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The Nanostructure of Human Brain

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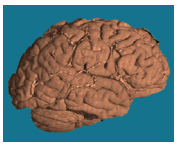
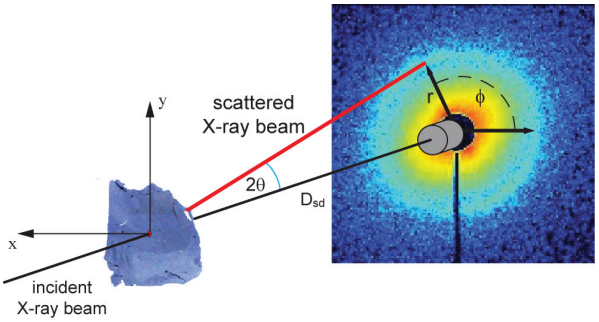
INTRODUCTION



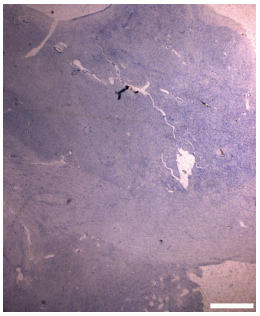
Histological analysis enables uncovering the microstructure of human brain tissue, whereas the nanostructure becomes accessible using X-ray scattering or diffraction. Conventional small angle X-ray scattering (SAXS) experiments detected oriented nanostructures inside human brain, for example myelin [2], but cannot be related to established histology because of the lack of localization. Using the scanning SAXS setup, which combines SAXS with a spatial resolution of a few micrometers in real space at the cSAXS beamline (SLS, PSI, Switzerland) [3], we are able to analyze the brain nanostructure including anisotropies over the entire slice. This method leads to a more detailed undestanding of the histological analysis of brain tissue slices and therefore is a valuable supplement for improving the generic brain atlas.

METHODS

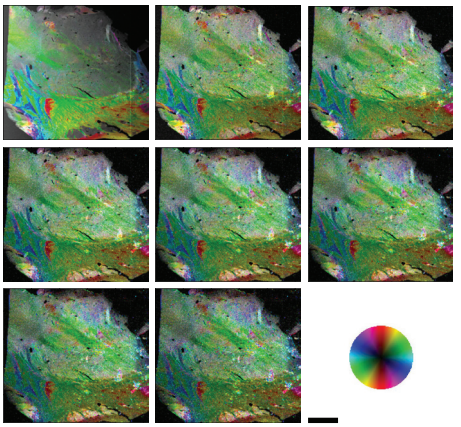


During the SAXS measurements at the cSAXS beamline the X-ray beam was focused to a spot size of 5 x 20 μm², whereas the PILATUS detector was placed at 7.2 m distance from the specimen (D_{sd}). For histological slices mounted on conventional microscopy glass plates an energy of 18.58 keV and for the slice placed in a polyimide sachet an energy of 11.2 keV was chosen. The slices were scanned through the beam in steps of 100 μm in x- and y-directions with an acquisition rate of 5 images per second.

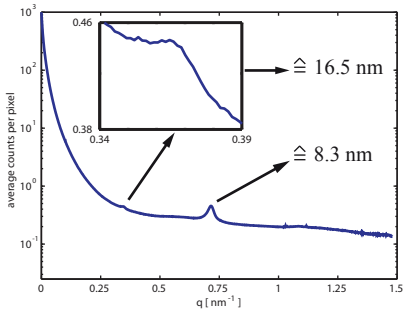
During histology, the thalamus block was cryosectioned and stained using myelin and NISSL staining. The image below shows a microscopy image of a NISSL stained slice used for the measurements. The length scale bar corresponds to 2 mm.

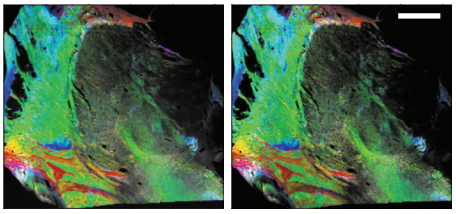


NO STAIN



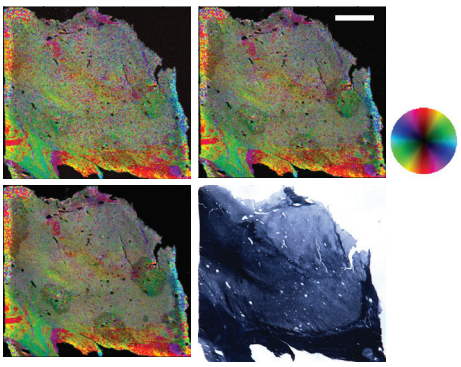
The images above correspond to orientation of nanostructures in the ranges of 5 to 16 nm, 33 to 50 nm, 66 to 83 nm, 99 to 117 nm, 134 to 152 nm, 159 to 182 nm and 217 to 240 nm of an unstained slice placed in a polyimide sachett. The bar corresponds to 5 mm. The radial intensity profile exhibits two peaks. The first peak corresponds to a typical myelin periodicity of 16.5 nm. The second peak corresponding to 8.3 nm is the second diffraction order signal. The figure at the bottom shows the unstained slice in the range of 8 to 9 nm. In the right image only the signal of the second myelin peak is shown.



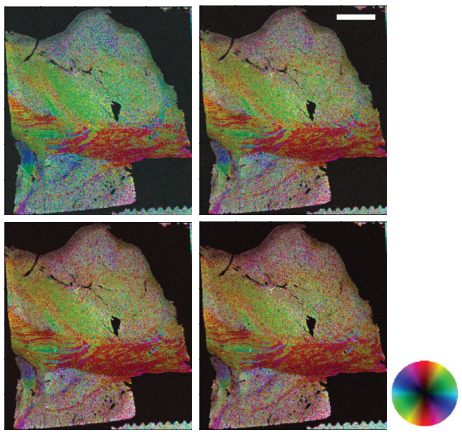


MYELIN STAIN

The figure below shows the processed scattering signals and the according microscopy image of a myelin stained thalamus slice mounted on a microscopy glass plate, in the ranges 70 to 80 nm, 102 to 110 nm and 131 to 145 nm from top left to bottom left. The orientation-dependent colors are according to the color wheel, their brightness is associated with nanostructure abundance. The bar corresponds to 5 mm. The first image shows no significant orientation inside the thalamus but in the adjacent region. During the next two ranges well defined regions with orientations of nanostructures (green, pink) appear inside the thalamus.



NISSL STAIN



The figure above shows orientation of nanostructures in the ranges of 40 to 50 nm, 50 to 60 nm, 60 to 70 nm and 70 to 80 nm (from top left to bottom right) of a NISSL stained thalamus slice mounted on a microscopy glass plate. The bar corresponds to 5 mm. Here as well, only a few smaller regions inside the thalamus show well defined orientation. The region outside the thalamus, which can be identified with the *internal capsule*, contains strongly oriented nanostructures.

CONCLUSION AND ACKNOWLEDGEMENT

Scanning SAXS allows uncovering the nanostrucutre of human brain tissue. Beside the localization, it also provides the orientation and texture. The supplemental information on the morphology of human brain improves the generic brain atlas.

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[1] B. Müller, et al. (2010) *European Journal of Clinical Nanomedicine,* **in press.**
[2] M. De Felici, et al. (2008) *Physics in Medicine and Biology* ***53****:5675-5688.*
[3] O. Bunk, et al. (2009) *New Journal of Physics* ***11****:123016.*