M2 Internship proposition (5-6 months)

2023

Project title:
INVICT-US
INTERACTION OF ULTRASOUND WITH IN VITRO 3D MICRO-ENVIRONMENT OF BONE CELLS

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Grant : 600€/month

Context and preliminary work

Bone tissue is a complex biological tissue, capable of adapting to its mechanical environment by optimizing its structure, a process known as bone remodeling. Ultrasound stimulation (UStim) of bone regeneration was discovered in the 1950s and has been widely studied since. However, the underlying mechanotransduction mechanisms (translation of mechanical stimuli into biological response) remain poorly identified and this lack of knowledge fuels controversy, preventing the development of efficient and optimized therapeutic tools [1].

The characterization and quantification of mechanical stresses induced by ultrasound stimulation on bone cells (osteocytes) is essential to understand these mechanisms.

To tackle this multiscale and multiphysics issue, the development of relevant models is a key-point. An in vitro UStim experimental set-up has been tested on 2D cell cultures (i.e. inside cell culture dishes) to prevent perturbations of the "acoustic dose" delivered within the cell medium [2]. This experimental set-up is coupled to an equivalent Finite Element (FE) model in order to monitor and tune the acoustic dose delivered to the cells and thus provide a relevant interpretation of future biological results [3]. However, in vivo, osteocytes are surrounded by a fluid (called pericellular matrix) inside the complex 3D lacuno-canalicular network embedded in the extra-cellular matrix (ECM). This 3D micro-environment affects the interaction of UStim with cells and must be taken into account in both the experimental and FE models. To this aim, a commercial porous 3D scaffold (AlvetexTM) has been bought and is currently implemented in the experimental set-up (Figure 1.a).

Objectives

The aim of the current internship is to describe and quantify mechanical stresses induced by fluid movements generated around osteocytes by ultrasonic waves by integrating their 3D microenvironment. To gain insight into this question, finite element numerical models will be developed under Comsol Multiphysics to identify the hydrodynamic phenomena, such as acoustic streaming, induced by ultrasound waves in the scaffold whose internal architecture will be

reconstructed from RX images (Figure 1.b). These models will progressively integrate the geometrical parameters and materials likely to influence the propagation of ultrasound waves and their mechanical interaction with the fluid inside the scaffolds. This internship is part of a larger ANR project (2023-2027) in collaboration with mechanics, acousticians and biologists to correlate the biological response of stimulated osteocytes to identified mechanical constraints.

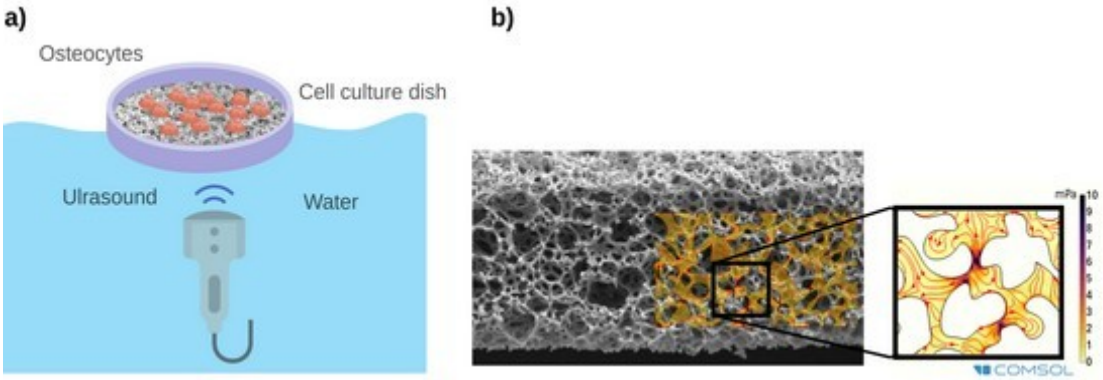

Figure 1: a) In vitro UStim of cells seeded in the 3D porous scaffold. b) Streaming velocities and fluid shear stress inside the 3D porous scaffold.

[1] F. Padilla et al., "Stimulation of bone repair with ultrasound: a review of the possible mechanic effects," Ultrasonics, vol. 54, no. 5, pp. 1125–1145, Jul. 2014, doi: 10.1016/j.ultras.2014.01.004.
[2] M. Majnooni et al., "Anti-reflection cover to control acoustic intensity in in vitro low-intensity ultrasound stimulation of cells," Acta Acust., vol. 6, 2022, doi: 10.1051/aacus/2022007.
[3] M. Majnooni et al., "Monitoring of In vitro ultrasonic stimulation of cells by numerical modeling," Ultrasonics, vol. 124, p. 106714, 2022, doi: 10.1016/j.ultras.2022.106714.

Prerequisites

The candidate should have academic knowledge in one or several disciplinary fields related to the subject: fluid and solid (bio)mechanics and acoustics. Skills in numerical modelling will be an asset to allow a quick handling of the implemented means.
He/she will have to show a spirit of synthesis, communication, rigour and methodology to be able to invest in the work requested and interact with the internship managers and the the laboratory environment in general.
It is possible to finance a thesis following this M2 internship.

Application

Candidates must send their application by e-mail, including a Curriculum Vitae, a letter of motivation, transcripts and a letter of recommendation from a previous internship at cecile.baron@univ-amu.fr and carine.guivier@univ-amu.fr.
After examining the application, a video interview will be proposed.