

Figure . Representative collagen patterns observed in human breast cancer tissue sections. Wavy (A) and straight (B). Dense (C) and well defined (D). Thick bundles (E) and thin strands (F). Discontinuous (G) and continuous (H). Crossing (I) and parallel (J). Scale bar is 10 microns.

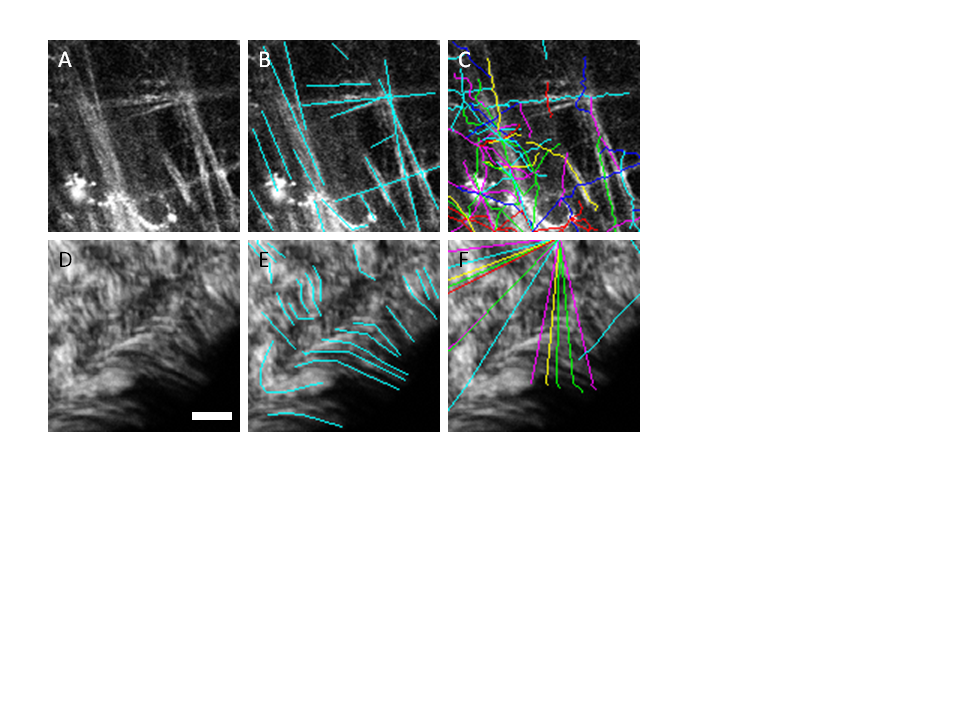


Figure . Fibers extracted by the FIRE algorithm without preprocessing. A and D are the original images, B and E are show manual segmentations of the fibers, D and F show the automatic fiber segmentations that are extracted by the FIRE algorithm. Scale bar is 25 microns.

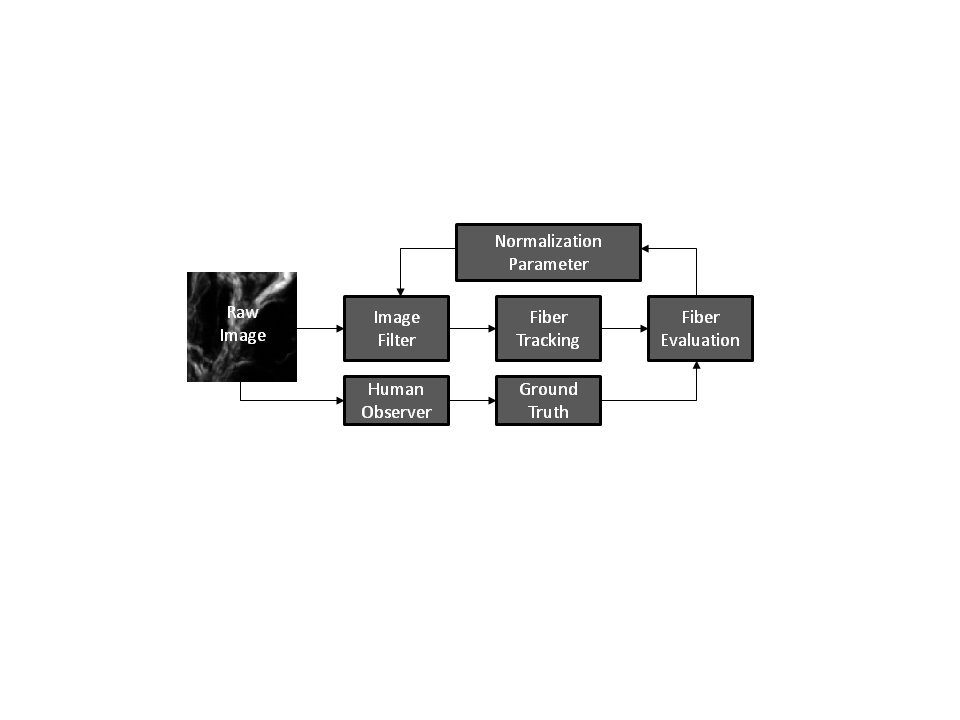


Figure . Diagram of the approach for quantitative collagen analysis showing the iterative process for optimizing the performance of a single image processing filter for fiber tracking. The raw image is processed by the image filter using an initial normalization parameter, the result of which is sent to the FIRE fiber tracking algorithm. Automated fiber extractions are compared against manually performed fiber extractions. Several normalization parameters are evaluated and one optimal parameter was selected for each filter that optimized the fiber evaluation result.

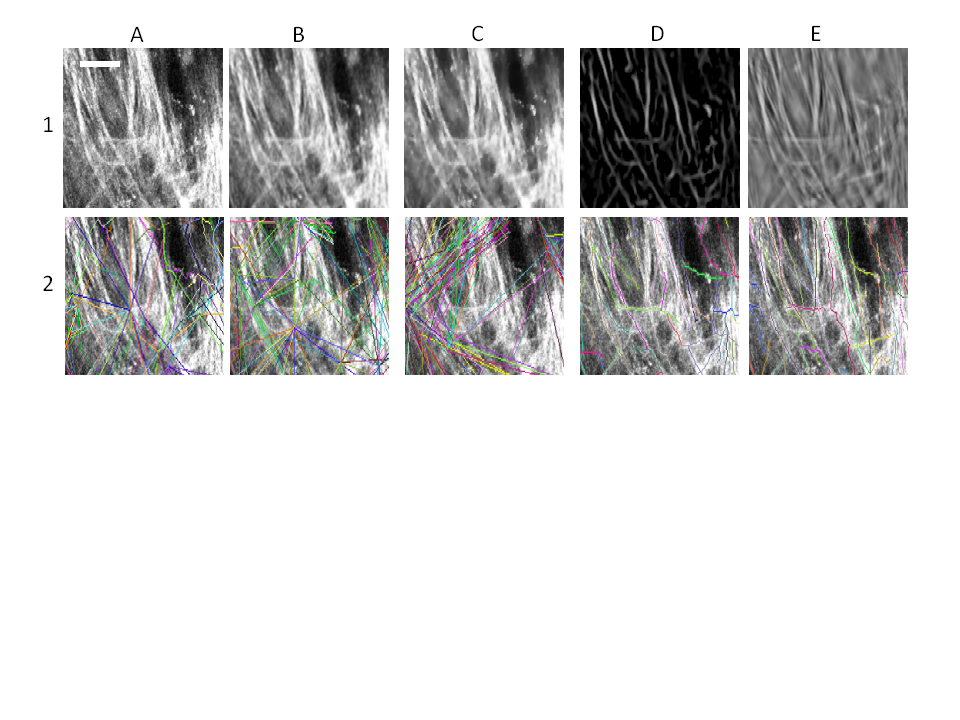


Figure . Output of the image processing techniques (row 1) and output of the fiber tracking algorithm (row 2) for a single test case. Column A is the result of no processing, B: GF, C: SPTV filter, D: TF, and E: CT. Scale bar is 25 microns.

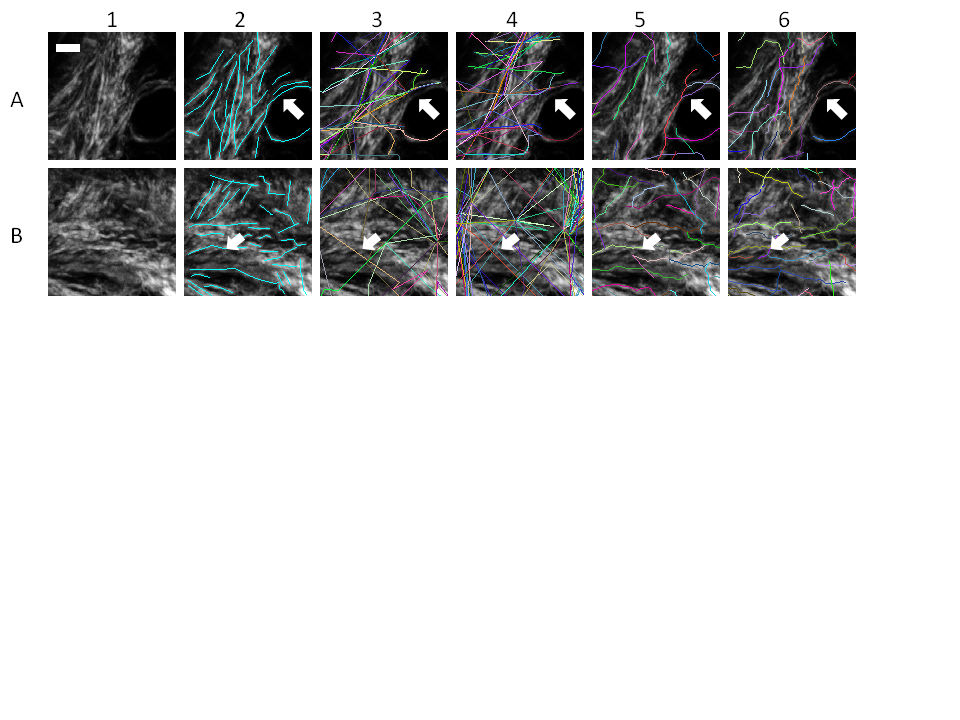


Figure . Two test cases (A&B), showing different processing methods in each column. The original image (column 1) is shown overlayed with a manual segmentation (column 2), GF (column 3), SPTV (column 4), TF (column 5), and CT filter (column 6). Scale bar is 25 microns.

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Figure . F measure result comparing the automated segmentation techniques to the manual segmentations of three independent raters, for 25 test cases, representing a total of 9290 fiber evaluations. The error bars indicate the standard deviation between average F measure scores of each of the raters.





Figure . Distribution of lengths (top row) and angles (bottom row) of all fibers in all simulated test cases. Ground truth data is on the left and the results of the automated CT+FIRE algorithm are shown on the right.

For the purposes of this paper, we separate existing computational algorithms into two categories, those capable of generating low-level features and those capable of generating high-level features. We define low-level features to be based on the pixels in the image, such as the number and density of pixels considered to be within fibers, the dominant fiber orientation at each pixel in the image, or the result of a filter at each pixel in the image. We define high level features to be based on the collagen fibers themselves, statistics such as fiber number, length, angle, curvature, and position. Our High level features are usually discovered by the tracking and extraction of individual fibers from an image. We suggest that both low and high-level information is important for understanding cellular interactions with individual collagen fibers. Tools should be able to extract both low and high level fiber based information from a heterogeneous collection of image morphologies and a wide range of image qualities. Although a number of researchers have developed tools for computer assisted collagen image analysis, to our knowledge no techniques exist for extracting fiber level information from the wide range of morphologies and image quality levels observed in practice.