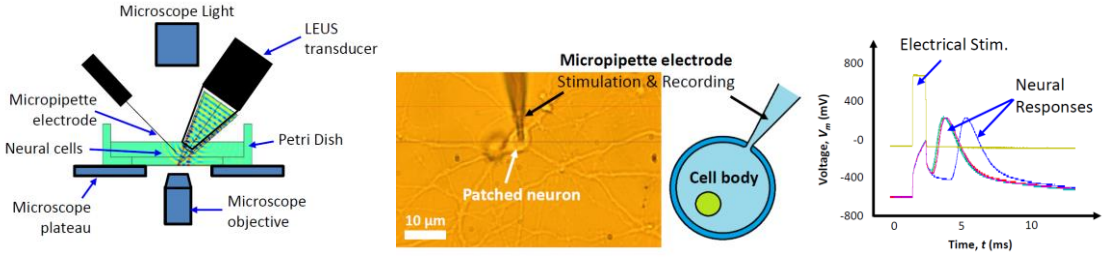
LABTAU
LABORATOIRE THÉRAPIE
ET APPLICATIONS ULTRASONORES

Master / Engineering student project – 6 months

Low Energy Focused UltraSound (LEFUS) stimulation of *in-vitro* neural cells

*Understanding the biophysical mechanisms developing a hybrid **LEFUS/patch-clamp/fluorescence imaging** platform*



Context of the study

The only way to induce and drive brain activity artificially has long been invasive electrical stimulation. Non-invasive alternatives exist (electrical, magnetic) but have limitations (targeting / selectivity, deep region access). This past decade, an increasing number of studies have shown the ability of Low Energy Focused UltraSound (**LEFUS**) to produce or modulate neural activity without the need for invasive (needle) procedures. It is possible to stimulate the cerebral cortex *in vivo* with low frequency ultrasound (250-600 kHz), despite an extended millimetric focal zone. *In vitro* stimulation of the retina with high frequencies (40 MHz) is also feasible with an extremely fine focal spot and high spatial accuracy. Investigations from the 1980s on superficial nerve stimulations (mechanoreceptors, auditory nerves, and in the 2010s (deep brain and retina stimulations) have reported analog conclusions: while LEFUS stimulation is technically sound, no description of biophysical processes is validated for understating and controlling the phenomenon. Various mechanisms have been proposed: **1)** an effect of the LEFUS beam inducing a global radiation force compressing/shearing neural structures, then modifying the membrane electrical potential; **2)** a local mechanical action of LEFUS-induced cavitation inducing electrical current; **3)** a global absorption of LEFUS energy leading to a local temperature increase affecting the neural excitability; **4)** involvement of neuronal or glia membrane channels or neurotransmission. The exact type of cells affected is also not known (neuron, astrocyte, both?). Finally, very few evidences of neuro**stimulation** (of a new activity) have been shown compared to neuro**modulation** (of an existing activity) and mechanisms involved in both phenomena are not sufficiently understood to control their efficacy/safety. **Our main project** aims at pursuing basic research investigations on the neurostimulation mechanisms, after initial works led by LabTAU (ANR T-ERC; https://anr.fr/Projet-ANR-16-TERC-0017), with the goal to develop new brain stimulation approaches.

Project objectives

In this project, the Master/Engineering student will continue the development of an advanced hybrid neurostimulation platform, involving **LEFUS stimulation tools, Patch-Clamp electrophysiology systems and Fluorescence imaging**, for studying ultrasound neurostimulation mechanisms at the cell scale. The feasibility to induce neural activations will be studied **in an *in-vitro* vertebrate model of Central Nervous System (CNS): Human neural progenitor cells (neurons, astrocyte cultures).** To generate **LEFUS**, dedicated LEFUS prototypes will be preliminary characterized acoustically in the context of **neurostimulation**. **Opportunity to apply for a PhD scholarship.**

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Project tasks

- Patch clamp electrical stimulation/recording of neural membrane potentials
- Chemical stimulations
- Fluorescence imaging of ions waves (Ca2+)
- LEFUS prototype characterization (modeling, electro-acoustical measurements)
- Comparison studies between electrical, chemical and LEFUS stimulations

Skills

The candidate must be an Engineering Student or a Master Student in one of the following fields: Biomedical Engineering, Electronic instrumentation, Acoustic instrumentation, Medical Imaging, System and Image

- Signal and image processing
- Basic skills in electrophysiology and neurosciences
- Programming skills: Matlab, C++
- Medical imaging: Ultrasound, MRI

Contacts

Send a CV and a motivation letter to:

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