Recent Advances in Scattered Light Imaging Enable New Insights into Brain's Nerve Fiber Architecture

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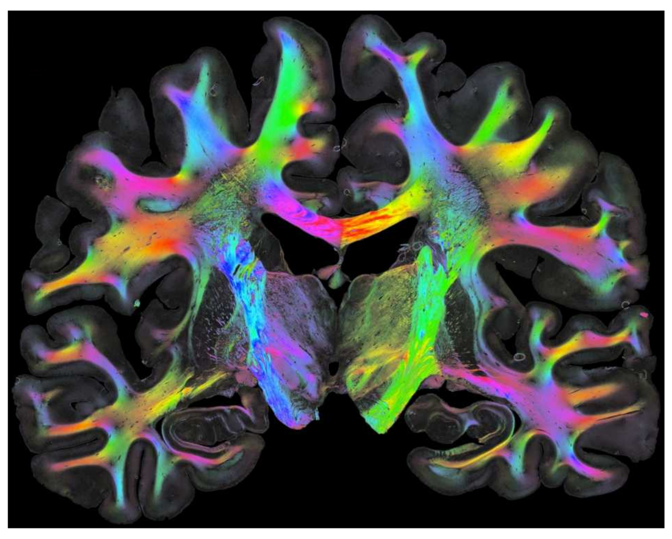
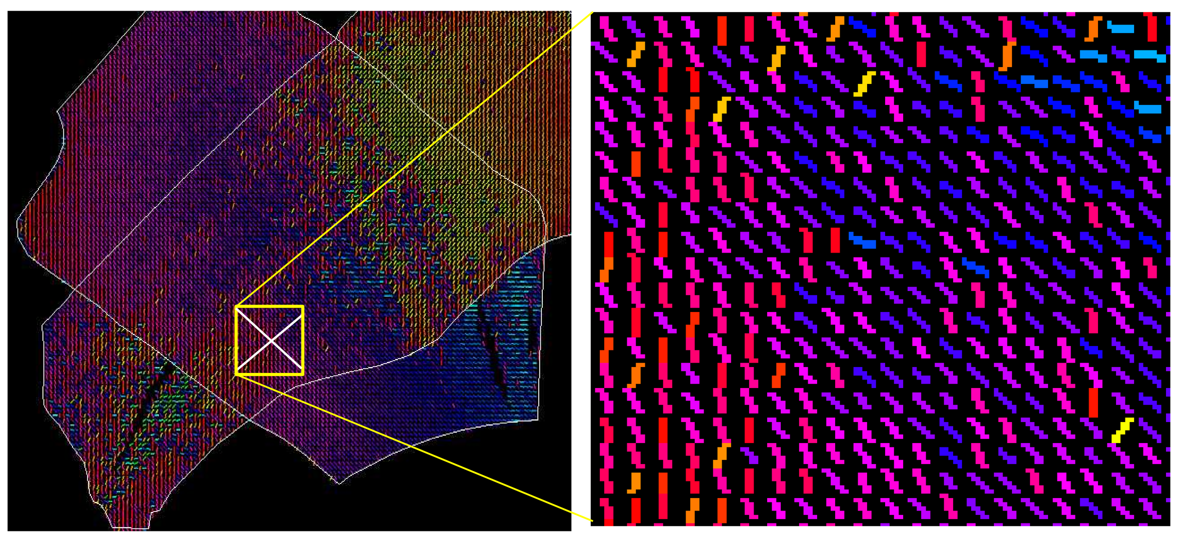
3D-Polarized Light Imaging (3D-PLI)

When generating a detailed network model of the brain, a correct reconstruction of crossing nerve fibers is crucial. 3D-Polarized Light Imaging (3D-PLI) reconstructs the brain's nerve fiber architecture by transmitting polarized light through histological brain sections and measuring their birefringence [1-2].

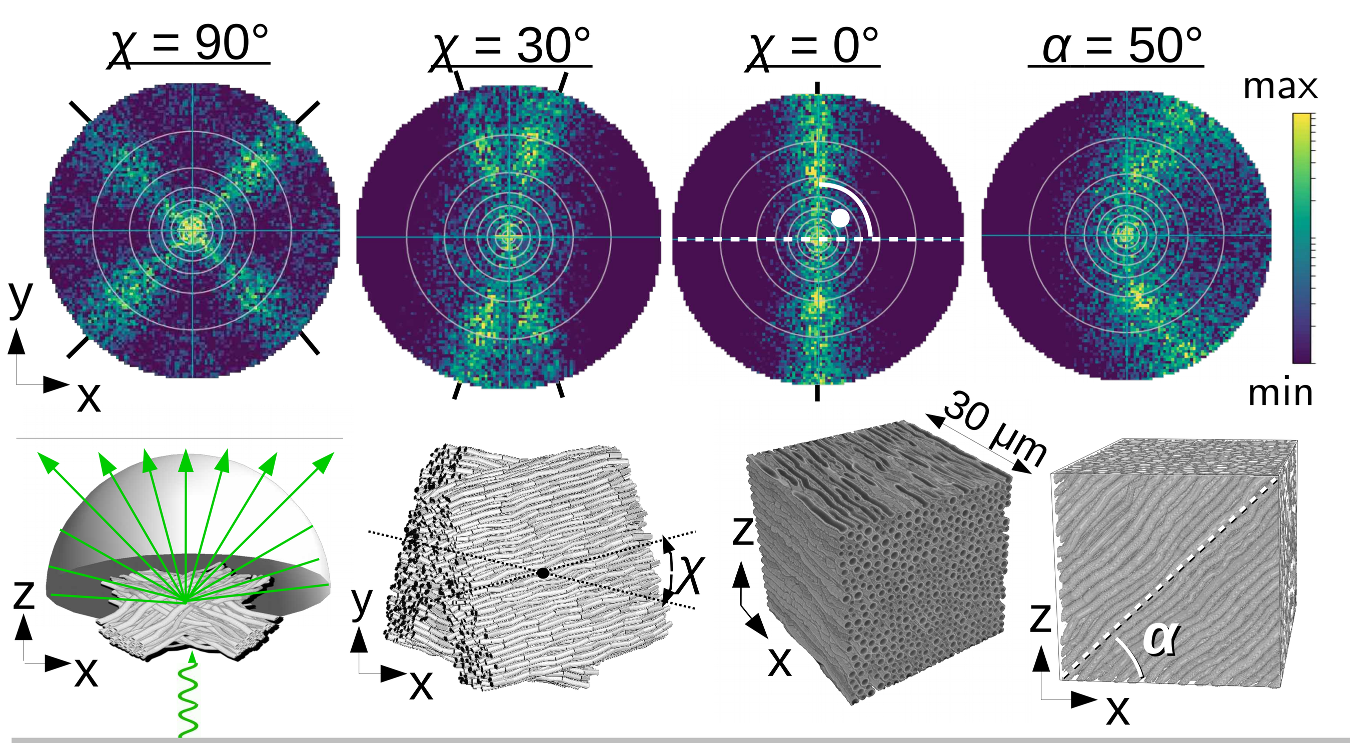


3D-PLI reconstructs the spatial nerve fiber orientation for each image pixel with micrometer resolution. However, the reconstruction of several, crossing nerve fiber pathways within one image pixel is not possible.

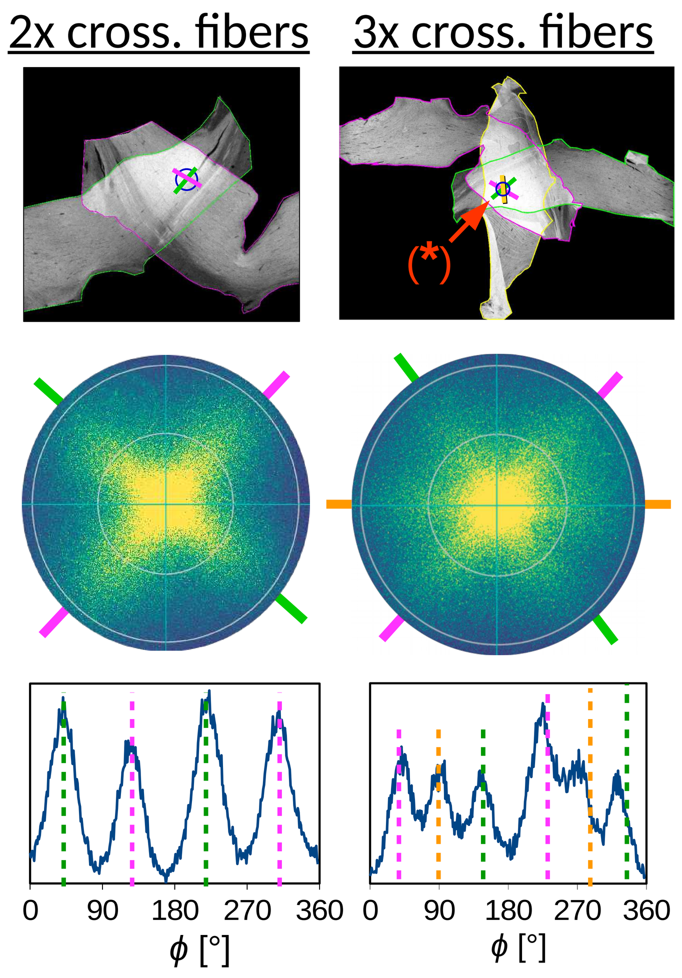


Simulated Light Scattering Patterns

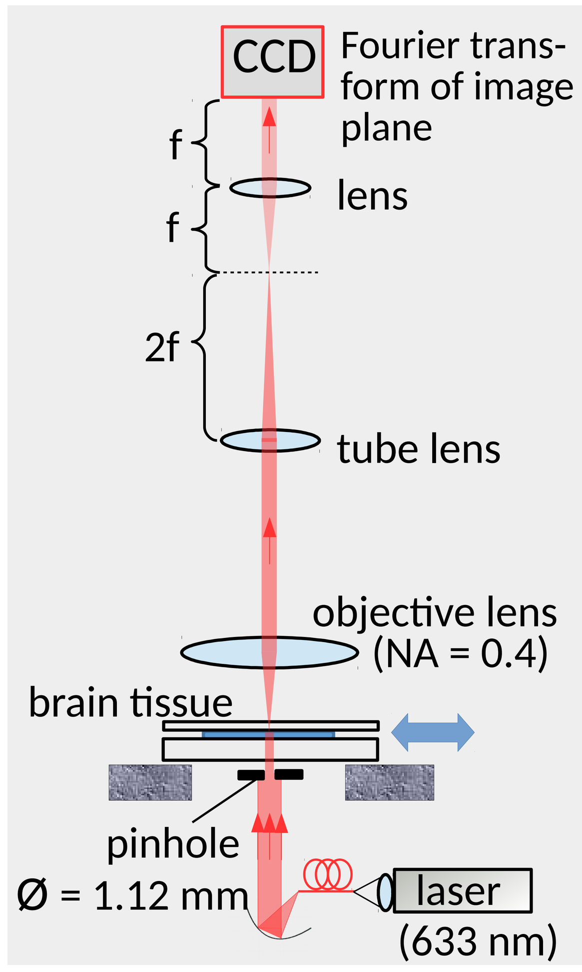
Simulations [3] have shown that the distribution of scattered light behind the sample (scattering pattern) gives additional information about the substructure of the tissue: For in-plane fibers, the light is always scattered perpendicular to the fiber orientation, so that the crossing angle χ of fibers can be reconstructed. For out-of-plane fibers with inclination α, the light is scattered more and more in the direction of the fibers (shown here exemplary for an inclination angle of α = 50°).



Coherent Fourier Scatterometry

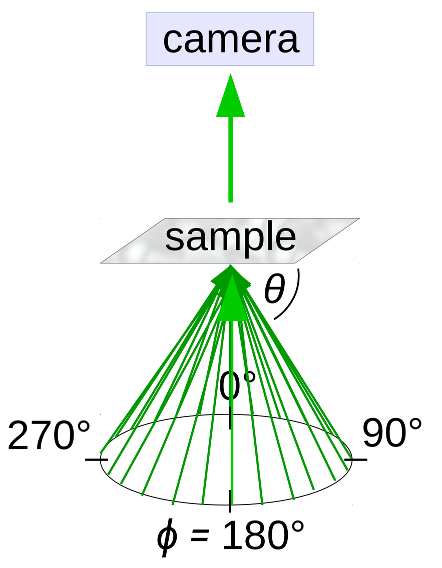


When illuminating a sample with a non-focused laser beam and measuring the Fourier transform of the image plane, we can measure the scattering pattern of the tissue. The measured patterns look similar to the simulated ones: the peaks indicate the (crossing) nerve fiber orientations [4].

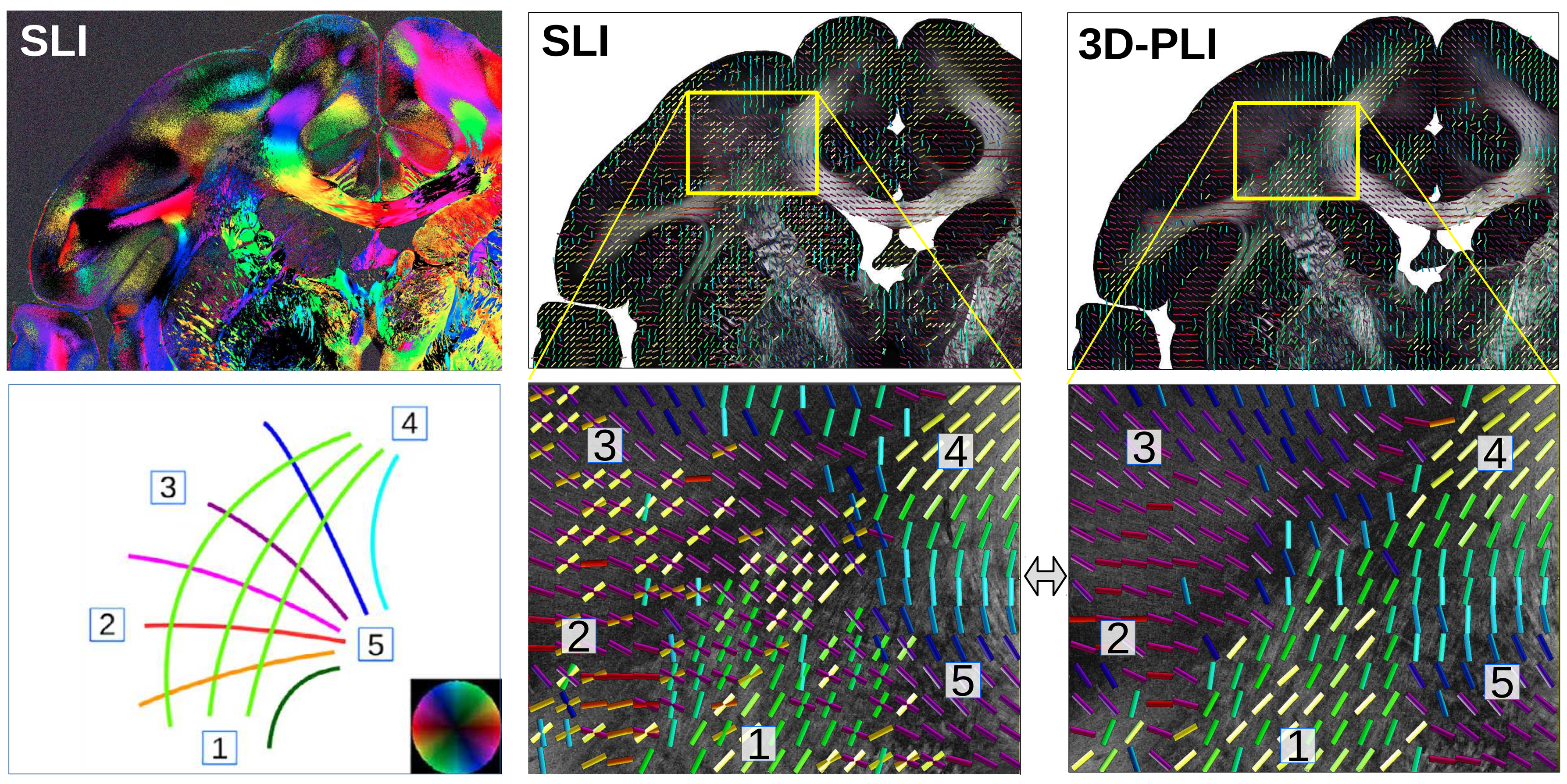


Scattered Light Imaging (SLI)

In SLI, we reverse the light path: Instead of illuminating the sample straight from below and measuring the light scattered in many different directions, we now illuminate the sample from different directions (along a circle) and measure the light transmitted straight into the camera [5-6].

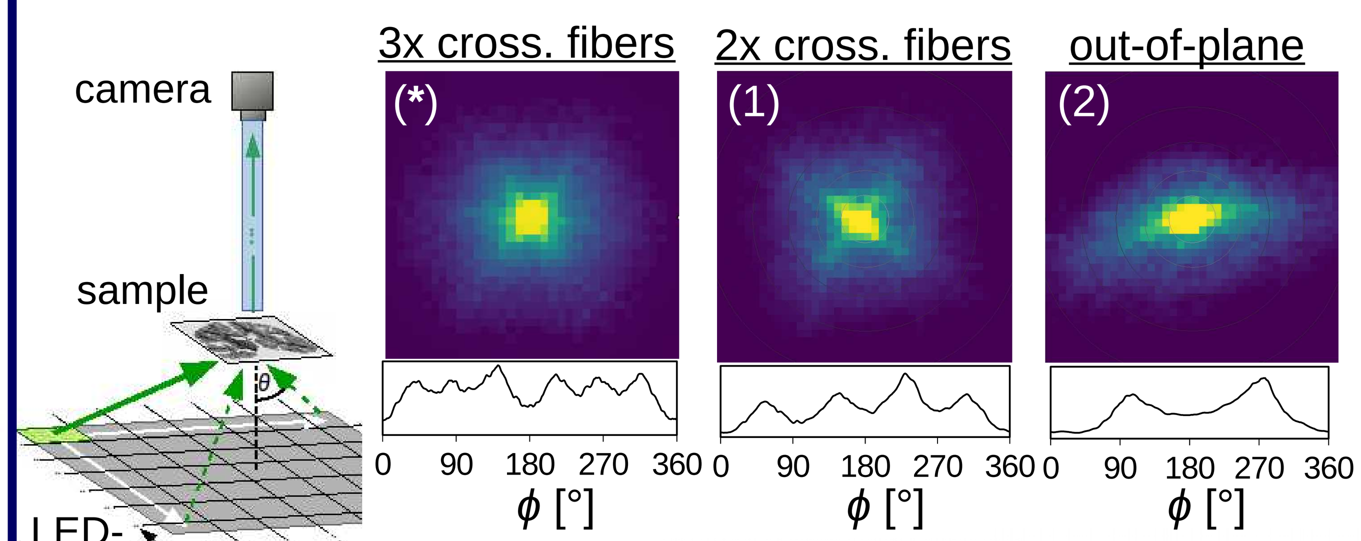


Each pixel in the resulting image series yields a characteristic intensity profile from which the (crossing) nerve fiber orientations can be determined. The images below show the reconstructed (crossing) nerve fiber orientations from SLI in direct comparison to those from 3D-PLI, for a coronal vervet monkey brain section (zoom: corona radiata). SLI allows the reconstruction of several crossing nerve fiber directions (where 3D-PLI yields only a single nerve fiber direction).

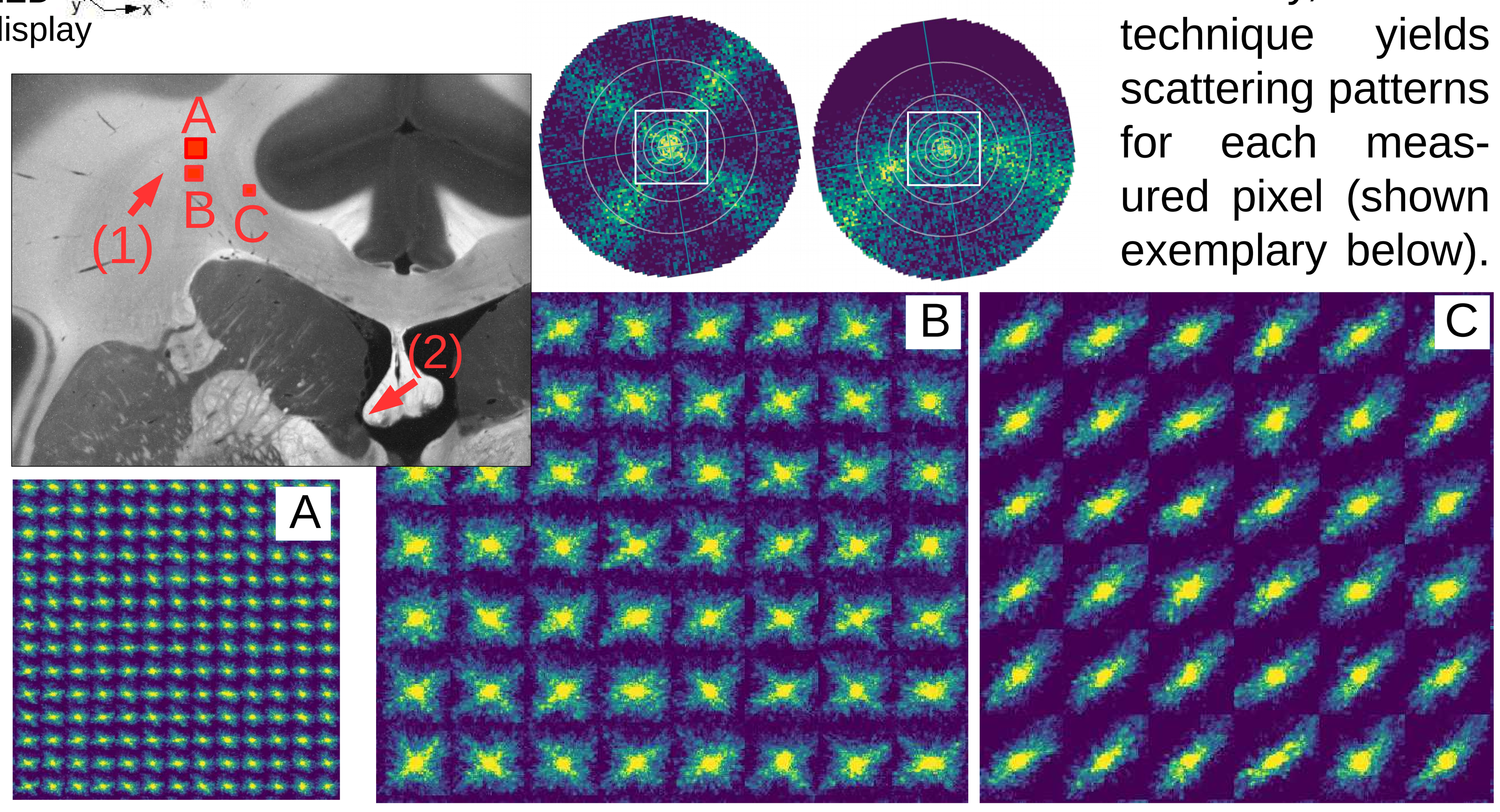


SLI Scatterometry

In SLI scatterometry, we use a display with individually controllable LEDs, so that the sample can be illuminated from all possible angles. This allows the measurement of scattering patterns for whole brain sections [7].



The scattering patterns of crossing and out-of-plane nerve fibers look similar to the simulated ones. In contrast to coherent Fourier scatterometry, the technique yields scattering patterns for each measured pixel (shown exemplary below).



Conclusion

While coherent Fourier scatterometry requires mechanical rasterizing of the sample and the object-space resolution is limited to about 100 μm [4], the here presented scatterometry measurements performed with Scattered Light Imaging allow the simultaneous generation of scattering patterns for all image pixels at once (limited only by the density of LEDs), which makes scatterometry on whole brain sections feasible for the first time.

Acknowledgement / References

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