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Enhanced determination of nerve fiber orientations by introducing iterative thresholds in Computational Scattered Light Imaging

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Abstract: We improve the determination of nerve fiber orientations in brain tissue sections that have been measured with Computational Scattered Light Imaging by close examination of low intensity signals with iterative thresholding.

1. Introduction

Computational Scattered Light Imaging (ComSLI) is a novel neuroimaging technique designed to reconstruct nerve fiber orientations in histological brain sections with micrometer resolution, also in regions with densely packed and crossing fibers [1–3]. By illuminating the brain section from different angles and measuring the normally through-scattered light with a camera, the scattering behavior of nerve fiber bundles can be analyzed. Previous studies showed that nerve fiber constellations yield characteristic light intensity profiles. The intensity profiles can be analyzed with the open-source toolbox SLIX [3]. By extracting number and position of the peaks and filtering prominent features, SLIX determines the in-plane fiber orientations in regions with flat, inclined, and crossing fibers. While the center of the field of view is illuminated from a similar polar angle θ during the measurement (cf. Fig. 1A), the borders of the field of view are illuminated from slightly different angles, yielding skewed light intensity profiles in these areas (cf. Fig. 1B). Especially in regions with low or ambiguous scattering signals, this might lead to incorrectly computed fiber orientations [2]. Also, when two peaks lie close together, as in intensity profiles of highly inclined fibers, they might be evaluated incorrectly if the second peak has a low prominence.

2. Material and Methods

To improve the peak detection and thus the determination of fiber orientations in these areas, we developed an iterative thresholding algorithm based on SLIX[1]. Previously, the peaks were filtered by a threshold that was chosen as best compromise between regions with inclined, flat and crossing fibers and set to a fixed value of 8 % of the normalized signal intensity [1]. Instead of a fixed threshold, we here introduce an adaptive threshold to find a user-defined target number of peaks. The algorithm follows an iterative approach: The tool starts with a threshold prominence of one, corresponding to the maximum intensity value of each light intensity profile. In each iteration, the threshold prominence is reduced and the number of prominent peaks is computed until the desired number of peaks is reached. From the positions of the determined prominent peaks, the fiber orientations are computed as in [1]. To demonstrate the performance of the algorithm, we measured a 60 µm thin, coronal vervet monkey brain section with ComSLI, using 15° azimuthal steps of illumination (cf. Fig. 1A). The fiber orientations were computed from the resulting intensity profiles both with SLIX (Fig. 1C) and the here proposed algorithm (Fig. 1D).

3. Results and Discussion

The proposed iterative threshold algorithm significantly improves the detected fiber orientations by also considering less prominent peaks in the light intensity profiles (cf. Fig. 1C-E). This is especially noticeable in regions with inclined or crossing fibers (green rectangles), or in regions at the border of the field of view (red rectangles). If crossing fibers yield an intensity profile with one low-prominence peak, the original SLIX algorithm yields no fiber orientation (white arrow in Fig. 1C). With the improved algorithm, 60% of the pixels that were not assigned a fiber orientation could be evaluated. If parallel fibers yield one low-prominence peak, the original SLIX algorithm misinterprets this intensity profile as inclined fibers. In Fig. 1B, the peak at the dotted red line is not detected

[1] https://github.com/3d-pli/SLIX

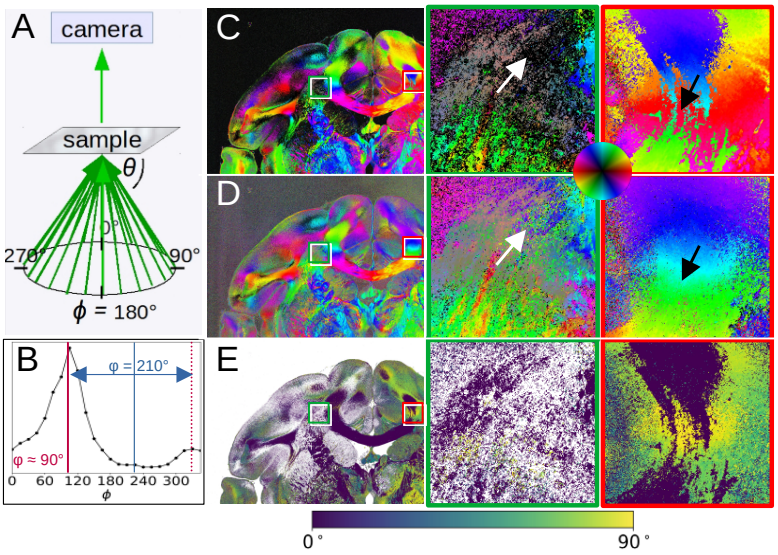

Fig. 1. (**A**) Measurement setup. A brain section is illuminated from different azimuth angles ϕ under a certain polar angle θ. (**B**) Exemplary light intensity profile of one image pixel belonging to an inhomogeneously illuminated region, indicated in (C) by a black arrow. The inhomogeneous illumination leads to a skewed intensity profile and an incorrectly computed fiber orientation with SLIX. (**C**) Color-coded fiber orientations (according to color wheel) computed with SLIX. The colored squares point out selections from a region at the center (green) and at the border (red) of the field of view. Black pixels were not evaluated. (**D**) Improved fiber orientations computed with the iterative threshold algorithm using a target number of four peaks. Much more regions with crossing fibers (green) are detected, and the reconstruction of fiber orientations at the border (red) has significantly been enhanced. (**E**) Absolute difference between the fiber orientations computed with SLIX and the proposed algorithm. White denotes pixels not evaluated in SLIX.

yielding a shift of ca. 120° in the detected orientation. Using measurements with a diffuser plate (homogeneously scattering sample) as calibration, inhomogeneous illumination at border regions could be corrected. However, with the iterative thresholding algorithm, it is possible to correct for even more artifacts and greatly enhance the reliability of the reconstructed fiber orientations. The results in regions with in-plane fibers remain mostly unchanged as the majority of them yield light intensity profiles without any minor peaks. This can be seen in Fig. 1E, where the corpus callosum shows a low difference between SLIX and the proposed algorithm (except for regions at the image borders). One drawback of this approach is that it assumes the same target number of peaks for all image pixels which can lead to misinterpretations, especially in gray matter regions of the brain. This could be fixed by defining a different target number of peaks per brain region, but this would require a-priori knowledge of the underlying fiber architecture. However, a peak number of four corresponding to two different fiber or blood vessel orientations per pixel is a good first approximation for almost every region in the white and gray matter. A bottom threshold for the peak prominence, low enough to avoid false negatives in the gray matter, could be introduced to avoid false positives in the deep white matter. In addition, light intensity profiles could be evaluated based on specific features like peak width or number of peaks for different prominence values in order to determine the most likely fiber configuration for this light intensity profile, using for example neural networks. In conclusion, the usage of a variable prominence for nerve fiber orientation detection in ComSLI is an important step towards a better reconstruction of the highly complex nerve fiber architecture of the brain.

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