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Mapping the neuronal circuits for smell with light, X-rays and electrons

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Integrating physiology and structure at the neuronal circuit scale can provide a mechanistic understanding on how that circuit works. The glomerular columns in the mouse olfactory bulb contain the first synapse of the olfactory sensory pathway, through a circuit that is compact, modular and accessible to optophysiology setups. A correlative multimodal imaging pipeline that combines in vivo 2-photon microscopy and synchrotron X-ray computed tomography with propagation-based phase contrast provides a robust and versatile approach to identify all neurons imaged in vivo in a multi-mm3 resin-embedded sample of brain tissue. Follow-up targeted imaging is possible with either X-ray nanoholotomography or volume EM, and doing so becomes simpler when milling the sample using a femtosecond laser. Finally, hard X-ray imaging can resolve fine structures in such samples, down to synapses. This approach allows harnessing the resolving power of multiphoton, hard X-ray and volume electron microscopy technologies to create detailed multiscale, multimodal maps of brain circuits.

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