Detection of Diabetic Retinopathy Using Blood Vessel Segmentation in Digital Fundus Image: A Review

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Abstract

Diabetic Retinopathy (DR) is the effect of diabetes mellitus to the human vision, which the major cause of blindness. Early diagnosis of DR is an important requirement in diabetes treatment and may allow easier medication to any other disease. Retinal fundus image is commonly used to observe the diabetic retinopathy symptoms. It can present retinal features such as blood vessel, optic disc, or macula and also captured the pathologies which may lead to DR. Blood vessel is one of retinal features which can show the retina pathologies. It can be extracted from retinal image by image processing with following stages: pre-processing, segmentation, and post-processing. This paper contains a review of public retinal image dataset and several methods from various conducted researches. All discussed methods are applicable to each researcher cases. However, there is further analysis to conclude the best method which can be used for general cases.

*Keywords:* DiabeticRetinopathy; Digital Image Processing; Segmentation Methods; Retinal Blood Vessel

The term Diabetes Mellitus (DM) is used to describe metabolic disorders from several etiologies of metabolism process such as carbohydrate, fat, and protein resulting from defects in insulin disorder [1]. According to Global Prevalence of Diabetes, in the year 2000, it was estimated that there were 171 million of diabetes patient in the whole world and it will be doubled to 366 million by 2030 [2]. While in Indonesia, World Health Organization (WHO) predicted that people with diabetes will rise from 8.4 million in 2000 to 21.3 million in 2030, or the 4th country with the highest number of people with diabetes in the world [3]. According to 2007 Basic Health Research (Riskesdas), death by DM proportion on 45-54 years old age group in urban areas were ranked 2nd with 14.7%, and in rural areas DM is ranked 2nd with 5.8% [4].

One of the diseases caused by the diabetes is retinal disease called Diabetic Retinopathy (DR). Diabetic retinopathy is a very specific retinal vascular complication of diabetes mellitus. It is the main cause of sight loss on people of working age in United States of America. Early diagnosis for diabetes and diabetic retinopathy is necessary for reducing the potential of sight loss [5].

Analysis and detection structural changes on the retinal blood vessel of fundus image is very important to diagnose and detect retinal disease such as diabetic retinopathy, hypertension, AMD, and arteriosclerosis [6]. Early symptoms of those diseases are indicated by retinal blood vessel’s features such as diameter, length, angle, and tortuosity [7]. Retinal blood vessel is the only part of the blood circulation that could be directly observed and studied in detail. Retinal imaging is further used to determine retinal normality and to diagnose or monitor retinal abnormalities. Changes in width and tortuosity of the retinal blood vessel are believed as indicators for diabetic retinopathy risk level [8].

Various researches regarding to blood vessel detection using advanced methods have been conducted by researchers in the last few years. From those researches, it may be concluded that blood vessel detection for diabetic retinopathy diagnosis in digital fundus image basically consists of three steps procedures; pre-processing, segmentation, and post-processing.

This paper is compiled in the following arrangement. In the first section contains elaboration of blood vessel detection on diabetic retinopathy. Afterwards, the second section will explain the used database and method components that used in blood vessel segmentation, such as pre-processing, segmentation, and post-processing. Finally, the last section will draw the conclusion.

1. Materials and Methods
   1. Retinal Image Database

The first step in image analysis process is to determine the retinal image to be analyzed. Retinal image may be collected from direct image shooting or from publicly available database. Some database which are available for retinal image processing, are as follows:

* + 1. DRIVE Database

DRIVE (Digital Retinal Image for Vessel Extraction) is a fundus image database which available for public. Fundus images in this database were collected through diabetic retinopathy screening program in Netherland, from 453 people in the age of 31-86 years old. Fundus images in this database sums up to 40 images with 20 training and 20 testing images [9].

* + 1. STARE Database

STARE Database contains 20 images for blood vessel segmentation, and 10 of them are contain the pathology. Image size on this database is 605x700 pixels with 8 bit per color channel [10].

* + 1. ARIA Online

This database was recorded in 2006 in a research collaboration between St. Paul’s Eye Unit, Royal Liverpool University Hospital Trust, Liverpool, UK, and the Department of Ophthalmology, Clinical Sciences, University of Liverpool, Liverpool, UK. The database consists of three groups: 92 images of age based macula degeneration group, 59 images of retinas that are infected with diabetes group, and 61 images of control group. Standard references used in this database are blood vessel, optical disc, and location of fovea. Images on this database are RGB images with 768x576 pixels with TIFF format [11].

* + 1. ImageRet

This database was recorded in 2008 and divided into two sub databases namely, DIARETDB0 and DIARETDB1. DIARETDB0 contains 130 retina images, 20 of them are normal images while the other 110 are images with various symptoms of diabetic retinopathy. Meanwhile, DIARETDB1 consists of 89 retina images with 5 healthy images and 84 images with light symptoms of diabetic retinopathy. These sub databases were determined by diabetic retinopathy symptoms such as microaneurysms, hemorrhages, hard exudates, and soft exudates. Image size on the database is 1500x1152 in PNG format [11].

* + 1. Messidor

Messidor project database is the largest database with 1200 retina images. These images were collected from 3 different ophthalmology department with the resolutions of 1440x960, 2240x1488, and 2304x1536 pixels. Images in this database were saved in TIFF format. Out of 1200 images, there are 800 images with pupil dilation [12].

* + 1. Review Database

This database contains retinal blood vessel images which used to estimate blood vessel’s width. This database was made by Department of Computing and Informatics, University of Lincoln, Lincoln, UK in 2008 [13].

* + 1. ROC Microaneurysm Set

This database consists of 100 colored fundus images with microaneurysm. The images in this database are 768x576, 1058x1061, and 1389x1383 pixels in JPEG format [11].

* + 1. VICAVR database

VICAVR database is a series of retina images used for AVR or Artery to Vena ratio. This database consists of 58 images with 768x584 pixels resolution [14].

* + 1. CHASE\_DBI database

CHASE\_DBI database is a dataset consist of 28 colored retinal fundus images from Child Heart and Health Study Program patients in England [15].

* + 1. Retinal Vessel Tortuosity Dataset

Retinal Vessel Tortuosity (RET-TORT) dataset consist of normal and hypertensive patient’s retinal image and the information about manually estimated tortuosity. Total of the images are 60 retinal vessel image [16].

* 1. Pre-processing

Pre-processing is used to remove the noise on retina images and to increase the image contrast value on fundus images. Moreover, pre-processing is also used for image normalization and brightness correction to increase the accuracy for the next step.

* + 1. Brightness Level Equalization
       1. Green Channel

Retina’s features or traits can be differentiated by using color as feature descriptor. Saleh et al. [17] identified that green channel generates maximum contrast on retina image, thus differentiating one feature to the other. In Manjiri’s et al. [18] research, green channel shows higher contrast intensity compared with red and blue channel, while Elbalaoui et al. [19] said that green channel has the best contrast compared with the red and blue channels.

* + - 1. Image Normalization

Image normalization is used to minimize intra-image variable in fundus images. Atur Kumar et al, stated that color normalization could be utilized for brightness correction, color modification, and contrast enhancement [20]. Fraz et al, in his research found a variation on intensity of the macula background to the surrounding area that may affect the segmentation process of the blood vessel. To minimize this variation, the reduction of background estimation from the original image is implemented by using 31x31 arithmetic mean kernel [21]. It was similar with L. Xu et al. who reduced background estimation from the original image using 25x25 median filter for background normalization [22]. Forachhia et al. made parameter model to estimate lighting and variable contrast for normalization. This method claimed that it could significantly reduce the image variation [23]. Vlachos et al. used this model for background normalization [24]. Goatman et al. proposed a method for contrast enhancement using image contrast to cover the whole pixel coverages for normalization [25]

* + - 1. Hue Channel

Hue channel in pre-processing plays a role in increasing the blood vessel’s contrast to the background by mapping the original intensity value between 0 and 1[9] [14].

* + - 1. Matched Filtering

Gaussian Shaped is method of matched filter to enhance the blood vessel from the retinal vessel cross section of retinal image. Thin vessel is the main problem of vessel enhancement process. Qin et al. [26] proposed a multiscale matched filter technique to solve this problem. The proposed method could detect both large and small vessels. This method delivers an efficient process to remove noise, so thin vessels can be identified with a precise width evaluation.

* + - 1. Homomorphic Filtering

Homomorphic filtering is a common technique for image enhancement and correction for normalizes the brightness of the whole image and increase the contrast since illumination and reflectance are the component that could not be separated. Two component should be used to improve the image appearance simultaneously, which is the brightness and contrast [27]

* + - 1. High Pass Filter

High pass filter is a technique that makes an image sharper and make the details of image clearer [27]. This method performs same process as low-pass filter with a different convolutional kernel.

* + 1. Contrast Enhancement
       1. Morphological Operation

Akram et al. proposed a morphological operation to soften the optic disc and brighten the lesions. Marwan et al. [28] used top-hat and bottom-hat transform for contrast enhancement and exhibited dark lesions with minimum background variations. K Sun et al. proposed a multiscale morphological operation for blood vessel’s enhancement [29]. Next, Giancardo et al. proposed a morphological reconstruction for vessel enhancement, such as vessel structure [30].

* + - 1. Gabor Wavelet

Gabor wavelet is used to enhance thin and barely seen vessel pattern. However, the result of Gabor wavelet have a slight blur effect, so non-sharp filter is used to sharpen the vessel’s edge in order to make the vessel clearer than its original image [31]

* + - 1. Histogram Equalization

Histogram equalization aims to distribute intensity value an image input to produce output with even intensity. Tamilarasi et al. used histogram equalization combined with smoothing filter to enhance retina image’s contrast [32]. Antal et al. use histogram equalization (CLAHE) that applied local histogram to deferent area of the input image[33]. in CLAHE, contrast limitation is applied to every pixel to avoid noise amplication. Elbalaoui et al. [34] used CLAHE because it can increase the contrast between contours. When enhancing the contrast image, two factors must be considered, spped and efficiency. Bhattacharjee et al. using CLAHE to enhance the contrast of fundus images which operates on a small region of retinal images, but can generate noise in image [35]. Other contrast enhancement method that can be done with adaptive histogram equalization is by contrast limited adaptive histogram [36]. In this method, the image is split to 8x8 sections and histogram equalization is applied locally to every section of the image [37]. This method is very effective in emphasizing local values in an image. However, this method also generates noise that can disturb the next process [38]. Other histogram equalization development is illumination equalization which uses Global Local Adaptive Histogram Equalization with Partially Overlapped Windows (GLAPOW) algorithm [39]. This technique has a good performance compared with other technique for image fundus. Other contrast enhancement method that also adopts histogram technique is Gray Level Grouping [40]. This method have similarities with histogram equalization technique, but differ on gray level grouping aspects based on its frequency of occurrences.

* 1. Retinal Blood Vessel Segmentation

Segmentation process is the core process in blood vessel detection on retinal fundus image. In this process, blood vessel will be detected on eye retinal fundus image. Detected blood vessel in this segmentation process can be used for further research. The segmentation method covered in this paper is divided in to three major groups namely, image based, pattern recognition based, and vessel tracking/tracing.

* + 1. Image based

Segmentation methods categorized in this group are based on digital image processing operations. These techniques were using image as the primary data. It differentiates these techniques from pattern recognizing technique which requires input image transformation process into values or features. This group may be divided into two major divisions, namely, edge/boundary based and region based or region growing.

* + - 1. Edge/boundary based
         1. Canny Edge Detection

*Canny edge detection* is used to detect edges [41] Smriti’s et al. [9] research applied canny edge detection method for each intensity profile to find the edge of the vessel. The weakness of this method is the lack of segmented image and feature to be extracted.

* + - * 1. Multiscale

Multiscale is a method for blood vessel segmentation in eye retinal fundus image. Uyens et al. [13] research used multiscale line detector method for blood vessel segmentation and Elahe et al. [42] proposed multiscale method for retinal blood vessel segmentation based on weighted two-dimensional (2D) medialness function.

Frangi et al. studied multiscale second order local structure of images (hessian) in the context of vessel filter’s enhancement [43]. Vessel dimensions were derived through Eigen value analysis of the hessian where the second order structure of the image can be outlined. This may directly give the smallest curvature direction along the vessel. Vessel’s dimension is defined using geometric ratio, Eigen value, and Frobenius norm matrix.

Martinez Perez et al. provided scale space analysis method, based on blood vessel’s width, size, and orientation [44]. This method uses two main geometrical features and the second order of the intensity (edge and maximum curvature) along the scale space that gives information regarding the image.

Vlascos et al. [45] proposed multi sale line tracking for blood vessel segmentation. Line tracking is initialized in various scale to accommodate various vessel widths.

Tsai et al. [46] proposed automatic vessel segmentation method using hessian matrix. They first choose 25 frames from the contrast’s angiogram to obtain the vessel structure. They subsequently define adaptive feature transformation equations using gray values and scale to improve feature response.

* + - * 1. Matched Filter Method

*Matched filter* is template based method that uses two dimensional linier structure element with Gaussian cross-profile section that is changed or rotated into three dimension to identify the blood vessels cross profile. The result of this process is a binary segmentation of the blood vessel. This method’s weakness lies in the image detection, small vessels are not defined and cannot be validated.

Chaudhuri et al. [47] Proposed two dimensional linear kernel with Gaussian profile for retinal blood vessel segmentation. Profile from the filter is designed to be matched with the blood vessel. Kernel is gradually rotated 15 degrees to fit in different vessels. The highest response of the filter is selected for every pixel and thresholding to generate binary image. Next process is to remove other features besides the vessel. Hoover et al. combined local traits and retinal blood vessel area for segmentation using threshold probing technique on image matched filter [48]. To increase the threshold, this method using iterative of MFR image area. Image analysis method MFR was formulated by Chaudhuri et al [47]. Thresholding with iterative probing is conducted on every parts for every pixel as vessel or non-vessel. Al-Rawi et al. [49] developed Chaudhuri’s et al. matched filter method using search optimization procedure to find the best parameter for matched filter size, deviation standard, and threshold value.

The other matched filter technique is proposed by Cinsdikici dan Aydin that developed a hybrid method from matched filter and *Ant Colony Algorithm* for retinal blood vessel segmentation [50]. Their experiments show the accuracy improvement of the matched filter. The next generation of matched filter method is developed by Odstrcilik et al. [51] and Fazli et al. [52]. Odstrcilik et al. [51] made automatic retinal blood vessel segmentation method. This concept develops two dimensional matched filter. It uses the correlation between local image area and 2D masks matched with vessels width. Fazli et al. [52] uses Gaussian matched filter and its first derivative for retinal blood vessel segmentation. Yao and Chen improved Odstrcilik method using 2D Gaussian matched filter for retinal blood vessel enhancement and simplified with Neural Network. Next 2D Otsu algorithm is used to find the best segmentation result and the vessel generated through regional connectivity analysis[53].

The new matched filter technique proposed by Fazli et al. [54] that conducted retinal blood vessel segmentation using matched filter with two different values from varians parameter. The used filtering techniques is classical matched filtering, proposed modified matched filtering, second derivative from Gaussian function filtering, K-means, and Fuzzy C-means clustering.

* + - * 1. Gabor filter

Gabor filter is widely used for image processing application including image segmentation and image analysis [26] Farnaz’s et al*.* [55] research applied Gabor filtering technique to detect blood vessels in retina image based on wavelet gabor because gabor filter are better for the segmentation. It can detect specific features in retinal image.

* + - 1. Region based/ Region Growing

The vessels segmentation process can also be prefixed with region growing technique to begin the process of reconstruction of blood vessels in retina of fundus image.

Elahe *et al.* [42] developed vessel reconstruction with vessels radius estimation based on information obtained from vessel *centerline* extraction use eigenvalueand result of medialness function and vessel reconstruction using the estimated radius and the vessel’s graph. while on research of Xiao *et al*. [56] applied *region growing* for vessel segmentation thin curved to solve the failing segmentation for retinal vessels by previous level set method.

* + 1. Pattern recognition based
       1. Feature Extraction

Segmentation process with classification technique require the features extraction. It is necessary for performing an efficient segmentation process. Not all pixels in the image are segmented but only certain features in an image. The process of defining the features or characteristics of the image that most efficient or more meaningful, which represents important information for analysis and classification. This stage extracts features of pixels in image [57].

* + - * 1. *Morphological Method*

Morphological method is used to extract image component and determine the region such as, feature, boundaries, and skeleton. Two main morphological operators which used are dilation and erosion*.* Dilationexpands the object with structuring the element, filling the *holes*, and connecting the area *disjoint*, while *erosion is* depreciation object to the structuring element. The other morphological operation is *closing* and *opening. Opening* is *erosion* followed by *dilation,* while closing is dilation followed by erosion.

Zana et al. combine morphological filter with cross curvature evaluation to segment vessel pattern [58]. The result of this method is relatively strong. Afterward, they merge morphological multiscale enhancement by using fuzzy filter and watershed transformation to extract vascular tree in *angiogram,*  using the method of Sun et al.[59]. This method get important information from shape and area of the vascular. And then, Fraz et al. proposed *vessel centerline detection* combination and *morphological bit plane slicing* to extract blood vessel of retinal image [60]. This method works perfectly in feature of vessel with Gaussian Shaped Profile, but it less suitable for retinal image where arterioles are clear. Other method to improved quality of retinal image is declared by *Singh* et al. [61] which proposed an approach to detect blood vessel with use the morphological to eliminate background and enhancement blood vessel with phase preserving noise removal algorithm. Vessel silhouette extracted by fixed threshold scheme. *Sindhu* et al. segmented blood vessel by using morphological operations with applied threshold [62]. This method is fast and efficient and can be applied to a large amount of images for automatic segmentation.

* + - * 1. *Pattern Classification and Machine Learning*

Pattern classification in blood vessel segmentation is divided into two categories, supervised method and unsupervised method. Supervised method uses label information before deciding whether the pixel is vessel or not, while unsupervised method segments vessel without previous labeling [11].

* + - * 1. *Convolutional Neural Network*

Convolutional Neural Network (CNN) is used as hierarchical features extraction, *e.g.* Shuangling et al. [63] Each targeted pixel, the raw pixel values from the rectangular window is centered and directly given as CNN input. These methods usually fail to capture some of good vessels, but actually these vessel are not essential to the clinical importance.

* + - 1. Classification
         1. *K-Nearest Neighbor (KNN)*

KNN classifier operate on the premise that classification of unknown intances can be done by relating it to the known according some distance or similarity function. Saranya et al. [64] classifying blood vessel using K Nearest Neighbor (KNN) classifier. This method has good performing in segmenting small blood vessel.

* + - * 1. *Neural network*

Neural network is one of the popular classification method in biomedical research. Smrity et al. [9] proposed a neural network classifier for classifying the pixel of vessel into artery and vein. This method gives good performance in classify artery and vein but its performance may be different in other cases. In the other research, Wilfred et al. [65] used backpropagation neural network to classify pixel of retinal image into vessel and non-vessel. It ensures the best performance in the classification stage.

* + - * 1. *Thresholding*

Farnaz et al. [17] proposed thresholding method to classify pixel into vessel and non-vessel. This method can classify image into separate component which changes the image into a binary image. The above method uses gray values for performing the pixel classification. Thresholding process is used for removing unimportant details. Quality of segmentation can be shown from select threshold value.

* + - * 1. *Clustering*

Saranya et al. [64] proposed segmentation method using fuzzy C-means (FCM). FCM is an overlapping clustering algorithm, where each point in image may belong to two or more cluster with different degree of membership. Features with high similarity in the image are grouped into the same cluster. The similarity is defined by the distance of the feature vector to cluster centers. Fuzzy partitioning is carried out through an iterative optimization of the object fuction.

* + - 1. Vessel tracing/ tracking

Vessel tracking method separates vessel between two points using local transformation and works only in one point, not all of the points. Vessel tracking is one of segmentation algorithm which is frequently used. Basically, vessel tracking is principal curve projection algorithm, *e.g.* research conducted by You et al. [36] which used vessel tracking method in segmenting vessel into three attributes of direction, width, and center point. The density distribution of the cross section of a blood vessel is estimated by using a Gaussian shaped function. Individual segments are identified by using a search procedure, which kept track of the center of the vessel and makes some decisions about the future path of the vessel based on certain vessel properties. However, the vessel-tracking method requires a user intervention and may be confused by vessel crossing and bifurcations. To deal with the problem of the central light reflex area in the tracking method, the vessel intensity profiles can be modeled as twin Gaussian functions, and a new method in which the tracking process started from the circumference of the optic disc and applied a Kalman filter as the base to estimate the next search location. It was developed by Chutatape et al. [66] that proposed tracking method with Gaussian and Kalman filter to detection retinal vessel in retinal images. Gaussian matched filter used for estimating the center point of vessel and Kalman filter used for estimating location next vessel segment. Thus, Delibasis et al. [67] proposed automatic tracing model to segment and estimate the vessel. The algorithm is used vessel parametric model. This model describe line as definition of parameter. MoM (measure of match) is used to calculate the similarity between model and image. Pixel initialization for tracking vessel is realized by using *multiscale vesselness filter* and divide the binary output and choose which pixel with null value as seed. Vessel tracking is obtained from the best stripe identification which is matched with the vessel by using the seed point, strip orientation, size of stripe and MoM. The new research of tracking method is tracing of retinal blood vessel through edge information by Khadijah et al. [68] that improved algorithm for tracking vessel. This method can be the basic for an automated detection disease such as stroke and diabetic.

* 1. Post-processing

Post-processing is the final process in the research. This process aims to increase, sharpen, and correct the segmentation process results. Post-processing makes a better result of detection and segmentation. The post-processing can also remove unnecessary region and focus to the vessel [61]

Some post-processing techniques are implemented to increase the accuracy of segmentation [26]. The segmented image then convolved with 3x3 median filter to reduce salt and pepper noise. Length filtering along with some morphological operators are used to remove isolated pixel [69] and Xiao et al. [56] proposed two steps of post-processing from the final segmentation result. The first step is combined with different retinal vessel segmentation results which derived from the level set method and region growing. The second step is to remove false detection of the isolated vessel pixels.

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| --- | --- | --- | --- | --- | --- |
| **Morphological Method** | | | | | |
| Paper | Year | Database | Sensitivity | Specificity | Accuracy |
| Zana et al. [58] | 1999 | DRIVE | 0.6971 | - | 0.9377 |
| Fraz et al. [60] | 2011 | DRIVE  STARE | 0.7152  0.7311 | 0.9769  0.9680 | 0.9452  0.9440 |
| Singh et al. [61] | 2014 | DRIVE  STARE | -  - | -  - | 0.9460  0.9521 |
| Sindhu et al. [62] | 2013 | DRIVE | 0.96 | 0.89 | 0.93 |
| **Matched Filter Method** | | | | | |
| Paper | Tahun | Database | Sensitivity | Specificity | Accuracy |
| Chaudhuri et al. [47] | 1989 | DRIVE  STARE | -  - | -  - | 0.8773 |
| Hoover et al. [48] | 2000 | STARE | 0.6751 | 0.9567 | 0.9267 |
| Al-Rawi et al. [49] | 2007 | DRIVE | - | - | 0.9535 |
| Cinsdikici dan Aydin [50] | 2009 | DRIVE | - | - | 0.9293 |
| Odstrcilik et al. [51] | 2013 | DRIVE  STARE | 0.7060  0.7847 | 0.9693  0.9512 | 0.9340  0.9341 |
| Fazli et al. [52] | 2013 | DRIVE | - | - | 0.9353 |
| **Vessel Tracking/ Tracing Method** | | | | | |
| Paper | Year | Database | Sensitivity | Specificity | Accuracy |
| Khadijah et al. [68] | 2014 | DRIVE  STARE | - | - | 0.9391  0.9335 |
| **Multi Scale** | | | | | |
| Paper | Year | Database | Sensitivity | Specificity | Accuracy |
| Martinez Perez et al. [44] | 1999 | DRIVE | 0.6389 | - | 0.9181 |
| Vlacos et al. [45] | 2013 | DRIVE | 0.747 | 0.955 | 0.929 |
| Tsai et al. [46] | 2013 | - | - | - | 0.9566 |
| Han et al. [70] | 2014 | DRIVE  STARE | 0.6770  0.7043 | 0.9871  0.9869 | 0.9473  0.9573 |

1. Conclusion

This paper evaluates methods for detection of diabetic retinopathy through vessel segmentation of retinal image. The processes involves image database, pre-processing, segmentation and post-processing. All discussed methods are applicable to each researcher’s unique cases. However, there is no further analysis to conclude the best method in general. Each method has advantages and disadvantages, which depends on the condition and needs of researchers.

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