Proposition de stage/thèse :

Tracking of single nanoparticles in deep tissues for measurements of molecular-motors dynamics in neurons

Intra-neuronal transport, mediated by different families of molecular motors, has been shown to be perturbed in neurodegenerative disorders such as Parkinson's and Alzheimer's diseases. Our team has already demonstrated the possibility to study several parameters of this transport in two-dimensional cultures using fluorescent nanodiamonds[1,2]. In order to be able to work in more complex structures and in deep biological tissues, we have developed a two-photon microscope that allows us to localize BaTiO3 nanoparticles (NPs of diameter ~100nm) with an accuracy of about 10nm (article in progress). Their nanometric size allows them to be internalized in cells by endocytosis, the vesicle containing the NP is then taken over by molecular motors and serves as a light probe for their displacement. From an optical point of view, the excitation in the infrared allows access to a transparency window of the biological tissues, the detected optical signal being in our case a non-linear second harmonic signal. The excitation beam is moved to probe the position of the NP using a fast digital holography device, capable of working at 22kHz. This setup allows to follow the dynamics of an NP with a temporal accuracy of 1 to 5 ms. To give an order of magnitude, a molecular motor typically makes a step of 10nm in about 10ms.

The objective of the internship, which contains an important part of experimental and analytical work, is to continue the development and optimization of the tracking microscope by measuring the displacement of an NP in a cell in culture. In particular, in order to access complex and diffusive systems such as mouse brain slices or in a zebrafish larva, it is necessary to implement an adaptive optics device that will have to be designed. If a literature has been emerging for a few years on this implementation in neuroimaging[3,4], it has never been implemented on a dynamic tracking device.

The PhD thesis would include the implementation of this adaptive optics device and its proof of concept on complex biological samples. This realization will allow the study of intracellular transport parameters in 3-dimensional neuronal structures with as yet unreached spatiotemporal resolutions.

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Références

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