, and trained medical professionals for monitoring progression of a disease, diagnosis of a disease (combined with retinal angiography), or in screening programs, where the photos can be analyzed later.

Figure 4: A Common Type of Mydriatic Topcon Retinal Camera

A fundus camera provides an upright, magnified view of the fundus. A typical camera views 30 to 50 degrees of retinal area, with a magnification of 2.5x, and allows some modification of this relationship through zoom or auxiliary lenses from 15 degrees which provides 5x magnification to 140 degrees with a wide angle lens which minimizes the image by half. Since the instruments are complex in design and difficult to manufacture to clinical standards, only a few manufacturers exist: Topcon, Zeiss, Canon, Nidek, and Kowa.

Generally the fundus camera is of two types, which is based on the dilation pupil of the eye. They are Mydriatic Fundus Camera (requires dilation of pupil). E.g.: Topcon TRC-50DX Retinal Camera and Non-mydriatic (no dilation of pupil is required) Fundus Camera. E.g.: Topcon TRC-NW8 Retinal Camera

4. Pre-requisite for Exudate Detection

The Optic Disc (OD) is the brightest feature of the normal fundus, and it has approximately a vertically slightly oval (elliptical) shape. In colored fundus images, the OD appears as a bright yellowish or white region. The OD is considered the exit region of the blood vessels and the optic nerves from the retina, also characterized by a relatively pale view owing to the nerve tissue underlying it. Measured relatively to the retinal fundus image, it occupies about one seventh of the entire image [11]. Alternatively, according to [14], the OD size varies from one person to another, occupying about one tenth to one fifth of the image.

The optic disc is considered one of the main features of a retinal fundus image for automatic detection of exudate [11], [12]. The OD often serves as a landmark for other fundus features; such as the quite constant distance between the OD and the macula-center (fovea) which can be used as a priori knowledge to help estimating the location of the macula [11], [13].

The OD is also used as an initial point for retinal vasculature tracking methods [13], [14]; large vessels found in the OD vicinity can serve as seeds for vessel tracking methods. Also, the OD-rim (boundary) causes false responses for linear blood vessel filters [15]. The change in the shape, color or depth of OD is an indicator of various ophthalmic pathologies especially for glaucoma [16], thus the OD dimensions are used to measure abnormal features due to certain retinopathies, such as glaucoma and diabetic retinopathies [14], [17]. Furthermore, the OD can initially be recognized as “one or more” candidate exudates regions one of the occurring lesions in diabetic retinopathies [16] due to
its similarity of its color to the yellowish exudates. Identifying and removing the OD improves the classification of exudates regions [18].

The process of automatically detecting or localizing the OD aims only to correctly detect the centroid (center point) of the OD. On the other hand, disc boundary detection aims to correctly segment the OD by detecting the boundary between the retina and the nerve head (neuroretinal rim). Some methods estimated the contour (boundary) of the OD as a circle or an ellipse (e.g., [11], [13], [17], and [19]) and other methods have been proposed for the exact detection of the OD contour (e.g., "snakes" which has the ability to bridge discontinuities of the edges [16]).

4.1 Detection of Optic Disc

Here the optic disc is detected using simple thresholding, morphological and edge detection technique. The size of the optic disc is approximately known and as it belong to the brightest parts of the image $f_i$ (luminance), on applying a simple area threshold, a binary image $b$, is obtained which contains some parts of the optic disc as well as bright appearing pathologies like exudates. Exudates are not very big, and they are far from reaching the size of the optic disc. Hence, the biggest particle of the image $b$ coincides with one part of the optic disc.

Here the red channel i.e. $f_r$ of the original image $f$ is considered in order to eliminate large gray level variations within the papillary region. Then filling the vessels is done by applying a simple closing operation with a structuring element $s_i$ that is bigger than the maximal width of vessels. In order to remove large picks, opening is done over the resulting image. Then to extract the contour of the detected optic disc, sobel edge operator is used. Figure 6(a) shows the detected optic disc.

Finally, the detected optic region is eliminated from the original image (Figure 6(c)). Here after only the optic disc eliminated image is used for further exudate detection process.

5. Exudate Detection Methods

Exudates are yellowish intraretinal deposits, which are usually located in the posterior pole of the fundus. The exudate is made up of serum lipoproteins, thought to leak from the abnormally permeable blood vessels, especially across the walls of leaking microaneurysms. They are often seen in either individual streaks or clusters or in large circinate rings surrounding clusters of microaneurysms. They have an affinity for the macula, where they are usually intimately associated with retinal thickening.

Global thresholding is used to detect the large exudates, while local thresholding is used to detect the lower intensity exudates [3]. Huiqi Li et al. proposed an exudate extraction technique by using a combination of region growing and edge detection techniques. The optic disc is also detected by principal component analysis (PCA). The shape of the optic disc is detected using a modified active shape model [16]. Sanchez et al. Combined color and sharp edge features to detect the exudates. The yellowish objects are detected first; the objects in the image with sharp edges are then detected using Kirsch’s mask and different rotations of it on the green component. The combination of results of yellowish objects with sharp edges is used to determine the exudates [24]. Hsu et al. presented a domain knowledge based approach to detect exudates. A median filter is used to compute an intensity difference map. Dynamic clustering is then used to determine lesion clusters. Finally domain knowledge is applied to identify true exudates [25]. Usher et al. detected the candidate exudates region by using a combination of RRGs and adaptive intensity thresholding [26]. Goh et al. used the minimum distance discriminant to detect the exudates. The spectrum feature center of exudates and background are computed and then the distance from each pixel to class center is calculated. The pixel is classified as exude if it falls within the minimum distance [27].

5.1 Comparison of various techniques

As stated in [19], it is the green channel ($f_g$), in which the exudates appear most contrasted. Hence, only green channel of the optic disc eliminated RGB image (Figure 6(d)) is going to be used for detection of exudates.

5.1.1 Morphological Approach.

The morphological approach used for detecting exudates is in accordance with [21]. Here, first the vessels are eliminated by a closing with structuring $s_i$ is larger than the maximal width of the vessels i.e. $c = f_g \bullet s_i$. Filling the holes by reconstructing the image from its borders is done in order to obtain the whole candidate regions rather than their borders. The candidate region is dilated in order to ensure that there are background pixels next to exudates that are included in the candidate regions. Then watershed is applied and with histogram matching and only the high intensity regions i.e.
exudates are obtained. Sobel edge detector is applied to get the contour of the exudates.

1. Find all connected components in \( S_g(x,y) \) and erode each connected components to one pixel; label all such pixels found as 1. All other pixels in \( S_g \) are labelled 0.

2. Form an image \( f_{gQ} \) such that, at a pair of coordinates \((x,y)\), let \( f_{gQ}(x,y)=1 \) if the input image satisfies the given predicate, \( Q \), at those coordinates; otherwise, let \( f_{gQ}(x,y)=0 \).

3. Let \( g \) be an input image formed by appending to each seed point in \( S_g \) all the 1-valued points in \( f_{gQ} \) that are 8-connected to that seed point.

4. Label each connected components in \( g \) with a different region label (e.g., 1,2,3,...). This is the segmented image obtained by region growing.

5.1.3 Fuzzy C-Means Clustering Technique.

The exudates can be segmented using Fuzzy C-means algorithm. The Fuzzy C-means (FCM) algorithm is an iterative clustering method that produces an optimal c partition, which minimizes the weighted, within group sum of squared error objective function \( J_q(U, V) \) [23]:

\[
J_q(U, V) = \sum_{k=1}^{n} \sum_{i=1}^{c} (u_{ik})^q d^2(x_k, v_i)
\]

where \( X = \{X_1, X_2, ..., X_n\} \subseteq \mathbb{R}^n \), \( n \) is the number of data items, \( c \) is the number of clusters with \( 2 \leq c \leq n \), \( u_{ik} \) is the degree of membership of \( x_k \) in the \( i \)th cluster, \( q \) is a weighting exponent on each fuzzy membership, \( v_i \) is the prototype of the centre of cluster \( i \), \( d^2(x_k, v_i) \) is a distance measure between object \( x_k \) and cluster center \( v_i \). A solution of the object function \( J_q \) can be obtained via an iterative process, which is carried as follows:

1) Set values for \( c, q, \) and \( \epsilon \).

2) Initialize the fuzzy partition matrix \( U \).

3) Set the loop counter \( b=0 \).

4) Calculate the c cluster center \( V^{(b)}_i \) with \( U^{(b)} \):

\[
V^{(b)}_i = \frac{1}{\sum_{k=1}^{n} (u_{ik}^{(b)})^q} \sum_{k=1}^{n} (u_{ik}^{(b)})^q x_k
\]

Figure 5: Flow Chart Representation

5.1.2 Region Growing Approach.

The seed based region growing approach can be used to segment exudates. Let \( f_g(x,y) \) denote an input image array \( S_g(x,y) \) denote a seed array containing 1s at the locations of seed points and 0s elsewhere and \( Q \) denote a predicate to be applied at each location \((x,y)\). Arrays \( f \) and \( S \) are assumed to be of the same size. Arrays \( f_g \) and \( S_g \) are assumed to be of the same size. A basic region-growing algorithm based on 8-connectivity may be stated as follows [22].
5) Calculate the membership \( U^{(b+1)} \). For \( k=1 \) to \( n \), calculate the following:

\[
I_k = \{ 1 \leq i \leq c, d_{ik} = \| x_k - v_i \| = 0 \}
\]

\[
\tilde{I}_k = \{ 1, 2, ..., c \} - I_k
\]

for the \( k^{th} \) column of the matrix, compute new membership values:

a) If \( I_k = \varnothing \), then

\[
u_{ik}^{(b+1)} = \frac{1}{\sum_{j=1}^{c} \left( \frac{d_{ik}}{d_{jk}} \right)^2 (q-1)} \]

b) Else \( \nu_{ik}^{(b+1)} = 0 \) for all \( i \in \tilde{I}_k \) and \( \sum_{i \in I_k} \nu_{ik}^{(b+1)} \); next \( k \).

6) If \( \| U^{(b)} - U^{(b+1)} \| < \varepsilon \), stop; otherwise, set \( b = b+1 \) and goto step 4.

5.1.4 K-Means Clustering Technique.

K-mean clustering (Figure 6(h)) is used to segment exudates. Let \( A = \{ a_i | i = 1, ..., f \} \) be attributes of \( f \)-dimensional vectors and \( X = \{ x_i | i = 1, ..., N \} \) be each data of \( A \). The K-means clustering separates \( X \) into \( k \) partitions called clusters \( S = \{ s_i | i = 1, ..., k \} \) where \( M \in X \) is \( M_i = \{ m_{ij} | j = 1, ..., n(s_i) \} \) as members of \( s_i \), where \( n(s_i) \) is number of members for \( s_i \). Each cluster has cluster center of \( C = \{ c_i | i = 1, ..., k \} \). K-means clustering algorithm can be described as follows [24].

1) Initiate its algorithm by generating random starting points of initial centroid \( C \).

2) Calculate the distance \( d \) between \( X \) to cluster centre \( C \). Euclidean distance is commonly used to express the distance.

3) Separate \( x_i \) for \( i=1...N \) into \( S \) in which it has minimum \( d(x_i, C) \).

4) Determine the new cluster centres \( c_i \) for \( i=1...k \) defined as:

\[
c_i = \frac{1}{n_i} \sum_{j=1}^{n(s_i)} m_{ij} \in S_i
\]

5) Go back to step 2 until all the centroid converges.

The sample results of all the various exudate detection techniques are show below in figure 6.

6. Analysis

The images used here in this project have been obtained from Dr. Agarwal’s Eye Hospital, Tirunelveli with a “CANON 12 Megapixel Camera” on “ZEISS FF450 PLUS Fundus Camera”. They provided with 15 digital retinal fundus images with exudates and also along with various retinal abnormalities which were obtained from different patients at various point of time. But many images does not meet with the criteria’s that were needed and only 5 images met with expected criteria.

The algorithms are implemented and the performance of each algorithm is measured by comparing the obtained results with the ophthalmologist’s hand-drawn ground truth. Eight performance measurements, namely, True Positive (TP, a number of exudates pixels correctly detected), False Positive (FP, a number of non-exudate pixels which are detected wrongly as exudate pixels), False Negative (FN, a number of exudate pixels that are not detected), True Negative (TN, a number of non-exudates pixels which are correctly identified as non-exudate pixels), Sensitivity, Specificity, Positive Predictive Value (PPV), and Accuracy are calculated.

Equations below show the computation of Sensitivity, Specificity, PPV (Positive Predicate Value) and Accuracy, respectively:

\[
\text{Sensitivity} = \frac{TP}{TP + FN}
\]

\[
\text{Specificity} = \frac{TN}{TN + FP}
\]

\[
\text{PPV} = \frac{TP}{TP + FP}
\]

\[
\text{Accuracy} = \frac{TP + TN}{TP + FP + FN + TN}
\]

The results of various algorithms used here are compared against the ophthalmologist’s hand drawn ground truth and their performances are tabulated below in Table 1. The average performance of all 4 techniques is plotted as graph (Figure 7 to Figure 10) below.
7. Conclusion

Here a detailed study on exudate detection techniques for early identification of Diabetic Retinopathy (DR). An automated DR detection system is a very important need due to the growing up number of diabetic patients around the world. For this automated system, in this paper a number of algorithms are surveyed and four algorithms are found to give better results as far as exudate detection is concerned. Here the performances of various algorithms have been presented with a small database. From the various performance metrics Fuzzy C-Means algorithm detects exudates more accurately than other 3 algorithms with a sensitivity of 92.08%, specificity of 99.52%, PPV of 86.66% and accuracy of 99.87% and also some lower amount of false positive regions are noticed. Even then due to its high accurate detection rate Fuzzy C-Means Algorithm is suggested for exudates detection of an automated system which aims at the mass screening of people with Diabetic Retinopathy.

Table 1: Analysis Table

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<th>FN</th>
<th>TN</th>
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<td>90.08</td>
<td>99.96</td>
<td>91.47</td>
<td>99.93</td>
</tr>
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SAMPLES OF OBTAINED RESULTS

6 (a) Original Image

6 (b) Optic Disc Detected Image

6 (c) Optic Disc Eliminated Image

6 (d) Green Channel Image
6 (e) Morphological Approach
6 (f) Region Growing Approach

(g) Fuzzy C-Mean Approach
6 (h) K-Mean Clustering Approach

6 (i) Ground Truth

Figure 6: Sample Results Obtained for Various Exudate Detection Techniques
Figure 7: Sensitivity Analysis Graph

Figure 8: Specificity Analysis Graph
Figure 9: Positive Predictive Analysis Graph

Figure 10: Accuracy Analysis Graph
8. References


