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Retinal image registration using topological vascular tree segmentation and bifurcation structures

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ABSTRACT

This paper presents a new retinal image segmentation and registration approaches. The contribution of this paper is two-fold. First, the conventional vessel-tracking methods use local sequential searching, which can be easily trapped by local intensity discontinuity or vessel rupture. The proposed method uses global graph-based decision that can segment the topological vascular tree with 1-pixel width and fully connection from retinal images. Staring from initial multi-scale ridge segmentation, the disconnected vessels are retrospectively connected and then spurious ridges are removed using a shortest path algorithm on a specially defined graph. The hypothesis testing is defined in terms of probability of pixel belong to foreground and background, which enables that the false detections could be removed. Second, the conventional point-matching methods largely depend on the branching angles of single bifurcation point. The feature correspondence across two images may not be unique due to the similar angle values. In view of this, structure-matching registration is favored. The bifurcation structure is composed of a master bifurcation point and its three connected neighboring pixels or vessel segments. The characteristic vector of each bifurcation structure consists of the normalized branching angle and length, which is fairly robust to be against translation, rotation, scaling, and even modest distortion. The experimental results are presented to demonstrate the superior performance of the proposed approach.

1. Introduction

Retinal image analysis is an intense field of research and development in the context of biomedical imaging analysis and computer-assisted diagnosis, due to its capability of automated localization and delineation of structures of interest [1]. This paper studies two fundamental challenges of retinal image analysis: segmentation and registration. Examination of blood vessels in the eye allows detection of eye diseases such as glaucoma and diabetic retinopathy [2]. Image registration is the process of establishing pixel-to-pixel correspondence between two images of the same scene [3]. Retinal image registration is challenging due to the difficulties of modality-varying and time-varying intensities of retinal images.

Retinal vasculature is instrumental in diagnosis and treatment of diseases such as diabetes, hypertension, and arteriosclerosis. For example, ophthalmologists examine the deterioration of diabetes by observing the changes in retinal vessels, such as curvature, width, and the presence of abnormal ruptures. As manual vessel labeling is tedious, the automatic detection and analysis of vasculature becomes a promising tool in screening of retinopathy. In this paper, a retrospective correction approach to obtain connected vessel segmentation is proposed. Staring from initial multi-scale ridge segmentation, the proposed approach retrospectively connects the disconnected vessels and removes spurious regions using a shortest path algorithm on a specially defined graph. Unlike the conventional vessel-tracking approaches, our approach is based on a global graph-based decision.

There are several challenges in retinal image registration. The first difficulty refers to multimodal registration which means medical imaging with different modalities, such as fluoroscein angiography, indocyanine green angiography, and red-free. The second is temporal registration of images taken at different times. In view of this, this paper proposes a new structural feature for feature-based retinal image registration. Different from point-matching techniques, the proposed method is a structure-matching approach. The bifurcation structure is composed of a master bifurcation point and its three connected neighbors. The characteristic

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vector of each bifurcation structure consists of the normalized branching angle and length. It is invariant against translation, rotation, scaling, and even modest distortion. Further analysis and simulation demonstrate that it can greatly reduce the ill-posed nature of the matching process.

The rest of this paper is organized as follows. In Section 2, a brief overview of related works in the area of retinal image segmentation and image registration is presented. Then, a topological vascular tree segmentation method is proposed in Section 3. The feature-based registration algorithm using the proposed bifurcation structure is developed and analyzed in Section 4. Experimental results are reported in Section 5. Finally, Section 6 concludes this paper.

2. Related works

2.1. Retinal image segmentation

Retinal vessels appear darker than the background in color retinal images. However, due to poor contrast and inhomogeneous background, the conventional intensity-thresholding techniques usually cannot yield satisfactory segmentations. This motivates the use of high-pass filtering techniques, such as matched filtering [4] and steerable filtering [5], which are robust to intensity inhomogeneity. More generally, the vessel segmentation problem can be referred to as a ridge detection problem that seeks to trace the center of the line object in retinal images. The ridge is mathematically defined as the local extreme point in the direction of the largest surface curvature. Such a direction can be estimated by computing the largest absolute eigenvalue of the Hessian matrix, making ridge detector invariant to vessel orientation. Ridge detector can identify the vessel centerlines reliably but may produce gaps and disconnections due to the effect of the noise. Resultant segmentation may also contain many spurious vessels due to the high-pass filtering nature of the ridge detector. To further improve the segmentation results, it is necessary to incorporate prior information about the vasculature, such as shape statistics, intensity, connectivity, etc. For example, such prior information can be obtained from a training dataset of manually labeled images [6]. Another example is topologically adaptive snake, which incorporates connectivity constraint into segmentation [7]. This approach extends the traditional snake model to a collection of snakes that are progressively expanded, shrunk, merged, split, and even removed to embrace the complex contours of main vessels.

The common characteristic of retinal vasculature is the spatial continuity of pixels within the vessel in addition to the intensity contrast across the boundary. Nevertheless, when spatial continuity and contrast is poor or in the vicinity of bifurcation points, the disconnection and truncation of vessels becomes a serious problem in forming a vascular tree. Therefore, another research direction involves of vessel tracking. It works by first detecting initial vessels and then exploiting local region properties to track vasculature. Eichel et al. proposes an algorithm based on sequential edge linking that assigns belief values to edges and paths according to a probabilistic model [8]. This method works in similar way to the boundary-based segmentation by tracking a bounded path [9]. The centerline-tracking approaches attempt to link vessels one-by-one based on sequential searching [10–13]. The only prior information needed by the tracking-based methods is the connectivity. However, the sequential searching is a local approach that can be easily trapped by local intensity discontinuity or vessel rupture [14–16]. Nguyen proposed an effective method for automatically extracting blood vessels from color retinal images [17]. Bhuiyan proposed a new technique to measure the retinal vessel caliber, which is an "edge-based" vessel tracking method [18]. In addition, the problem of removal of spurious vessels is not fully addressed.

2.2. Retinal image registration

The registration methods can be classified into several categories including feature-based techniques, gradient approaches, and correlation methods [1]. In feature-based methods, salient and distinctive objects (e.g. edge and corner) are manually or automatically selected for estimating the transformation between image pair, such as translation, rotation, scaling, and distortion. Gradient approaches, originated from optical flow, estimate the translation parameters using linear partial difference equations. The idea behind correlation methods is quite straightforward as that the cross-correlation between the delayed signal and the reference will have a peak at the delayed time. According to Fourier shift property, the Fourier transform of a shifted function is the transform of the un-shifted function multiplied by the phase. Hence, phase correlation method identifies the translation from the normalized cross-spectrum. In similar fashion, rotation and scaling can be estimated with the aid of polar Fourier representation [19].

These motivate the exploitation of robust features such as vasculature and optic disk instead of intensity in retinal image registration [20]. Generally speaking, the feature-based techniques can be classified into region- and point-matching categories. The region-matching approaches consider all the features in a region as a whole and identify the transformation parameters by minimizing the similarity measures. For example, the cost function in [21] is defined as the error between two binary vessel images with consideration of affine, bilinear, and projective transformation models. The similarity measure is formulated as the entropy-based mutual information [22]. The shortcomings of region-matching methods lie in their huge searching space and local convergence when involving of high-order transformation models and inconsistent features.

Point-matching methods, on the other hand, rely on the matched features in both images. The technique consists of two steps: feature matching and transformation estimation. The feature matching process establishes the correspondence between two feature groups. Once the matched feature pairs are reliable, the transformation parameters can be identified easily and accurately. Most of the point-matching methods use bifurcation point as landmark since it is a prominent indicator of vasculature. In [23], the branching angles of each bifurcation point are used to produce a probability for every point pair. Since some bifurcation points may have more than one matched counterpart, a hierarchical method is proposed to solve this dilemma in [24]. The correspondences are refined gradually from the coarse translation model to the fine quadratic model. This idea is extended to the dual-bootstrap *iterative closest point* (ICP) algorithm [25]. The location, branching angle and width of landmarks are taken as the similarity metric. Starting from low-order initial estimates that are only accurate in small bootstrap regions, the dual-bootstrap ICP iteratively decides the optimal transformation model from simple to complex, and expands the bootstrap region from local to global. Another possible way is to search the minimal error by imposing the transformation to any combination of feature points [26]. This exhausted search needs huge computations when the number of feature points increases. The *self-organizing maps* (SOM), an unsupervised neural network that can train itself, provide promising results for multimodal registration [27]. It is well known that when more robust landmarks can be obtained with less computational complexity, the performance of feature-based methods will be improved greatly. However, the aforementioned methods largely depend on the branching angles of single bifurcation point. As such angles have coarse precision leading to similar bifurcation points;