X-ray tomography for Circuit Neuroscience – Towards X-ray Connectomics

Carles Bosch[1], Yuxin Zhang[1], Safe Khan[1], Alexandra Pacureanu[2], Andreas T. Schaefer[1]

Affiliation: [1]Francis Crick Institute, London, UK, [2]ESRF **andreas.schaefer@crick.ac.uk**

The brain is one of the most complex structures known. In order to understand how information is processed in mammalian brains, one needs to combine functional measurements with structural information across scales from cm to nm. In this talk, I will discuss our multi-modal, multiscale approaches, combining functional imaging *in vivo* in mice with different synchrotron X-ray tomography techniques[1,2]. I will illustrate how nano-holotomography can reveal circuit structure at scale, sufficient to describe input-output relationships in a brain area. Moreover, advanced sample preparation approaches[3,4] make it possible to not only prepare samples optimised for X-ray tomography but also to subsequently perform targeted volume electron microscopy with multiple samples. I will conclude by providing an outlook on what the key challenges are for X-ray tomography to delineate neural circuitry at microscopic level[5] and how to scale these approaches up to entire brains.
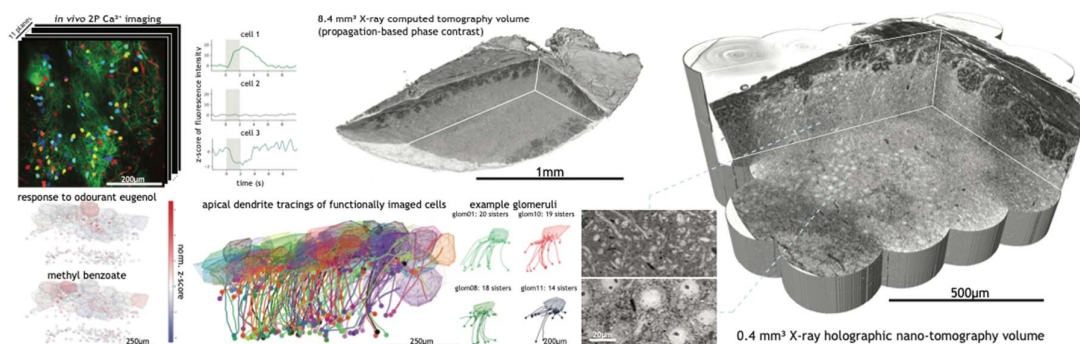
Figure 1: A correlative workflow – combining functional imaging *in vivo* with parallel beam- and holographic synchrotron X-ray nanotomography

References

[1] - Bosch, C., Ackels, T., Pacureanu, A., Zhang, Y., Peddie, C.J., Berning, M., Rzepka, N., Zdora, M.C., Whiteley, I., Storm, M., ,,,, and A.T. Schaefer, Nature Communications 13, 2923. (2022).

[2] - A. Laugros, J. Livingstone, P. Cloetens, A. Pacureanu , A. T. Schaefer. Program No. 144.05. 2023 Neuroscience Meeting Planner. Washington DC: Society for Neuroscience (2023).

[3] - Bosch, C., Lindenau, J., Pacureanu, A., Peddie, C.J., Majkut, M., Douglas, A.C., Carzaniga, R., Rack, A., Collinson, L., Schaefer, A.T., and H. Steigmann. Appl Phys Lett 122, 143701. (2023)

[4] - Zhang, Y., Ackels, T., Pacureanu, A., Zdora, M.-C., Bonnin, A., Schaefer, A.T., and Bosch, C. Frontiers in Cell and Developmental Biology **10**. (2022)

[5] - Bosch, C., Diaz, A., Holler, M., Guizar-Sicairos, M., Aidukas, T., Pacureanu, A., Mueller, E., Peddie, C.J., Collinson, L., Zhang, Y., … A. Diaz, A. Wanner and A.T. Schaefer. bioRxiv 2023.11.16.567403. (2023)