Retinal Vessel Detection and Measurement for Computer-aided Medical Diagnosis

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Abstract Since blood vessel detection and characteristic measurement for ocular retinal images is a fundamental problem in computer-aided medical diagnosis, automated algorithms/systems for vessel detection and measurement are always demanded. To support computer-aided diagnosis, an integrated approach/solution for vessel detection and diameter measurement is presented and validated. In the proposed approach, a Dempster–Shafer (D–S)-based edge detector is developed to obtain initial vessel edge information and an accurate vascular map for a retinal image. Then, the appropriate path and the centerline of a vessel of interest are identified automatically through graph search. Once the vessel path has been identified, the diameter of the vessel will be measured accordingly by the algorithm in real time. To achieve more accurate edge detection and diameter measurement, mixed Gaussian-matched filters are designed to refine the initial detection and measures. Other important medical indices of retinal vessels can also be calculated accordingly based on detection and measurement results. The efficiency of the proposed algorithm was validated by the retinal images obtained from different public databases. Experimental results show that the vessel detection rate of the algorithm is 100 % for large vessels and 89.9 % for small vessels, and the error rate on vessel diameter measurement is less than 5 %, which are all well within the acceptable range of deviation among the human graders.

Keywords Computer-aided medical diagnosis · Image processing · Computer vision · Artificial intelligence

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Introduction

The eyes of a human are the window of his/her vascular system, which is uniquely accessible for doctors to study the health of people. Many research studies have shown that retinal vessel appearance is an important indicator for many diseases which include blood pressure, diabetes, hypertension, arteriosclerosis, etc. These diseases can be analyzed and diagnosed by studying and measuring vessel features, such as vessel diameter, tortuosity, and branch geometry. These features can also provide great help in calculating other cardiovascular-related characteristics such as volumetric flow, velocity of flow, velocity profile, and vessel wall shear stress for circulatory and respiratory systems. For vessel feature measurements, delineation of the boundary, centerline, and diameter of blood vessels is the fundamental of the measurement of other features. It is a sophisticated issue to calibrate these measures correctly, objectively, and automatically. For the applications, such as automatically measuring the features of retinal vessels, the essential task is to design a reliable and intelligent system in which the knowledge of medical image analysis, computer vision, and decision making are integrated properly for accurate feature measurement. Figure 1 shows the eyeball structure and a retinal image captured through a retinal imaging device.

The developed methods for vessel detection can be roughly classified into three categories: the edge detection-based, the segmentation-based, and the probing-based. The edge detection-based algorithms use gradient masks to identify edge points between regions in a retinal image. Vessel boundary is then located according to the intensity discontinuity. The simplest method to find edge points is through the use of an N by N convolution mask kernel. Gradient operators, such as Sobel operators, line masks, etc., can be used for edge detection as well. For the images degraded by noise, mathematical morphology techniques and optimal methods are good to be

Fig. 1 **a** Eyeball structure and **b** retinal image

used to obtain accurate detection results (see [1]). In the edge-detection-based methods, one well-known method is utilizing matched filter response (MFR) [2] for vessel detection. Several modified versions of MFR are reported in [4]. A recent development of using multiscale-matched filters for retinal vessel centerline extraction is proposed in [5]. The strength of MFR is its ability to stress the edge points while degrading the other non-edge points. However, an important weakness of MFR is its high computational cost and unguaranteed convergence.

For the segmentation-based methods, the simplest one is using a single threshold to partition a retinal image into background and vessel. Optimal threshold methods can provide a considerable improvement over a simply choosing global threshold. Localized or boundary information-based thresholding methods are alternative options. The method reported in [7] is designed for vessel detection in red-free and fluorescein retinal images by using the first and the second spatial derivatives of the intensity image. Deformable model-based segmentation methods, such as the method proposed in [8], are also utilized to detect blood vessel or vessel-like pattern in 2D and 3D space. In [9], Staal et al. propose a ridge-based vessel segmentation method to identify vessel centerlines. The AdaBoost method [10] is also proposed for retinal pixel classification by analyzing a high-dimensional feature vector extracted for each image pixel. For the images with inhomogeneous illumination distribution and/or heavy noise, the correctness of vessel segmentation is difficult to be guaranteed, and its computational cost is expensive as well.

The probing-based methods utilize a profile model to incrementally step forward along the inspected vessel, and identify vessel boundary during probing. In [11], Hough transform is first used to locate a start point for the inspected vessel in a retinal image. Then, vessel tracing operation is started from the selected start point. The probing will be stopped when some predefined criteria are met. Zhou et al. propose a method [12] that relies on a 1D-matched filter with priori knowledge on retinal-vessel properties. In a recent study reported in [13], a vessel parametric model is proposed for actively tracing vessel and building vessel tree via retinal vessel model and bifurcation analysis. The merit of this kind of methods is that their 1D or 2D matched filter/model can

provide more accurate results on vessel edge measurement and diameter than the methods of the other categories if the initial settings of the matched filter/model are assigned properly. Its drawback is the proclivity for termination or wrong decision at vessel bifurcations, vessel crossovers, and the places where a sharp direction change happens to a vessel. Another limitation is their reliance upon the initial direction estimation made at the start point.

In this paper, an integrated approach for detecting and delineating blood vessels in retinal images is addressed. The proposed method utilizes the strengths of both the edge detection- and the probing-based methods. Once the start point and the end point of a vessel of interest in a retinal image have been selected by a doctor or a grader, the vessel path, boundary, centerline, and diameter of the vessel can be automatically and accurately identified, measured, and displayed in real time.

The paper is organized as follows. The details of the proposed approach are described in “[Retinal Vessel Detection and Diameter Measurement](#)” section. In the “[Experimental Results](#)” and “[Application on Arteriolar-to-Venular Ratio Estimation](#)” sections, some experimental results and a sample application are reported to demonstrate the efficiency of the proposed approach. The paper ends with a “[Conclusions](#)” section.

Retinal Vessel Detection and Diameter Measurement

To measure a vessel of interest, the edges of the vessel needs to be detected first and its path should be identified automatically as well for measurement. In order to do that, initial vessel edge information and a vessel map for an input retinal image should be obtained and created by the vessel detection and measurement algorithm/system to provide the convenience for the user (either a doctor or a grader) to select the vessel of interest. An information fusion-based edge detector, called Dempster–Shafer fusion-based detector, is developed in this paper to generate a vessel map with more accurate and continue vessel edge information by leveraging the strengths of both Laplacian and Canny edge detection filters. After a start and end points of a vessel of interest have been selected

by the user, a global search algorithm, called A*-based search, is proposed to be used to identify the vessel path quickly no matter how many vessel crossovers and bifurcations will happen between the start and end points, which is a big challenge for the probing-based vessel detection methods. Once the path has been identified, the diameter of the vessel of interest is measured accordingly based on the information provided by the vessel map. Then, mixed Gaussian-matched filters are called to refine the vessel detection and measurement result in real time. The proposed algorithm is a fully automatic approach on detecting and measuring retinal vessel individually, but an interactive and semi-automatic algorithm on detecting and measuring all vessels of a retinal image. In computer-aided medical diagnosis, people are more interested in measuring some vessels of a retinal image than the results of the whole image. Another advantage of using the proposed approach is that the detection and measurement operation for a vessel of interest can be completed in real time and provides accurate detection and measurement results at the same time. The details for the proposed approach are provided in the following sections.

Generating Vascular Map via a Dempster–Shafer-Based Edge Detector

An integrated edge filter is proposed to improve the accuracy of vessel edge detection by combining the outputs of a Laplacian of Gaussian (LoG) filter and a Canny filter via a probability-based fusion method, known as Dempster–Shafer fusion (D–S) [14]. To make edge detection more accurate on diameter measurement and more robust to noise, edge thinning and noise reduction operations are integrated in the filter as well.

LoG and Canny Filters

LoG filter is a 2D isotropic measure of the second spatial derivative of a Gaussian while Canny filter [15] can be approximated as a 2D isotropic measure of the first spatial derivative of a Gaussian. For a LoG filter, its output image, the convolution result of the second spatial derivative of a Gaussian and a retinal image, will be processed by a zero-crossing detector to decide which pixels of the output image are edge pixels. A classical LoG filter can be briefly described as follows:

$$g(x, y) = \nabla^2 h * I(x, y) \quad (1.a)$$

$$h(x, y) = \exp\left(-\frac{x^2 + y^2}{2\sigma^2}\right) \quad (1.b)$$

$$\nabla^2 h = \left(\frac{x^2 + y^2 - \sigma^2}{\sigma^4}\right) \exp\left(-\frac{x^2 + y^2}{2\sigma^2}\right) \quad (1.c)$$

where $g(x, y)$ is an output image, $I(x, y)$ is an input image, σ is standard deviation (scaling factor), $h(x, y)$ is a 2D Gaussian function, $\nabla^2 h$ is a LoG filter. Figure 2 shows some examples of the gradient magnitude of an input image at different scales.

A Canny filter considers the mathematical problem of deriving an optimal smoothing filter given the criteria of detection, localization, and minimizing multiple responses to a single edge. Its Gaussian function acts as an image smoother to perform noise reduction. In the edge detection process, a Canny filter uses four filters to detect horizontal, vertical, and diagonal edges. The edge detection operator, which can be Roberts, Prewitt, or Sobel for example, used in a Canny filter returns a value for the first derivative in the horizontal direction (G_y) and the vertical direction (G_x). From the value, the edge gradient and direction can be determined.

$$G = \sqrt{(\partial_x I(x, y))^2 + (\partial_y I(x, y))^2} \quad (2.a)$$

$$\theta = \arctan\left(\frac{G_y}{G_x}\right) \quad (2.b)$$

where $G_x = \partial_x I(x, y)$ and $G_y = \partial_y I(x, y)$. The direction angle of the edge is rounded to one of four angles representing vertical, horizontal, and the two diagonals (0° , 45° , 90° , and 135° for example). Canny filter also introduces the notion of nonmaximum suppression, which means that given the presmoothing filter, edge points are defined as points where the gradient magnitude assumes a local maximum in the gradient direction.

Compared with LoG filter, Canny filter is more sensitive on edge detection in noisy environments and more accurate on identifying edge location. But, one drawback of a Canny filter is that its detection result may contain many broken edges as shown in Fig. 3b because of its localization consideration, and thus cause some boundary information loss. Another drawback is some detected edges are located either inside or outside of the true edge. On the other hand, a LoG filter can generate more continuous edges than a Canny filter does, as shown in Fig. 3c, and thus get more consistent detection results. More discussion on how to use the first and the second derivatives on edge detection in retinal images can be found in [16].

D–S-based Fusion for Edge Detection

To take the advantages from both a LoG filter and a Canny filter, the D–S theory is proposed to be used for fusing the results of LoG filtering and Canny filtering to achieve more accurate and stable results on vessel edge detection. Dempster–Shafer theory developed by Arthur P. Dempster and Glenn Shafer is a mathematical theory of evidence based on *belief functions* and *plausible reasoning*, which is used to

Fig. 2 Multiscale convolution by LoG filtering. **a** Original image. **b** $\sigma=3$. **c** $\sigma=6$. **d** $\sigma=9$

combine separate pieces of information (evidence) to calculate the probability density of an event. More details of the D–S theory can be found in [14]. Since LoG filter applies the second spatial derivative of a Gaussian for edge detection while Canny filter focuses on using the first spatial derivative of a Gaussian for edge detection, they are two independent methods. Therefore, Canny filter and LoG filter can be considered as evidences and their outputs can be taken as events for the D–S fusion. By fusing these events with their confidence score by the D–S rule, more accurate and stable results on vessel edge detection can be expected.

The critical conception of Dempster–Shafer theory is the Dempster rule on combination. The measures of *belief* and *plausibility* are derived from the combined basic assignments. Dempster's rule combines multiple belief functions through their basic probability assignments (m). These belief functions are defined on the same frame of discernment, but are based on *independent* arguments or bodies of evidence. The independence issue is a critical factor when combining evidence and is an important research subject in Dempster–Shafer theory. The Dempster rule of combination is purely a conjunctive operation (AND). The combination rule results in a belief function based on conjunctive pooled evidences. Specifically, the combination, called the joint $m_{1\oplus 2}(A)$, is calculated from the aggregation of two basic probability assignment (bpa)'s m_1 and m_2

$$m_{1\oplus 2}(A) = \frac{\sum_{B \cap C=A} m_1(B)m_2(C)}{1-K} \text{—when } A \neq \phi \quad (3.a)$$

$$m_{1\oplus 2}(\varphi) = 0 \quad (3.b)$$

$$K = \sum_{B \cap C=\varphi} m_1(B)m_2(C) \quad (3.c)$$

where A , B , and C are event sets generated by the D–S fusion, a LoG filter, and a Canny filter, respectively; $m_{1\oplus 2}(\varphi)$ is defined to ignore the conflicting events caused by a LoG filter and a Canny filter; and K represents basic probability mass associated with conflicts determined by summing the products of the bpas of all sets where the intersection is null.

As the outputs of a LoG filter and a Canny filter can be anyone of $\{\text{edge}, \text{non-edge}\}$, which can be denoted as $\{E, N\}$, edge confidence of the LoG filter (m_1) and edge confidence of the Canny filter (m_2) can be considered as two masses. The D–S rule expressed in Eq. (3) becomes

$$m(E) = \frac{m_1(E)m_2(E)}{1-m_1(E)m_2(N)-m_1(N)m_2(E)} \quad (4)$$

where $m(E)$, $m_1(E)$, and $m_2(E)$ are edge confidence of D–S fusion, LoG filter, and Canny filter, respectively. $m_1(N)$ and $m_2(N)$ are non-edge confidence of the LoG filter and the

Fig. 3 Edge detection results with different edge detectors. **a** Original image. **b** Canny filtering. **c** LoG filtering. **d** D–S-based filtering

Canny filter. Non-edge confidence of D–S fusion can be computed by $m(N)=1-m(E)$. The confidence score of the output of the LoG filter can be estimated by

$$m_1(E) = \frac{g(i,j)}{g_{\max}} \quad (5)$$

where $g(i,j)$ is the gradient magnitude of an image pixel (i,j) and $g_{\max}$ is the maximum gradient magnitude of the image. The confidence score of the output of the Canny filter can be calculated by

$$m_2(E) = \frac{g(i,j)}{\text{Threshold}} \quad (6)$$

where *Threshold* is either the max intensity gradient value of the pixels when using the high threshold for low edge sensitivity or the max intensity gradient value of the pixels when using the low threshold for high edge sensitivity.

A confidence map will be obtained by computing edge confidence score ($m(E)$) to each image pixel of the input image. For each $m(E)$, if $m(E)$ is larger than a preset experimental confidence value, its corresponding point (image pixel) will be classified as an edge point. When the preset confidence value is increased, the edges generated by the D–S fusion become thinner and thus some small edges might be lost. On the other hand, when the preset confidence value is decreased, the edges detected by the D–S fusion become thicker and more small edges are able to be detected. One example of using a D–S-based edge filter is shown in Fig. 3. As we can see, Fig. 3 shows the D–S filtering has better performance on vessel edge detection than LoG and Canny filtering can achieve.

In our study, before conducting edge detection, all input image pixels were converted to gray scale and normalized into the range of 0–255. The unit of Sigma value of LoG filter is in pixel size and the threshold is in the range of 0–1.0. To determinate the optimized parameter settings of the LoG filter, a coarse-to-fine search strategy (multiscale search) was applied to find the best parameter settings. The same search strategy was also applied to the Canny filter to identify its best parameter settings. Note that besides LoG and Canny filters, the other edge detectors including more sophisticated filters can also be considered to replace the LoG filter and/or the Canny filter for the D–S fusion. Since the multipixel width edges of a blood vessel will reduce the diameter measurement accuracy, edge thinning operation is needed to reduce vessel edges from multipixel width to single-pixel width. In our implementation, an edge thinning operator and a contour-following-based noise filter for noise reduction are integrated (Fig. 4).

Finding Appropriate Vessel Path via Graph Search

By using the proposed D–S fusion edge detector, a vascular map, also known as vascular network, will be generated for the input retinal image. To measure a retinal vessel of interest, people need to indicate which vessel is the vessel of interest. The vessel of interest can be indicated by the user (a doctor or a grader) through simply selecting its start point and end point of the vessel. Once the two points have been selected by the user, the path of the selected vessel will be identified from the vascular map automatically by our proposed A*-based graph search no matter the vessel is overcrossed with one or more vessels or not.

Identifying Vessel Path

Once the two points (the start point and the end point) on or near the vessel of interest have been indicated by the user, the A*-based graph search (a best-first graph search algorithm) will be executed to identify the path of the vessel from the vascular map regardless of how complex the vascular structures might be and how many vessel crossovers and bifurcations it would have.

First if the start point and the end point are not a vessel edge point, two vessel edge points will be identified automatically for the two points via the nearest point search. The two edge points will be named as the start point and the end point to replace the initial ones. Then, a crossing line perpendicular to the vessel edge is generated, which is drawn from the start point and stopped at the opposite edge of the vessel. The line between the start point and the intersection point of the opposite edge is called as Start Line. With the same operation, the End Line can be identified as well.

A region-growing process is conducted to fill up the local region enclosed by the vessel boundaries, the start line, and the end line as illustrated in Fig. 5a. Then, a thinning operation is executed to identify the vessel centerlines which construct a local skeleton map as illustrated in Fig. 5b.

If the vessel has no over-cross with other vessels or no bifurcation between the start line and the end line, the local skeleton map will be a single curve. In this case, no path search is needed. The curve will be the centerline of the vessel of interest. But in most cases, the vessel has one or more crosses with other vessels, and/or bifurcations. Path search in the local skeleton map is needed to identify the correct (the desired) path, which is not a trivial problem. Here, a graph theory-based search algorithm, named A* search [17], is proposed for finding the vessel path. One search example is shown in Fig. 5c.

A*-based Path Search

A* is a best-first graph search algorithm that finds the least-cost path from a given start node to the end node (goal node) when all image nodes (image pixels) are represented by a tree

Fig. 4 Example of vascular map generation with the D–S-based edge detector. **a** Input image (350×260 pixels). **b** Result after D–S-based edge detection. **c** Result after edge thinning. **d** Result after the contour-based filtering with a predefined filter size (10 pixel length)

structure. It uses a distance-plus-cost heuristic function (usually denoted as $f(n)$) to determine the order of the nodes which the search will visit. The distance-plus-cost heuristic is a sum of two functions:

$$f(n) = e(n) + h(n) \quad (7)$$

where n is the order of the n th node (image pixel) in the tree, $e(n)$ is the actual shortest Euclidian distance traveled from the start node to the n th node, $h(n)$ is the estimated (or “admissible heuristic”) distance from the n th node to the end node.

The search algorithm starts to probe the vessel path from the start node. The neighboring nodes of the current path node (the start node) will be probed by calculating their f value. After f value calculation, the probed nodes are pushed into an empty priority queue. In the priority queue, the lower the f value of a given node is, the higher its priority is. The node with the lowest f value will be popped out from the queue and become the current path node. The neighboring nodes of the new current path node are probed by calculating their f value and are pushed into the priority queue. If some neighboring nodes of the current path node have already been pushed into

the queue, they will not be pushed into the queue again, but their f value will be updated accordingly. After that, a new path node, which has the lowest f value in the current queue, will be popped out to start a new path search step. The process will repeat until the end node is probed. In our implementation, to assure the correctness of the path search, a new cost factor, named $c(n)$, is included into the distance-plus-cost function, to enhance the continuousness of vessel width during the path search.

$$f(n) = e(n) + h(n) + c(n) \quad (8)$$

where $c(n)$ is the difference of vessel width between the current path node and its predecessor. The new factor will force the path probe go along with the direction which has the less change on vessel width, which means the probing will stay with the vessel of interest well and avoid any possible wrong probing at the overcrosses with other vessels.

Compared with the conventional probing-based methods, the A*-based search method has the advantage of global optimal as it considers all possible paths between the start point and the end point, and chooses the most appropriate path

Fig. 5 Example of vessel path search. **a** Region-growing for vessel path search. **b** Local skeleton map after thinning. **c** Final result (the desired vessel path) after graph search

for the vessel of interest. In the example shown in Fig. 5, the vessel of interest has two overcrosses with another vessel and two bifurcations of itself. In this case, the proposed algorithm can identify the path correctly via graph search while other methods (e.g., the probing-based methods described in [11, 12]) cannot find the right path or provide a wrong output as they only consider the local information (e.g., the centerline direction at the current path node, the change of the local vessel width, the consistency of the local centerline direction, etc.) for path probing.

Vessel Diameter Measurement

Once the path of the vessel of interest has been identified, the diameter of the vessel will be measured automatically. Since the boundary of a vessel of interest was already detected by the proposed edge detector and the vessel centerline was identified during the path search, the initial diameter measure of the vessel of interest can be calculated simply through automatically generating crossing lines perpendicular to the vessel centerline, where each crossing line will have two intersection points with the edges of the vessel, and measuring the distance of the two intersection points for each crossing line.

Vessel Detection and Measurement Refinement by Using Mixed-Gaussian Matched Filters

Vessel edge detection and diameter calculation addressed in the previous sections are under the assumption that the vessel edge after the edge thinning operation will be the true edge. However, many researchers argue this assumption. In this section, a Gaussian-shaped model is used to refine the edge detection results and diameter measurement estimated in the previous sections. The model is based on the fact that the gray density profile along the cross-section of a blood vessel is a Gaussian curve [12] as illustrated in Fig. 6a, b. Once a Gaussian-shaped model has been fitted to a vessel of interest with the initial value estimated in the previous sections, more accurate edge information (edge boundary) and diameter measure can be derived from the Gaussian-shaped model.

In recent years, researchers already noticed that the gray density distributions along the cross-section of a vein and an artery are different. The cross-section of a vein has a single-peak shape as the vein contains a lot of carbon dioxide while the cross-section of an artery has a double-peak shape as the artery contains a large amount of oxide. Based on the fact, a single Gaussian model (see Eq. (9)) and a mixed (twin) Gaussian model (see Eq. (10)) are designed for vein and artery respectively and described as follows:

$$s(p; a) = a_1 \exp \left(- \left(\frac{p - a_2}{a_3} \right)^2 \right) + a_4 \quad (9)$$

Fig. 6 Cross-section of a retinal vessel. **a** Vein. **b** Gray density distribution of the cross-section shown in **a**. **c** Artery. **d** Gray density distribution of the cross-section shown in **c**. Note that *Y*-axis (vertical) of **b** and **d** represents gray value while *X*-axis (horizontal) of **b** and **d** represents width of the vessel

where a_1 is the amplitude of the Gaussian function, a_2 locates the peak position of the curve along the p axis, while a_3 indicates the spread of the Gaussian curve, and a_4 is the gray level of the background.

$$s(p; a) = a_1 \exp \left(- \left(\frac{p - a_2}{a_3} \right)^2 \right) - a_4 \exp \left(- \left(\frac{p - a_5}{a_6} \right)^2 \right) + a_7 \quad (10)$$

where a_1 and a_4 are the amplitude of the two Gaussian functions, respectively, a_2 is the peak position of the first Gaussian curve, and a_5 is the peak position of the second Gaussian curve, while a_3 and a_6 are the spread of the Gaussian curve and a_7 is the gray level of the background. In our current implementation, whether a vessel of interest is vein or artery still needs to be decided manually. Then, an appropriate matched filter will be executed accordingly.

In the proposed algorithm, a nonlinear Levenberg–Marquardt (LM) [18] method is proposed to estimate the coefficients of the mixed Gaussian matched filter. A recursion formula for the LM is defined as:

$$a_{\text{next}} = a_{\text{cur}} - K \times \nabla \chi^2(a_{\text{cur}}) \quad (11)$$

where a_{next} is the new coefficient of the matched filter, a_{cur} is the previous coefficient, K is a constant value, ∇ is the vector of first order derivatives for the steepest descent, and χ^2 is the merit function which is described as:

$$\chi^2 = \sum_{i=1}^N \left[\frac{q_i - f(p_i; a)}{\sigma_i} \right]^2 \quad (12)$$

where P_i is the position along the cross-section, q_i is the gray value of P_i , $f(p_i; a)$ is the current profile model of the Gaussian curve used for P_i , N is the pixel number of the cross-section, σ_i is the permitted standard deviation and changed from pixel to pixel in a certain range. σ_i works as a weighting function to control the contribution of the fitting error of $f(p_i; a)$. When the position P_i is getting closer to the center of the cross-section, its σ_i is becoming smaller.

Before applying LM, an average filter is used to smooth the profile of the cross-section for noise reduction. It is also necessary to rotate the cross-section to horizontal for dimension reduction before conducting the LM-based fitting. Note that the convergence and the executing speed of LM are very sensitive to its initial settings. LM can provide a high accurate estimation on coefficients, but with inappropriate initial values (not close to the true value), LM cannot converge to its global optimum and its computational cost is very expensive as well. Since the initial value of these coefficients will directly affect LM's convergence and calculation cost, LM is not practical on vessel measurement for a long time, which also block the use of mixed Gaussian-matched filters on vessel detection. But in the proposed approach, LM will converge very quickly because the fairly accurate vessel edges and their diameters have already been calculated and set as the initial values for LM. In our study, the computational cost of LM is reduced by a factor of seven on average and the rate of nonconvergence cases is close to zero.

When a Gaussian curve is modeled, the center of the modeled curve will be on the centerline of the vessel and the vessel diameter can be estimated from the σ . In [12], the vessel diameter was suggested as $d=1.98\sigma$ ($\sigma = \sqrt{a_3/2}$), which is based on the fact that the integration within $\pm 0.99\sigma$ reaches 95 % of the integration of the whole domain. But, a more general model expressed in Eq. (13) can provide a closer estimation to the measures made by human, which is taken as the ground truth.

$$d = a\sigma + b \quad (13)$$

where d is vessel width, a and b are a constant value. $d=2.09\sigma+0.96$ were tested. Compared with $d=1.98\sigma$, the accuracy rate of $d=2.09\sigma+0.96$ has an improvement from 89.6 to 95.1 % on average and the detection accuracy on vessel edge boundary are improved accordingly. A visual example given in Fig. 7 demonstrates the difference of the before and the after using a matched filter for edge detection and diameter measurement. More testing results are reported in “Experimental Results” section.

Experimental Results

Twenty red-free retinal images were collected at 30° of field of view (FOV) with the size of 1,520×1,140 pixels (24-bit true

Fig. 7 Vessel edge detection and diameter measurement with and without matched filtering. **a** Measurement before matched filtering. **b** Measurement after matched filtering

color) for algorithm evaluation. The collected images were segmented manually by a trained grader. To make the collected images comparable with the retinal images of the public databases (e.g., STARE and DRIVE), the resolution of the collected images was reduced by half to 760×570. Besides these collected images, the retinal images of STARE (also known as HOOVER database), a public database made available by Hoover et al. [3], were tested as well. STARE consists of 20 red-free retinal fundus images captured at 35° of field of view. Each STARE image was digitized to a 605×700 image with 24-bit true color. The images provided by DRIVE [9], another public database, were also tested for algorithm evaluation. DRIVE has 40 red-free retinal images captured at 45° field of view with size of 768×584 and 8 bits per color channel. The DRIVE images were divided into two sets (one for testing and one for training) with 20 images each. One advantage of the use of STARE and DRIVE images is to provide a common baseline for the comparison with other vessel detection algorithms. All retinal images provided by these databases were segmented manually, which means the databases also provide the ground truth for performance evaluation. In our tests, all these red-free retinal images (RGB images) were converted to grayscale images before conducting vessel detection and measurement.

Tests on Initial Vessel Detection

Except some minor (very thin) vessels smoothed out during vascular map generation, almost all vessels were detected, segmented, and measured successfully by the proposed D–S fusion-based edge detector. For quantity evaluation and validation, 900 vessels including large and small vessels were randomly selected from the collected retinal images and the public available retinal images. These vessels were measured by the proposed algorithm and the results were compared with the ground truth. The success rate on vessel detection is 100 % for large vessels (diameter, ≥ 6 image pixels) and 89.9 % for small vessels (diameter, ≥ 3 pixels and < 6 pixels) as shown in Table 1.

Table 1 Results of initial vessel detection

	Large vessel	Small vessel
Total number	613	287
Detected	613	258
Success rate	100 %	89.89 %
Accuracy rate on edge detection	96.51 %	87.47 %

The accuracy rate on edge detection was also calculated by comparing all detected edge pixels with the true edge pixels delineated by the grader and computing the ratio of the number (N_m) of the matched edge pixels and the number (N_g) of all true edge pixels. More specifically, we first mapped all the detected vessel edges and the ground truth (true vessel edges) to the retinal images and marked them with different status symbols (“detected” and “true”). For each detected edge pixel, if the pixel also marked as “true”, we added a new status symbol (“matched”) for the pixel. If not, we searched all neighboring pixels of the detected edge pixel to see if one or more true edge pixels are its neighbor, and added a new status symbol (“matched”) for the pixel if there is one or more true edge pixels. Once we finished the matching process for all detected edge pixels, the accuracy rates for large-vessels detection and small-vessels detection can be estimated respectively and given in Table 1.

Tests on Vessel Path Search

To evaluate the performance of the proposed path search method, the 900 retinal vessels selected in the previous test were used again for test. For each vessel, the proposed path-search module was executed to identify a vessel path. Through the comparison of the search result and the ground truth (the manual result), we classified the search result as either a proper path or a wrong path. In some cases, path search cannot be completed due to the background noise or the vessel size (too tiny). These failures, denoted as “Track not started”, were also considered as wrong paths. The success rate of the proposed algorithm for path search can reach 97.6 % as listed in Table 2.

Table 2 Results of path search

Category	Vessel
Total number	900
Appropriate path	878
Wrong path	13
Track not started	9
Success rate	97.56 %

Tests on Vessel Detection and Measurement Refinement

Table 3 shows some comparison results on vessel detection and diameter measurement by using LoG, Canny, D–S fusion, and the mixed Gaussian-matched filtering separately. Since the edge detection accuracy of both D–S fusion and matched filtering can reach 0.1 image pixel level, we extended the output accuracy of LoG and Canny edge detectors to 0.1 image pixel level by running one test for ten times with and then using the average result as the final. At each time, we adjusted their thresholds and/or sigma of Gaussian around their optimum values. Then, we averaged these results and got the final result for the test. In this comparison study, the selected 900 vessels were used again for vessel diameter accuracy comparison. The measurement error rate was estimated by computing the difference of the results made by the grader and the proposed algorithm.

$$\delta = \frac{|M_g - M_c|}{M_g} \times 100\% \quad (14)$$

where δ denotes the measurement error rate, M_g and M_c represent the measurement value of the grader and the measurement value obtained with the proposed algorithm. As shown in Table 3, the average measurement error rates of LoG, Canny, D–S fusion, and the mixed Gaussian-matched filter are 13.6, 10.1, 7.0, and 4.5 %, respectively, which shows the mixed Gaussian filtering has the best performance on vessel diameter measurement. Six sample results are also listed in Table 3 to provide some level of details on vessel diameter measurement. Receiver operating characteristic (ROC) curves of these four edge detection operators are provided in Fig. 8 for comparison analysis. Note that these ROC curves were calculated by using the data and method described in “Comparison with Other Vessel Detection and Measurement Algorithms” section.

Comparison with Other Vessel Detection and Measurement Algorithms

The error and accuracy rates of Hoover's method [3], Jiang's method [6], Staal's method [9], and most likely class for STARE images were calculated and reported in [9]. In order to compare the proposed algorithm with others, we repeated the tests reported in [9]. We first detected all retinal vessels located in the FOV (650×550) for all STARE images (20 images) and then calculated the error and accuracy rates for the proposed method. More specifically, according to the vessel detection results, we classified all FOV image pixels of the STARE images into two categories: background and vessel. By comparing with the manually labeled results provided by the database, we calculated the total number of all missed vessel pixels as the number of false negatives (FN), and the total number of all false classified vessel pixels as the number of false positives

Table 3 Comparison of diameter measurement by using LoG, Canny, D–S fusion, and Matched Filter

Vessel (pixel)	Grader result	Result by LoG	Result by Canny	Result by D–S fusion	Result by Matched filter
V1	7.0	7.8	6.8	7.2	7.1
V2	5.0	6.0	4.7	5.0	5.0
V3	3.0	3.8	2.8	3.3	3.2
V4	4.0	4.6	4.5	4.6	4.4
V5	7.0	7.1	5.8	7.0	7.0
V6	4.0	5.0	4.8	4.9	4.5
Measurement error rate (V1–V6)		14.23 %	10.70 %	7.22 %	4.14 %
Avg. measurement error rate of 900 vessels		13.57 %	10.13 %	7.01 %	4.54 %

(FP). Then, we took the total number of all FOV pixels as the sum of true positives (TP), true negatives (TN), FP, and FN. The error rate in this test was computed by

$$e = \frac{FP + FN}{TP + TN + FP + FN} \times 100\% \quad (15)$$

where e is the error rate. The accuracy rate can be calculated by $(1 - \text{error rate})$.

In the test, the vessels with width less than 3 image pixels were also measured if these vessels were reported in the ground truth. Since the error and accuracy rates of the proposed method for STARE images were calculated in the same way as that of Hoover's method, Jiang's method, Staal's method, and most likely class (MLC) reported in [9], we can compare our error and accuracy rates with the others directly. Table 4 lists all rates including ours. From the table, we can see that the proposed D–S fusion-based edge detector has the second best performance on vessel detection compared with the other methods. It is only after Staal's method. However, with the enhancement made by the mixed Gaussian matched filter (MF) the overall performance of our proposed method (D–S fusion plus MF) on vessel detection is the best. ROC curves of Hoover's method, MLC, D–S fusion,

and D–S fusion plus MF are provided in Fig. 9 for comparison analysis. Note that the ROC curves of Hoover's and MLC were calculated by using our implementation of Hoover's method and MLC.

All STARE images were manually segmented by two trained observers. The first observer (grader A) segmented 615,726 pixels as blood vessel and 5,293,034 as the background (10.4 % vessel) while the second observer (grader B) labeled 879,695 pixels as blood vessel and 5,029,065 as the background (14.9 % vessel). The second observer segmented more details (many smaller vessels) than the first observer did. As we can see, there is an obvious variability between the two observers. By the suggestion given in [9], the performance of the proposed method was evaluated based on the segmentations of the first observer as the ground truth because of his stable performance and all experiment were done on the FOV only. Two examples of using STARE images for performance comparison are given in Figs. 10 and 11.

Processing Speed

The algorithm was implemented by Visual C++ in MS Windows environment. For the PC machine with CPU (P4 2.4 GHz) and 4 GB memory running Windows XP operation system, the algorithm can generate the vascular map for a retinal image in near real time. For instance, the average computational time of creating a vascular map for a retinal image with resolution of 760×570 is around 4 s on average.

Fig. 8 ROC Curves of LOG, Canny, D–S, and D–S&MF**Table 4** Comparison results on vessel detection

Method	Error rate (%)	Accuracy rate (%)
Hoover's method	7.25	92.75
Jiang's method	9.91	90.09
Staal's method	4.84	95.16
Most likely class	10.42	89.58
D–S fusion	7.08	92.92
D–S plus MF	4.34	95.66

Fig. 9 ROC curves of Hoover, MLC, D-S, and D-S&MF

The operations of identifying the path of a vessel of interest and measuring vessel diameters are run in real time.

Application on Arteriolar-to-Venular Ration Estimation

Other important indices of retinal vessels can be calculated through the vessel detection and measurement results. In this section, a sample application on indices estimation, arteriolar-to-venular ratio (AVR), was calculated and tested to demonstrate the efficiency of the proposed vessel detection and measurement approach.

1AVR Measurement

An early marker for cardiovascular risk monitoring is the narrowing of retinal blood vessels. To quantify the degree of the narrowing, AVR is calculated by measuring the diameters of individual retinal arteriolar and venular calibers. A low AVR value is associated with high blood pressure and the increased risk of stroke, diabetes, and hypertension. Here, a traditional method on AVR estimation, known as Parr–Hubbard formula based on the Wisconsin protocol [19], was implemented and tested. Before the AVR calculation, two measures, central retinal artery equivalent (CRAE) and central retinal vein equivalent (CRVE), need to be estimated first. The formula for CRAE, CRVE, and AVR ratio can be described as the follows:

$$W_{\text{CRAE}} = (0.87W_a^2 + 1.01W_b^2 - 0.22W_aW_b - 10.76)^{\frac{1}{2}} \quad (16)$$

where W_{CRAE} is the width of the trunk arteriole (CRAE), W_a is the width of a small artery, and W_b is the width of a large artery.

$$W_{\text{CRVE}} = (0.72W_a^2 + 0.91W_b^2 + 450.05)^{\frac{1}{2}} \quad (17)$$

where W_{CRVE} is the width of the trunk vein (CRVE), W_a is the width of a small vein, and W_b is the width of a large vein.

$$\text{AVR} = \frac{W_{\text{CRAE}}}{W_{\text{CRVE}}} \quad (18)$$

Fig. 10 Results of a normal retinal image. **a** Retinal image. **b** Grader A (ground truth). **c** Grader B. **d** Result of Hoovers's method. **e** Result of most likely class. **f** Result of D-S fusion plus MF

Fig. 11 Results of an abnormal retinal image (pathological case). **a** Retinal image. **b** Grader A (ground truth). **c** Grader B. **d** Result of Hoover's method. **e** Result of most likely class. **f** Result of D–S fusion plus MF

More detailed definition of CRAE and CRVE can be found in [19]. AVR is calculated based on the calibers of all arterioles and venules passing through a concentric ring, which is defined as the range of 0.5–1.0 disc diameter (DD) [20] from the optic disc margin. DD is the diameter (about 2×1.5 mm across) of the optic nerve which is a circular to oval white area and centered at the retina. During the calculation of CRAE or CRVE, vessels are paired according to a predefined pattern, where the largest vessel is combined with the smallest vessel, the second largest is with the second smallest, and so on. This process will repeat until the vessels are merged to one. During the iteration, if there are an odd number of vessels, the residual vessel will be carried to the next iteration.

Tests on AVR Measurement

To evaluate the performance of the proposed algorithm on vessel characteristics measurement, CRAE, CRVE, and AVR

were computed for some randomly selected vessels. The error rate defined in “Tests on Vessel Detection and Measurement Refinement” section was calculated as well. Since the coefficients of the equations for computing CRAE and CRVE were estimated based on the data with physical measurement unit (in micrometer), it requires physical measurement values as inputs when the equations are used, which means it needs to convert vessel width from pixel size to physical size before using these equations to compute CRAE and CRVE. The conversion between physical unit and image pixel of our collected images (760×570) is known as $12.8 \mu\text{m}$ per pixel while the conversions of STARE and DRIVE images are unknown. Therefore, only the retinal vessels from our collected retinal images were selected for the evaluation. In the tests, retinal vessels located in the range of 0.5–1.0 disc diameter were selected for CRAE, CRVE, and AVR estimation. The average error rates of CRAE, CRVE, and AVR are shown in Table 5 together with four sample results. From the table, it can be seen that the error rates

Table 5 Results of CRAE, CRVE, and AVR computation

Artery (μm)	Grader result	Auto. result	Vein (μm)	Grader result	Auto. result	AVR	Grader result	Auto. result
CRAE1	182.42	173.82	CRVE1	201.38	192.21	AVR1	0.91	0.90
CRAE2	177.59	190.91	CRVE2	205.62	199.14	AVR2	0.86	0.96
CRAE3	188.54	180.58	CRVE3	203.24	206.88	AVR3	0.93	0.87
CRAE4	189.81	182.19	CRVE4	208.09	197.82	AVR4	0.91	0.92
Error rate for C1–C4	5.11 %		Error rate for C1–C4	3.61 %		Error rate for A1–A4	4.51 %	
Avg. error rate (20 retinal images)	4.13 %		Avg. error rate	4.79 %		Avg. error rate	3.74 %	

of CRAE, CRVE, and AVR can be reduced to as low as 4.1, 4.8, and 3.7 %. Note that if a more advanced algorithm on AVR estimation is selected, lower error rates are expected. The discussion on AVR algorithm selection and implementation is out of the scope of the paper. Interested readers are suggested to read the references ([20, 21, 22]) for more details on AVR, CRAE, CRVE definition, and estimation.

Conclusions

An efficient approach for retinal vessel detection and diameter measurement is addressed. To detect and measure retinal vessel automatically, a D–S fusion-based edge detector and the A*-based graph search were developed to obtain the path of a vessel of interest and its relevant information, such as vessel edge, centerline, and diameter in real time. Then, Gaussian-mixed matched filters were designed and applied to achieve more accurate measures for both veins and arteries. Based on the vessel detection and measurement results, other vascular characteristics can be calculated accordingly. The effectiveness of the proposed approach was validated by our collected retinal images and the public retinal images. The average error rate of the approach on vessel diameter measurement is less than 5 %. Moreover, the proposed approach can be extended for many other applications, such as line-like pattern detection and measurement.

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