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3D brain tissue imaging using Compton microscopy

Compton X-ray microscopy exploits inelastic X-ray scattering at 60 keV photon energies to generate quantitative electron density maps of biological samples [1], while delivering reduced radiation dose compared to conventional phase-contrast techniques. Using novel wedged multilayer Laue lenses [2] it can achieve resolution comparable to—or even surpassing—that of phase-contrast imaging. These lenses are capable of sub-10 nm focusing even at high energies, currently limited only by the coherence of available high-energy X-ray sources. Unlike widely used SEM-based slicing and imaging approaches [3], Compton microscopy is non-destructive, preserving specimen integrity for correlative studies. In this presentation, we report the first successful demonstration of 3D Compton tomography applied to mouse brain tissue, achieving 250 nm isotropic resolution and highlighting the method's potential and possible challenges for high-resolution, dose-efficient structural biology and connectomics, where radiation damage currently sets the limit on achievable resolution.

[1] Li, T. et al. *Light Sci Appl* 12, 130 (2023).

[2] Bajt, S. et al. *Light Sci Appl* 7, 17162 (2018).

[3] Knott, G. et al. *J Neurosci* 28 (12) 2959-2964 (2008).

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