

Robust Segmentation of Corneal Fibers from Noisy Images

Jia Chen
Department of Computer
Science
University of California, Irvine
jiac5@uci.edu

James Jester
School of Medicine
University of California, Irvine
jjester@uci.edu

M. Gopi
Department of Computer
Science
University of California, Irvine
gopi@ics.uci.edu

ABSTRACT

Corneal collagen structure, which plays an important role in determining visual acuity, has drawn a lot of research attention to exploring its geometric properties. Advancement of nonlinear optical (NLO) imaging provides a potential way for capturing fiber-level structure of cornea, however, the artifacts introduced by the NLO imaging process make image segmentation on such images a bottleneck for further analysis. Especially, the existing methods fail to preserve the branching points which are important for mechanical analysis. In this paper, we propose a hybrid image segmentation method, which integrates seeded region growing and iterative voting. Results show that our algorithm outperforms state-of-the-art techniques in segmenting fibers from background while preserving branching points. Finally, we show that, based on the segmentation result, branching points and the width of fibers can be determined more accurately than the other methods, which is critical for mechanical analysis on corneal structure.

CCS Concepts

•Computing methodologies → Computer graphics; Image processing;

Keywords

Image Segmentation; Branching Point Detection; Linear Structure Extraction

1. INTRODUCTION

Cornea, the outermost layer of the eye, serves not only as a protective outer cover but also as the primary refractive element responsible for focusing light back to the retina. M. Winkler, et al. [25] reveal that the cornea is composed of a large number of collagen fibers, and the three-dimensional structural organization of these collagen fibers controls the mechanical properties of cornea, thus further defines its refractive function. Therefore, the fiber level structure of

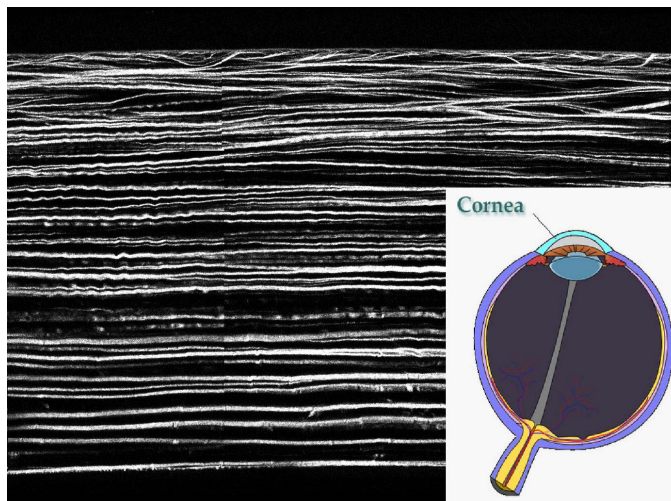


Figure 1: A NLO image of a rabbit's corneal collagen structure. Right bottom: schematic diagram of the eye showing the cornea (Mikael Haggstrom, CCO 1.0)

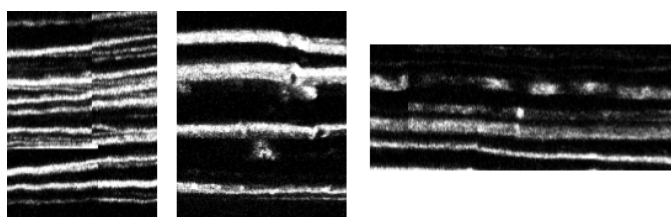


Figure 2: Typical artifacts in NLO image. Left: stitching artifacts Middle: noises Right: missing parts

cornea plays an important role in determining visual acuity, and a large number of research efforts have been devoted to exploring the structure and biomechanical properties of the corneal collagen structure [14] [18]. However, as the fibers within the cornea are approximately only $1\mu\text{m}$ in diameter, researchers have long suffered from lack of imaging technique for capturing such microstructural details.

On the other side, the recent advancement of nonlinear optical imaging (NLO), primarily in the form of second harmonic generation (SHG) imaging, yields very high lateral and axial resolution ($\sim 1\mu\text{m}$) [18]. The high resolution has

Permission to make digital or hard copies of all or part of this work for personal or classroom use is granted without fee provided that copies are not made or distributed for profit or commercial advantage and that copies bear this notice and the full citation on the first page. Copyrights for components of this work owned by others than ACM must be honored. Abstracting with credit is permitted. To copy otherwise, or republish, to post on servers or to redistribute to lists, requires prior specific permission and/or a fee. Request permissions from permissions@acm.org.

ICVGIP, December 18-22, 2016, Guwahati, India

© 2016 ACM. ISBN 978-1-4503-4753-2/16/12...\$15.00

DOI: <http://dx.doi.org/10.1145/3009977.3010051>

made it possible to detect single collagen lamellae and study structural relationship between them. However, the NLO imaging suffers from limitations of signal capturing, and inevitably leads to three major types of image defects, as shown in Figure 1:

(1) **Stitching artifacts:** The range that can be captured by NLO imaging relies on the focal volume of the femtosecond laser beam, therefore the SHG can only be captured in a small field of view (FoV) compared to the whole cornea area[18]. Thus, to generate an image for the whole cornea, a stitching process is required to merge all small captured region together, and this process causes stitching defects, as shown in Figure 1(a).

(2) **Imaging noise:** To achieve NLO imaging’s high precision, the signal receiver used is highly sensitive to even minor noises caused by various factors such as displacement of imaging subject, or environmental change.

(3) **Missing parts:** NLO imaging, which takes advantage of cornea’s anisotropic properties, is able to capture the fibers only when the angle between fiber plane and the signal receiver lies in a limited range. When the angle falls out of the range, the corresponding parts cannot be captured. So when the fibers go in and out of the fiber plane, some portions of the fibers are captured, while the other portions of the same fiber are missed.

In order to extract geometric properties from the corneal images and support further 3D reconstruction and mechanical analysis, a segmentation method robust to the above defects is desired. Although most of the previous image segmentation methods handle image noises to some degree, when applied to corneal image, they tend to diminish branching points while enhancing the linear structure. As the branching points are critical for analysing the fibers’ density, connectivity and distribution [25], preserving branching points is especially important for corneal images, so a segmentation method that is robust to the defects as well as preserving the branching points is desired.

In this paper, we propose a hybrid image segmentation method based on seeded region growing[20] and iterative voting[17]. As seeded region growing is good at preserving minor parts, it avoids two adjacent fibers being falsely merged when they are close to each other, and more importantly, it enhances the branching regions and makes branching point detection easier. Iterative voting robustly identify the linear structural parts and repair broken parts using a pixel’s nearby structure. The integration of seeded region growing and iterative voting finds a balance between linear structure and branching regions. We evaluate the algorithm on images captured by NLO imaging, and compare the result by applying it on two typical jobs of mechanical analysis : branching point detection and linear structure extraction. Results show our algorithm is robust to the typical artifacts in corneal image, and outperforms state-of-the-art algorithms.

2. RELATED WORK

In this section, we give an overview of related work and analyze the previous methods’ performance on noisy images like corneal images.

2.1 Image Segmentation

Image segmentation has a long history in computer vision research. Most of the image segmentation methods

are based on two basic properties of the pixels in relationship to their local neighbourhood: discontinuity and similarity [10]. Popular approaches include: thresholding techniques[24], Snakes[12][7], graph cut algorithms[19] [4], geodesic active contours[6][27], watershed segmentation[23], region growing[1][8][20], level sets[16] etc.

Among them, combinatorial graph cut algorithms have been successfully applied on natural image segmentation [19] [4]. However, the graph cut based methods are used mostly in interactive mode, and when the segmented target is fine structure, it is hard for graph cut algorithm to preserve the fine details.

In medical domain, region-based methods such as [8][20] are popular as they are more immune to noises than edge detection approach. The main disadvantage is there are chances of under segmentation and over segmentation of the regions in the image. For medical images, the edge based methods like Snakes, geodesic active contours are typically not suitable for segmentation purpose since the edge pixels identified are based on local intensity variation and are not necessarily well-connected to form closed boundaries. Although edge detection can be used to supplement other segmentation techniques, for images like corneal image, the edges detected often lead to over segmentation.

2.2 Junction Detection

Junction detection is a challenging task to locate junctions and determine their angles. Corner detection techniques like Harris corner detection [11] are good at detecting sharp corners, but tend to detect too many false positives, and when the angle is small, those methods often fail to detect the junction. [3] extracts interest points in a 2D image using topologically constrained grouping process. It is a generic process that uniformly describes all types of junctions, however, in complicated images such as corneal images, the topology is hard to predefine. [22] proposes a method for junction detection in 2D images with linear structures. The Hessian information and correlation matrix measurements are combined to select the candidate junction points. The potential junction branches of candidate junctions are found, based on the idea that the linear structure should have a higher intensity compared to the background in structured images. Then the locations of the junction centers are refined using template fitting at multiple scales. The main drawback of this algorithm is the Gaussian blur applied in the process weakens branching region, which is critical for corneal image analysis. [26] introduces a *contrario* (ACJ) detection theory and method. Compared to other methods, this approach requires fewer parameters, and is able to inhibit junctions in textured areas. But for corneal image, when the distance between fibers is short, this algorithm tends to misclassify the two fibers as one textured fiber.

2.3 Linear Structure Extraction

Linear structure extraction, which finds the centerline and estimates the width of linear structure, is a critical step in many applications, ranging from road network recognition in 2D aerial image to modeling lung bronchi, blood vessels and dendritic arbors in 3D biomedical image stacks[21]. The cornea structure, composed of fibers, shares a lot of common properties with linear structure, but most of previous methods aim at tree-like structures, when applied to corneal collagen structure, they mostly fail to distinguish the fibers

which are near or close to each other.

One popular linear structure extraction methods is Hessian-based approaches, and was first proposed in [9]. This method applies Hessian (the multiscale second order local structure) to estimate the probability that a pixel or voxel lies on a centerline. The advantage of the methods in this category is that, when applied with multiscale analysis, the linear structures in a large range of diameters can be captured. The main drawback of these approaches is that the required amount of Gaussian blur to compute the Hessian may result in confusion between adjacent structures, especially when they are thick and close to each other, which is a common case in the corneal image. Recently,[21] applied machine learning technique to solve this problem, where a regressor is trained to return the closest centerline in scale-space which is identified as the regressors' local maxima. However, to train such a regressor, a large number of training samples is required, which is hard to obtain from the corneal data set.

3. ALGORITHM OVERVIEW

In this paper, we develop an image segmentation method that separates the foreground collagen fibers from the background. As the mechanical analysis of the corneal collagen structure which uses the segmentation results is mainly based on fiber's connectivity and distribution of branching points, we focus mostly on preserving branching region and connectivity of fibers during segmentation. Based on this consideration, we propose a hybrid method based on seeded region growing and iterative voting.

Corneal fibers have varying widths, and are often close to each other. On one side, previous methods tend to diminish the gap between fibers, which leads to under segmentation and underestimation of the number of branching points. On the other side, the noises in NLO image are often falsely classified as fiber gap, which leads to over segmentation and further misleads the estimated distribution of branching points. Thus, to preserve the weak gaps, we first apply seeded region growing to enhance the gap region as well as making the pixels which belong to the same fiber connected. As most of the noises appear as isolated regions, in the growing process, noises are less likely to be connected with fiber structures. Region growing divides the image into three spaces: negative, positive and undecided spaces. In order to resolve the stitching artifacts and missing parts inside fibers, we apply an iterative voting method to improve the classification of pixels. During the iterative process, the direction and size of voting region is updated after each iteration, so that small defects inside fibers can be repaired using nearby fiber structure.

4. SEEDED REGION GROWING

Seeded region growing is based on the observation that similar pixels are usually connected with each other and mostly belong to the same object. So seeded region growing based methods start with a few seed points by manual pick or automatic selection, and gradually grow each region until certain scenario is reached. As it is robust, rapid, and free of tuning parameters, seeded region growing are widely applied in automatic image segmentation[1][8][20]. In this paper, as the branching points have special interests for us, the region growing method has the advantage of enhancing

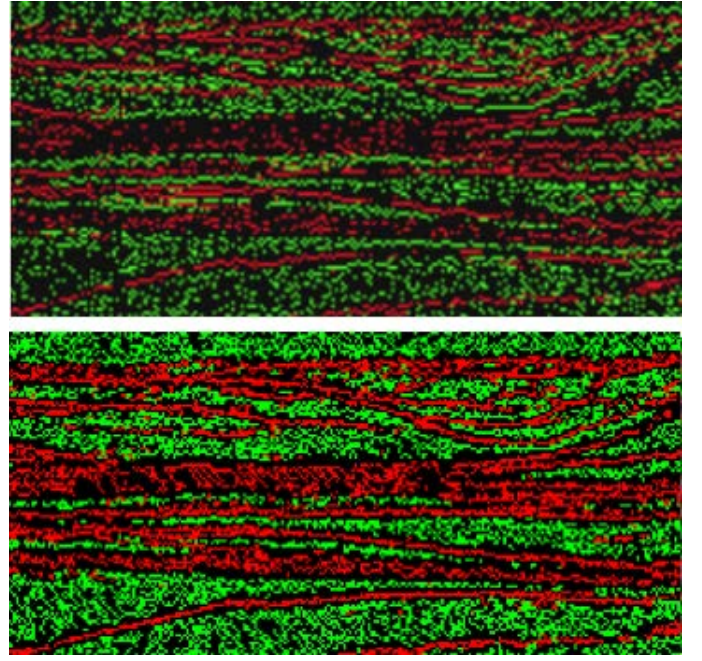


Figure 3: Top: initial seed points. Bottom: regions after growing. (Red as foreground, green as background, black as unknown)

even minor branching regions. Thus, we apply the idea of seeded region growing to generate an initial segmentation in which the minor gaps between fibers are preserved, and the regions which we are not so sure with are left as undecided, waiting for further processing.

Preprocessing: Like most of previous work, first of all, we apply gray level adjustments on the images to enhance the contrast. Histogram equalization is applied so that image intensity is mapped to fill the entire tonal range.

Initial seed points selection: Initial seed points greatly affect the segmentation results, so we choose only a small portion of pixels as seed points. Considering that the intensity may be unequally distributed in the entire image, a global thresholding is not desirable. As most of the cornea structures are composed by near-horizontal fibers, we compute average intensity value for each row of the image, and for pixels with intensity lower than α times of average value, we mark them as background seed points, for pixels with intensity higher than β times of average value, we mark them as foreground seed points. As it is a common mistake to merge two adjacent fiber into one in corneal image segmentation, in order to enhance the gap regions, we choose $\alpha = 0.2$, and $\beta = 1.5$ in our experiment, which initializes more background seed points than the foreground seed points. The top image in Figure 3 shows the initial seed points for both background and foreground.

Region growing strategy: Most of seeded region growing methods apply a growing strategy in which each set/region starts from a single seed point, and then assign the unallocated pixels to the above sets in a flood fill manner[1]. And after each step, the initial seeds are further replaced by the centroids of the generated homogeneous regions. This algorithm is robust and stable, but its quality strongly relies on the initial seed point selection. Unlike such methods, in this

Algorithm 1 Algorithm for Region Growing

```
1: procedure REGIONGROW
2:   for each pixel  $p$  in image do
3:      $label_p = 0$ 
4:   while true do
5:     for each pixel  $p$  in image do
6:       if  $label_p == 0$  then
7:         search  $p$ 's 8 neighbors,  $q \leftarrow \operatorname{argmin}|I_p - I_q|$ 
8:
9:         if  $label_q \neq 0$  then
10:            $label_p = label_q$ 
11:
12:       if no pixel's label changed then
13:         break
```

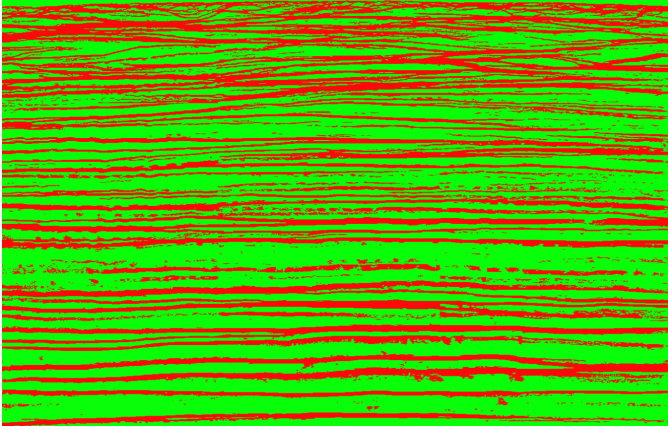


Figure 4: The regions after first round of voting.

paper, rather than aiming at separating image into regions, we would like to (1) preserve connectivity of pixels which belongs in the same fiber (2) preserve the gap between adjacent fibers (3) label only those pixels which we are sure to be foreground or background, and leave those which we are not so confident to later processing. Therefore, the strategy in Algorithm 1 is applied. For each iteration, this strategy searches the 8 neighbors of each unknown pixel p , and finds the neighbor pixel q whose intensity value is the most close to p . If the found pixel q is known to be foreground or background, we mark p to the same as q , if not, we leave p as unknown. After iterations, when no pixel's label is changed any more, the process terminates. Since at least one pixel is labeled in each iteration, time complexity of the algorithm is linear to the number of pixels in the image.

5. ITERATIVE VOTING

After seeded region growing, the labels of a large portion of pixels in the image are still unknown. Since there exist missing parts and stitching artifacts in the image, it will lead to a lot of segmentation errors if we classify the pixels merely by their intensity values, and as the cornea structure shows certain mesh-like pattern, it is desirable to not only rely on the intensity value but also consider the shape of model. Therefore, we iteratively apply an oriented kernel to determine the labels of the remaining pixels, which is also known as iterative voting [17] [2]. The steps of our iterative voting method are listed as below:

Parameter initialization: We define the voting window as a rectangle shaped region, and the initial voting area and voting magnitude affects the speed of iterative voting's convergence, so we would like to initialize the voting window based on the shape pattern in the image. We consider the region surrounded by two adjacent fibers as the shape pattern in the image that determines the voting window. In order to obtain a estimation of the shape pattern's aspect ratio, we calculate the dominant Eigen vector \vec{v} of the image's Hessian matrix:

$$\vec{v} = \frac{1}{n} \sum_{j \in D} \vec{v}_{j2}$$

where D is the range of the image, \vec{v}_{j2} is the first Eigen vector for the image's Hessian matrix at pixel j . The direction of \vec{v} is identical to the fiber's tangent direction, and the magnitude of \vec{v} indicates the shape pattern's aspect ratio. Thus the medial direction of the voting region is defined as

$$\vec{v}_{voting} = \frac{\vec{v}}{|\vec{v}|}$$

The shape of voting region is

$$h = \phi$$

$$w = \phi(1 + |\vec{v}|)$$

where h, w are height and width of the voting region respectively. ϕ is a variable to control the size of voting region, and in our experiment, $\phi = 8$ is good for most images.

Voting computation: For each pixel, we let the nearby pixels vote for its classification. As the pixels which are close to each other are more likely to belong to the same classification, when we apply voting, we consider the pixels near the center of voting region is more important than those far away, we would like to make the center pixels with higher weights. Thus, for each pixel, we first construct a normalized 2D gaussian filter with h and w as height and width, and \vec{v}_{voting} above as medial direction. Then we apply this filter on both the original grayscale image and current voting map, and the voting value S_j for pixel j is computed as

$$S_j = \theta G \cdot I(j) + \gamma G \cdot V(j)$$

where I is the original image (normalized to $[0, 1]$), G is Gaussian filter, V is the voting map in which foreground, background and unknown are represented as 1,-1,0 respectively. θ and γ control how much we would like to preserve the initial region growing result. In our experiment, we use θ as 0.4, and γ as 0.7, and if $S_j > 0.2$ we mark pixel j as foreground, otherwise background.

Update the voting window: As there exists stitching artifacts and missing parts in the image, we apply voting as a way to recover those misplaced and lost parts. After each iteration, we update the voting window according to the latest voting results, so that the voting results reflect more features of the nearby structure. After each iteration, each pixel's h, w , and v_{voting} is updated using the same way as parameter initialization, but the range is not the whole image, but their current voting window. In essence, our method is consistent with the idea of directional filter bank, but by voting iteratively, our method not only gradually adjusts directions, but also the filter window size, which makes it easier to deal with the varying width of fibers. Figure 5 shows the result after our iterative voting, the whole iterative voting process plays a dual role as reducing the noise and repairing broken fibers.

6. RESULTS AND APPLICATIONS

In this section, we compare our approach against three

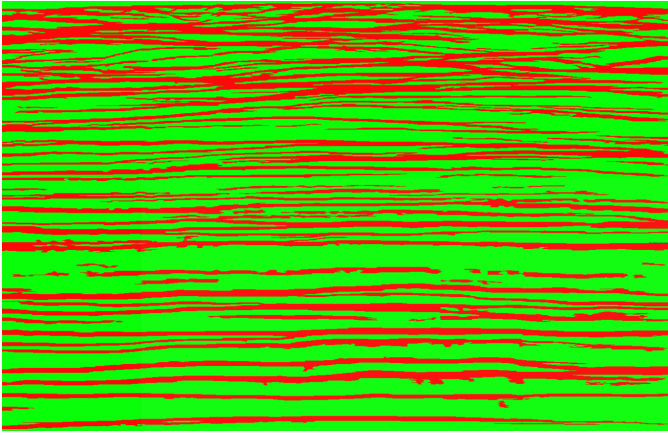


Figure 5: Regions after iterative voting

of the most powerful image segmentation methods: GrabCut[19], edge based active contour[6], and region based active contour [13]. For GrabCut method, we initialize the mask image by labeling low intensity pixels (lower than 50) as background and high intensity pixels (higher than 200) as foreground, and then run GrabCut algorithm implemented in OpenCV[5] to get segmentation result. For edge based active contour and region based active contour methods, we use the implementation of Image Segmenter App in Matlab. As we would like to compare the result of automatic image segmentation, for all the four methods, no manual intervention is applied. To evaluate the methods, we apply all the segmentation methods on 150 corneal images, obtained from 15 animals species including rabbit, hawk, dog, etc., and for each method we detect branching points and fiber structures based on the segmentation result.

As shown in Figures 7, due to the smooth step in GrabCut algorithm, GrabCut tends to merge two adjacent fibers together, and when there are missing parts in fiber, GrabCut tends not to extend further to connect them. And edge based active contour loses most of the details near branching point as it strongly depends on the edges detected. Region based active contour method preserves the most details among all the methods, but since our goal is to detect branching points and linear structure, the noises retained by region based active contour method may lead to poor result in later analysis. In summary, our algorithm preserves essential fiber details as well as branching regions.

6.1 Branching Point Detection

As branching points play an extremely important role in determining cornea’s mechanical properties, we evaluate our results by using it to detect branching points. For determining branching points, like most of the previous works[22], we assume sharp corners are branching points. The directional filter bank is applied to determine the type of junction, from which T type and Y type junction are classified as branching points.

As usually done to evaluate junction detection results, we prepare ground truth images by manually labeling each branching point. As the ground truth data itself can be inaccurate in terms of exact pixel location of the branching point, we introduce a tolerance factor ρ to perform plot precision-recall(PR) curves analysis, and if a detected branching point

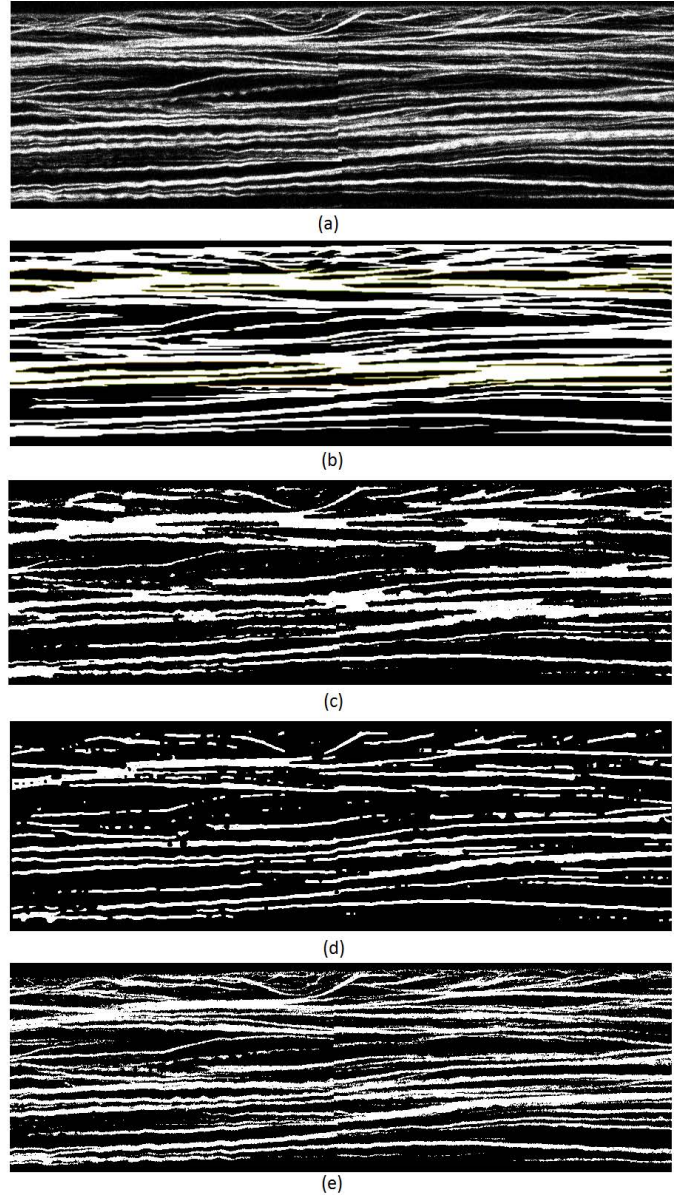


Figure 6: Corneal image segmentation results: (a)original image (b) ours (c) GrabCut (d)edge based active contour (e)region based active contour

is at most ρ distant from a ground truth branching point, it is considered to be a true positive. We generate a PR curve for each of the four methods for different values of ρ . As shown in Figure 10, we adjust the parameters in each method to achieve a certain recall rate (the ratio between the detected branching points and benchmarked branching points), and we plot the corresponding precision rate (the ratio of the true branching points among all detected branching points) in the figure. The result in the figure shows our algorithm outperforms all the others for all the relevant ranges of precision and recall.

6.2 Linear Structure Extraction

Linear structure extraction aims to extract the fibers’ cen-

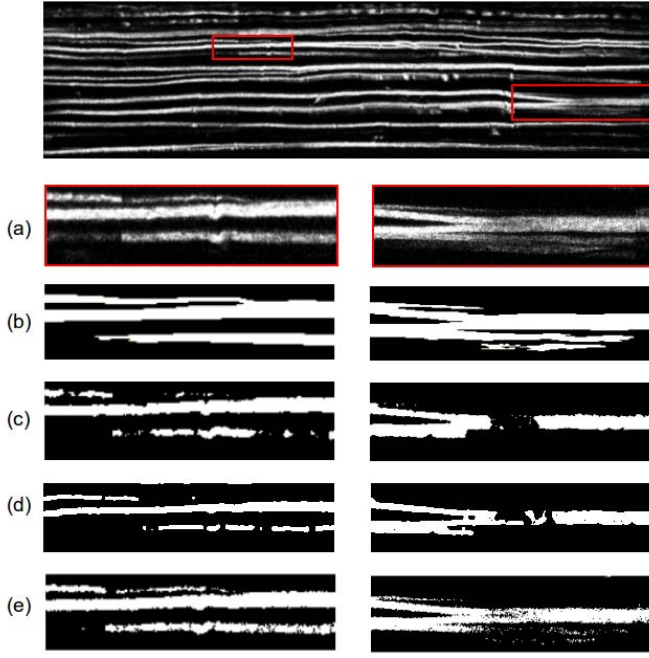


Figure 7: Rabbit corneal image segmentation results: (a)original image (b) ours (c) GrabCut (d)edge based active contour (e)region based active contour

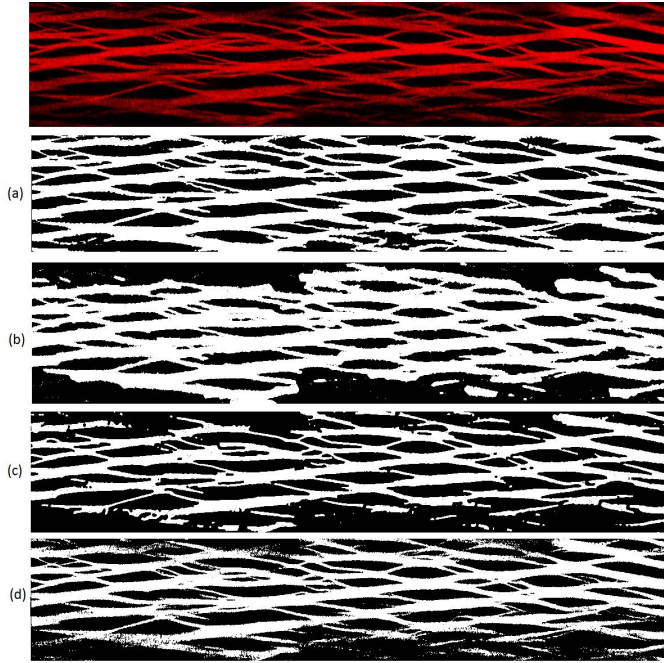


Figure 8: Hawk corneal image segmentation results: (a) ours (b) GrabCut (c) edge based active contour (d)region based active contour

terlines and width at each position, and image segmentation often works as one of its preprocessing steps. To evaluate our algorithm's performance on linear structure extraction,

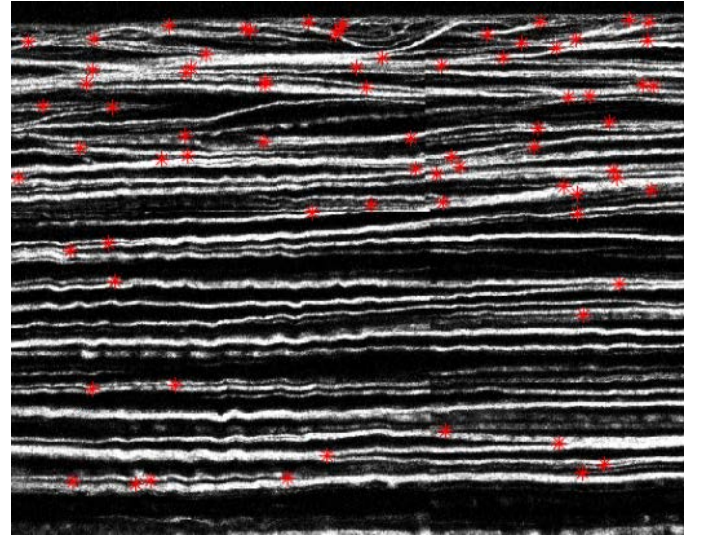


Figure 9: Branching points detection result, each star symbol represents a detected branching point

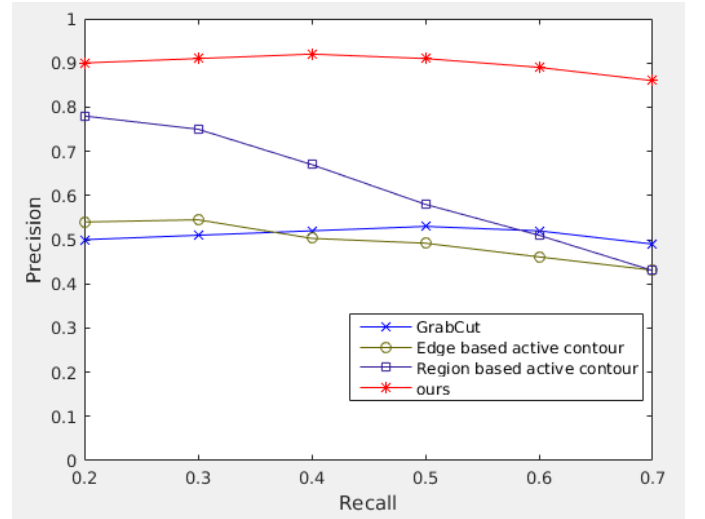


Figure 10: Precision-recall curves for branching point detection when $\rho = 5$

again, we follow the same evaluation methodology for evaluating branching point results. We apply Hessian based linear structure detector [21] to extract fibers' centerline based on segmentation results of GrabCut, region-based active contour, edge-based active contour and our method. To measure the extraction precision, we introduce another tolerance factor δ , and for each pixel in the extracted centerline, if we can find a pixel in benchmark centerlines that is at a distance less than δ , then the pixel is considered as true positive. Figure 11 shows the precision-recall curves for all the four methods we evaluate. According to the precision-recall curves, the result of our algorithm outperforms all the other methods. Figure 12 shows the application of our algorithm on computing the fibers' widths using [15], the estimated widths can be taken as input of further mechanical analysis.

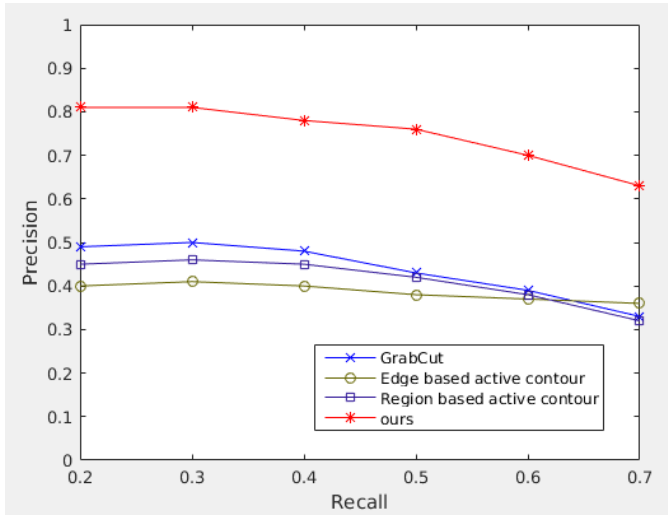


Figure 11: Precision-recall curves for branching point detection when $\delta = 8$

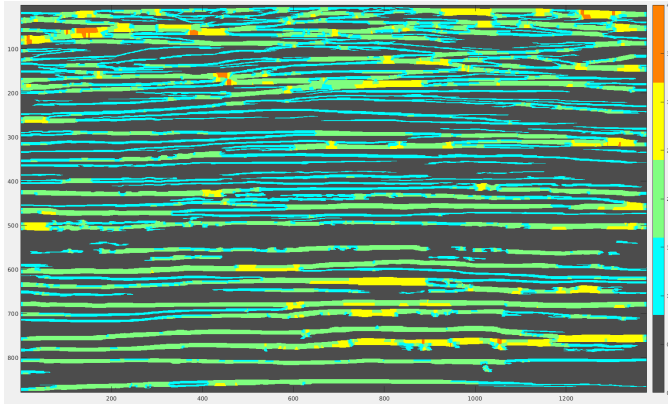


Figure 12: Estimation of linear structure's width

7. DISCUSSION AND FUTURE WORK

Our work provides a novel hybrid image segmentation method that integrates seeded region growing and iterative voting. The seeded region growing plays a dual role as (1) preserving the gap between the two adjacent fibers to prevent them from being falsely merged, especially when they are close to each other (2) enhancing the branching regions to make them easier to detect. After the region growing step, in order to eliminate false regions, for each pixel, its nearby pixels are used to vote for its label, and we iteratively adjust the voting window according to its local structure. This process preserves the major fiber structure as well as repairs missing parts inside fibers.

We show that the two of the three major artifacts in corneal images, namely the noises and stitching seams have little effect on the result of our method. The third artifact, namely the missing regions, is properly handled by our method when the missing region is relatively small. However, when the missing region is too large, higher level knowledge about the structure is required. Another potential improvement is to apply the branching points detection result to assist linear structure extraction.

8. REFERENCES

- [1] R. Adams and L. Bischof. Seeded region growing. *IEEE Transactions on pattern analysis and machine intelligence*, 16(6):641–647, 1994.
- [2] Y. Al-Kofahi, W. Lassoued, W. Lee, and B. Roysam. Improved automatic detection and segmentation of cell nuclei in histopathology images. *IEEE Transactions on Biomedical Engineering*, 57(4):841–852, 2010.
- [3] R. Bergevin and A. Bubel. Detection and characterization of junctions in a 2d image. *Computer Vision and Image Understanding*, 93(3):288–309, 2004.
- [4] Y. Y. Boykov and M.-P. Jolly. Interactive graph cuts for optimal boundary & region segmentation of objects in nd images. In *Computer Vision, 2001. ICCV 2001. Proceedings. Eighth IEEE International Conference on*, volume 1, pages 105–112. IEEE, 2001.
- [5] G. Bratski. *Dr. Dobb's Journal of Software Tools*, 2000.
- [6] V. Caselles, R. Kimmel, and G. Sapiro. Geodesic active contours. *International journal of computer vision*, 22(1):61–79, 1997.
- [7] L. D. Cohen. On active contour models and balloons. *CVGIP: Image understanding*, 53(2):211–218, 1991.
- [8] J. Fan, D. K. Yau, A. K. Elmagarmid, and W. G. Aref. Automatic image segmentation by integrating color-edge extraction and seeded region growing. *IEEE transactions on image processing*, 10(10):1454–1466, 2001.
- [9] A. F. Frangi, W. J. Niessen, K. L. Vincken, and M. A. Viergever. Multiscale vessel enhancement filtering. In *Medical Image Computing and Computer-Assisted Intervention (MICCAI98)*, pages 130–137. Springer, 1998.
- [10] J. Freixenet, X. Muñoz, D. Raba, J. Martí, and X. Cufí. Yet another survey on image segmentation: Region and boundary information integration. In *European Conference on Computer Vision*, pages 408–422. Springer, 2002.
- [11] C. Harris and M. Stephens. A combined corner and edge detector. In *Alvey vision conference*, volume 15, page 50. Citeseer, 1988.
- [12] M. Kass, A. Witkin, and D. Terzopoulos. Snakes: Active contour models. *International journal of computer vision*, 1(4):321–331, 1988.
- [13] S. Lankton and A. Tannenbaum. Localizing region-based active contours. *IEEE transactions on image processing*, 17(11):2029–2039, 2008.
- [14] K. M. Meek and C. Knupp. Corneal structure and transparency. *Progress in retinal and eye research*, 49:1–16, 2015.
- [15] H. Mirzaalian and G. Hamarneh. Vessel scale-selection using mrf optimization. In *Computer Vision and Pattern Recognition (CVPR), 2010 IEEE Conference on*, pages 3273–3279. IEEE, 2010.
- [16] S. Osher. Level set methods. In *Geometric level set methods in imaging, vision, and graphics*, pages 3–20. Springer, 2003.
- [17] B. Parvin, Q. Yang, J. Han, H. Chang, B. Rydberg, and M. H. Barcellos-Hoff. Iterative voting for inference of structural saliency and characterization of subcellular events. *IEEE Transactions on Image Processing*, 16(3):615–623, 2007.

- [18] A. J. Quantock, M. Winkler, G. J. Parfitt, R. D. Young, D. J. Brown, C. Boote, and J. V. Jester. From nano to macro: studying the hierarchical structure of the corneal extracellular matrix. *Experimental eye research*, 133:81–99, 2015.
- [19] C. Rother, V. Kolmogorov, and A. Blake. Grabcut: Interactive foreground extraction using iterated graph cuts. In *ACM transactions on graphics (TOG)*, volume 23, pages 309–314. ACM, 2004.
- [20] F. Y. Shih and S. Cheng. Automatic seeded region growing for color image segmentation. *Image and vision computing*, 23(10):877–886, 2005.
- [21] A. Sironi, V. Lepetit, and P. Fua. Multiscale centerline detection by learning a scale-space distance transform. In *Computer Vision and Pattern Recognition (CVPR), 2014 IEEE Conference on*, pages 2697–2704. IEEE, 2014.
- [22] R. Su, C. Sun, and T. D. Pham. Junction detection for linear structures based on hessian, correlation and shape information. *Pattern Recognition*, 45(10):3695–3706, 2012.
- [23] L. Vincent and P. Soille. Watersheds in digital spaces: an efficient algorithm based on immersion simulations. *IEEE transactions on pattern analysis and machine intelligence*, 13(6):583–598, 1991.
- [24] M. H. Wilkinson, T. Wijnbenga, G. De Vries, and M. A. Westenberg. Blood vessel segmentation using moving-window robust automatic threshold selection. In *Image Processing, 2003. ICIP 2003. Proceedings. 2003 International Conference on*, volume 2, pages II–1093. IEEE, 2003.
- [25] M. Winkler, G. Shoa, Y. Xie, S. J. Petsche, P. M. Pinsky, T. Juhasz, D. J. Brown, and J. V. Jester. Three-dimensional distribution of transverse collagen fibers in the anterior human corneal stroma: corneal collagen fiber angle quantification. *Investigative ophthalmology & visual science*, 54(12):7293–7301, 2013.
- [26] G.-S. Xia, J. Delon, and Y. Gousseau. Accurate junction detection and characterization in natural images. *International journal of computer vision*, 106(1):31–56, 2014.
- [27] A. Yezzi, S. Kichenassamy, A. Kumar, P. Olver, and A. Tannenbaum. A geometric snake model for segmentation of medical imagery. *IEEE Transactions on medical imaging*, 16(2):199–209, 1997.