

Title : High-resolution deep imaging of brain slices using Lattice Light-Sheet Microscopy

Authors : Magali Mondin¹, Maxime Malivert¹, Angela Getz² & Mathieu Ducros¹

1 : Univ. Bordeaux, CNRS, INSERM, Bordeaux Imaging Center, BIC, UMS 3420, US 4, F-33000 Bordeaux, France

2 : Univ. Bordeaux, CNRS, Interdisciplinary Institute for Neuroscience, IINS, UMR 5297, F-33000 Bordeaux, France

Fluorescence imaging is essential for studying the brain, but conventional techniques such as confocal and multiphoton microscopy suffer from limitations in imaging depth, resolution, and phototoxicity. Lattice Light-Sheet Microscopy (LLSM) has brought significant advancements to neuroscience, enabling fast imaging of brain slices with low phototoxicity while maintaining a good balance between resolution and acquisition speed. However, resolution and penetration depth remain limited due to optical aberrations induced by thick tissue samples.

Adaptive Optics (AO) applied to Lattice Light-Sheet Microscopy enables real-time correction of these aberrations, significantly improving image quality at greater depths. We demonstrate that this approach enhances the visualization of neuronal structures in thick brain slices, allowing high-resolution imaging down to 60 μm below the tissue surface. Additionally, we combine AO-LLSM with super-resolution microscopy using the DNA-PAINT technique to achieve nanometric resolution of synaptic structures in brain slices.

These advancements open new perspectives for exploring the organization and dynamics of synapses in complex brain tissue, providing imaging tools for neurobiology and the study of synaptic mechanisms at the nanoscale.