

Accelerating connectomics with X-ray holographic nanotomography

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Mapping the connections between neurons in tissue is a fundamental requirement in neurosciences and it remains out of reach due to the necessary spatial resolution and to the complexity of the circuitry spanning over extended areas. State of the art techniques are based on electron microscopy [1-2]. While these techniques enable 3D high resolution imaging, the covered volumes are very limited and they rely on tissue ultrathin slicing. Our aim is to accelerate the connectomics field by developing adequate X-ray holographic nanotomography. By joining forces of cutting edge X-ray focusing optics [3], together with highly brilliant sources and exceptional sensitivity of phase contrast in the hard X-ray regime [4], we can achieve sufficient spatial resolution for connectomics (Figure 1) while covering in hours volumes of views which require months of continuous seamless operation of EM based instruments [2].

[1] Wei Allen Lee, Vincent Bonin, Michael Reed, Brett J Graham, Greg Hood, Katie Glattfelder, Clay R Reid. "Anatomy and function of an excitatory network in the visual cortex." **Nature**, 532, 7599, 370-374 (2016)

[2] C Shan Xu, Kenneth J Hayworth, Zhiyuan Lu, Patricia Grob, Ahmed M Hassan, José G García-Cerdán, Krishna K Niyogi, Eva Nogales, Richard J Weinberg, Harald F Hess "Enhanced FIB-SEM systems for large-volume 3D imaging" **eLife** 6:e25916 (2017)

[3] Julio Cesar da Silva, Alexandra Pacureanu, Yang Yang, Sylvain Bohic, Christian Morawe, Raymond Barrett, and Peter Cloetens, "Efficient concentration of high-energy x-rays for diffraction-limited imaging resolution," **Optica** 4, 492-495 (2017)

[4] Anna Khimchenko, Christos Bikis, Alexandra Pacureanu, Simone E. Hieber, Peter Thalmann Hans Deyhle, Gabriel Schweighauser, Jürgen Hench, Stephan Frank, Magdalena Müller-Gerbl, Georg Schulz, Peter Cloetens, Bert Mueller. "Hard X-Ray Nanoholotomography: Large-Scale, Label-Free, 3D Neuroimaging beyond Optical Limit", **Advanced Science**, 2198-3844, doi:10.1002/advs.201700694 (2018)

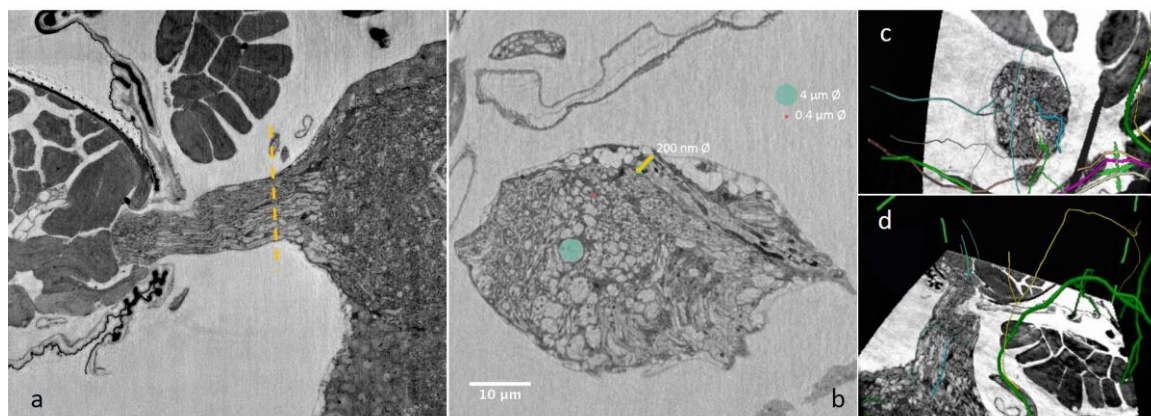


Figure 1: Resolving circuitry controlling locomotion in drosophila with X-ray holographic nanotomography. **a-b:** Regions of interest in reconstructed orthogonal slices (dotted line in panel **a** indicates position of slice illustrated in panel **b**) showing the connections between the ventral nerve cord, which makes most of the central nervous system, and the leg. **c-d:** snapshots illustrating segmentation of the axons using a virtual reality software.