Super-resolution imaging in brain slices with lattice light-sheet microscopy

Internship context

"Molecular & functional specificity of synapses" is a new team within the FGA Lab at CNCR, VU Amsterdam. The aim of our research is to understand the molecular processes that establish synapse-type-specific functional diversity and plasticity in neuronal networks. Our team combines advanced molecular tools and imaging techniques for visualizing and manipulating synaptic organization and function in integrated experimental models, using brain slice preparations. This includes fast 4D and super-resolution (SR) imaging of the molecular dynamics and nanoscale organization of synaptic proteins with lattice light-sheet microscopy (LLSM).

LLSM is a high-performance imaging technique for studying sub-cellular dynamics in live 3D samples (Chen et al., 2014; Getz et al., 2022). The high optical sectioning offered by a thinner light-sheet over a larger field of view allows very high spatial and temporal resolution with minimal photobleaching and phototoxicity.

However, two challenges remain. (1) To image synaptic plasticity at the molecular scale, nanometric resolution is necessary, but diffraction limits the resolution of optical systems around ~250 nm. (2) Imaging thick samples is essential to image integrated structures *in situ*, but optical aberrations, increasing with depth, degrade spatial resolution of images. We are building a LLSM setup and developing (1) SR imaging with single molecule localization microscopy (SMLM) techniques to study synaptic nanoscale organization, and (2) adaptive optics (AO) techniques to resolve these structures in depth (Malivert et al., 2022).

Offer description

The aim of this optics-focused Master-2 internship will be to assist in the design, assembly, alignment and validation of a new home-built LLSM setup, using classical and SR imaging modalities combined with AO techniques. The candidate's objectives will include (1) mounting of optical-optomechanical subassemblies, (2) lasers and optics alignment of the microscope paths, (3) engineering work and 3D design to develop new system functionalities, (4) experiments on standard and biological samples to validate microscope performance and (5) development of SMLM and AO protocols on LLSM. The candidate will be required to use several digital tools such as 3D design software and image analysis software (Image J, Imaris) during the internship. Additional opportunities to develop skills in programming and biological sample preparation are available.

The student will be jointly supervised by Maxime Malivert, a postdoctoral researcher leading the LLSM and super-resolution imaging development project, and Angela Getz, team leader.

Candidate profile

We are looking for a Master-2 level student to conduct a 6-month internship in the fields of physics, optics, imaging, and/or microscopy. Experience with engineering work in a research laboratory or in an R&D department is desired. Previous skills in 3D design, programming, image analysis and wet-lab experience would be an asset. The candidate must demonstrate curiosity for discovery and the ability to work autonomously.

Position location

Vrije Universiteit Amsterdam, De Boelelaan 1085, 1081 HV Amsterdam

Application

Please send your application by e-mail, with a CV, a motivation letter and any other useful documents, to the following:

Postdoctoral advisor – Dr. Maxime Malivert: m.malivert@vu.nl
PI – Dr. Angela Getz: a.m.getz@vu.nl