

Master internship - Photoacoustic imaging for neurobiology

Position: Master internship - PhD position available following the internship

Topics: photoacoustic imaging, image-signal processing, neurosciences, calcium imaging

Research labs: [Timone Neuroscience Institute](#) (Marseille, France), [Fresnel Institute](#) (Marseille, France)

Private partner company: [DeepColor imaging](#) (Nantes, France)

Application: send CV, transcripts, cover letter, and contact details of two academic references to frederic.chavane@univ-amu.fr and thomas.chaigne@fresnel.fr

Deep photoacoustic imaging for *in vivo* calcium activity monitoring in small animals

Motivation

The study of large-scale neuronal circuits throughout the brain is a major goal in neurobiology yet currently one of the biggest technical challenges. Indeed, high resolution non-invasive imaging of activity in large neuronal populations is limited to shallow depths due to prominent light scattering beyond one millimeter. Photoacoustic imaging is a promising approach to overcome this issue. This fascinating technique relies on ultrasound generation upon the absorption of a light pulse, thus enabling to probe optical absorption contrast at large depth in biological tissue.

Photoacoustic imaging has been used to record the activity of neurons through variations in the optical properties of specific molecules ("proxies"), and ultrasound being much less scattered than light, up to several millimeters deep in the intact brain. The optical contrast underlying the photoacoustic signal can be endogenous (such as that provided by blood - thus hemoglobin - via its concentration in tissue or its oxygen saturation), or exogenous (such as calcium sensitive indicators [1]). Importantly, it has recently been shown that genetically encoded fluorescent markers can generate a photoacoustic signal, as these molecules are primarily optical absorbers [2]. Furthermore, recent proofs of concept have demonstrated that, using such fluorescent indicators, it is possible to image *changes* in their absorption due to neuronal activity [3]. However, these studies were limited by sub-optimal molecular probes and low-frequency piezoelectric ultrasonic sensors, which severely limited spatial resolution.

The *all-optical* photoacoustic imaging approach allows overcoming this limitation. Based on optical interferometric measurement of the acoustic field using a Fabry-Perot cavity [4], this technology can provide high-resolution 3D images (<50-100 μm). A new imaging system of this kind, built by the startup company Deepcolor Imaging, has been acquired as part of a joint project between INT (where the system is installed and where most of the work will be carried out) and the Fresnel Institute.

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The goal of this project is to:

- (i) explore, validate and optimize high-resolution photoacoustic imaging of neuronal activity *via* calcium indicators in brain and/or spinal cord slices *in-vitro*, using a multimodal device that combines the photoacoustic imaging system with a wide-field epifluorescence microscope for the simultaneous recording of the fluorescent signals and with an ultrathin multi-electrode array chip for additional simultaneous electrophysiological recordings [5].
- (ii) develop image and signal processing pipelines to extract neuronal activity from the three-dimensional photoacoustic images (volumetric time series).
- (iii) identify which of the available genetically encoded fluorescent indicators are best suited to this technique, both *in-vitro* and *in-vivo*.
- (iv) demonstrate the applicability to small animals (rodent and, possibly, small non-human primates) by performing photoacoustic imaging of calcium activity in anaesthetized and/or awake animals.

Why you should apply

By joining our research groups at the [Fresnel Institute](#) and the [Timone Neuroscience Institute \(INT\)](#) in Marseille, you will gain hands-on experience in cutting-edge optical imaging approaches and neurobiology. We are seeking talented and enthusiastic students motivated to participate in groundbreaking research.

This is a unique opportunity to gain experience in a wide range of skills, from optics and electronics to *in-vitro* and *in-vivo* imaging in tissue slices and awake small animals, along with image and signal processing.

You will build upon both the existing equipment as well as the combined expertise of the PIs and company involved in the project, regarding photoacoustic imaging, optical microscopy, signal processing and neurobiology. In addition to technical skills, you will also gain a strong understanding of the biology and neuroscience behind our research.

On top of a thrilling research environment, the city of Marseille offers a high quality of life, with limited living costs and a unique combination of a culture and nature.



From left to right: the INT - Timone Neuroscience Institute (10 minutes by bike or public transportation from the city center), the Fresnel Institute (30 minutes by bike or public transportation from the city center); the city center and the old harbour – the heart of Marseille; the “Calanques”, less than an hour by public transportation from the city center

Requirements

To be considered for this master internship, you should have a strong background in physics, optics, electrical engineering, neuroscience (with some solid experience in optical imaging) or any related field. Programming skills are a required (Matlab or Python), as well as a certain taste for tinkering. As you will be evolving in an international environment, you must be fluent in English (at least C1) and exhibit excellent communications capabilities (written and spoken).

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References

- [1] T.-W. Chen *et al.*, "Ultrasensitive fluorescent proteins for imaging neuronal activity," *Nature*, vol. 499, no. 7458, pp. 295–300, juillet 2013, doi: 10.1038/nature12354. Available: <http://www.nature.com/nature/journal/v499/n7458/full/nature12354.html>. [Accessed: Jul. 01, 2016]
- [2] G. S. Filonov, A. Krumholz, J. Xia, J. Yao, L. V. Wang, and V. V. Verkhusha, "Deep-Tissue Photoacoustic Tomography of a Genetically Encoded Near-Infrared Fluorescent Probe," *Angewandte Chemie International Edition*, vol. 51, no. 6, pp. 1448–1451, Feb. 2012, doi: 10.1002/anie.201107026. Available: <http://doi.wiley.com/10.1002/anie.201107026>. [Accessed: Mar. 10, 2017]
- [3] X. L. Deán-Ben *et al.*, "Functional optoacoustic neuro-tomography for scalable whole-brain monitoring of calcium indicators," *Light: Science & Applications*, vol. 5, no. 12, p. e16201, Aug. 2016, doi: 10.1038/lisa.2016.201. Available: <http://www.nature.com/doifinder/10.1038/lisa.2016.201>. [Accessed: Dec. 02, 2016]
- [4] E. Zhang, J. Laufer, and P. Beard, "Backward-mode multiwavelength photoacoustic scanner using a planar Fabry-Perot polymer film ultrasound sensor for high-resolution three-dimensional imaging of biological tissues," *Appl. Opt., AO*, vol. 47, no. 4, pp. 561–577, Feb. 2008, doi: 10.1364/AO.47.000561. Available: <http://www.osapublishing.org/abstract.cfm?uri=ao-47-4-561>. [Accessed: Nov. 28, 2016]
- [5] M. J. Donahue *et al.*, "Multimodal Characterization of Neural Networks Using Highly Transparent Electrode Arrays," *eNeuro*, vol. 5, no. 6, Nov. 2018, doi: 10.1523/ENEURO.0187-18.2018. Available: <https://www.eneuro.org/content/5/6/ENEURO.0187-18.2018>. [Accessed: Apr. 09, 2024]