# PhD subject proposal

Title : Mechanobiological modeling and simulation of coupled fluid-structure interaction using homogenization : application to the lacunocanalicular network for bone mechanotransduction.

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Location : Laboratory of Engineering Sciences, Informatics and Imagery (ICUBE), University of Strasbourg, CNRS, France.

National and international collaborations :

- Institut de Biomécanique Humaine George Charpak, ENSAM Paris Tech : Dr. Rachele Allena – Local modeling of cell to cell communications
- Laboratoire de bioingénierie et bioimagerie ostéo-articulaire (B2OA, Paris 7) : Prof. Hervé Petite, Dr Morad Bensidhoum – Bone cell experiments
- University del Aquila, La Sapienza, Rome : Prof. Francesco dell'Isola – Theoretical modeling
- Technical University Varsovie (TUW) : Prof. Tomasz Lekszyck – Theoretical modeling and optimization
- Tehran University : Dr. Majid Baniassadi – Statistical homogenization
- LEM3 (Nancy) : Dr Cédric Laurent – Bioreactor experiments
- Team MécaFlu (ICube) : Prof. Yannick Hoarau – Fluid flow modeling and fluid-structure interaction.

National collaboration network : CNRS Federation Engineery Mechanobiology Osteo-Articular (IMOA) FR2003

Resume :

The proposed subject deals with bone mechanobiology and more specifically with the coupled phenomena between mechanics, fluids and biology at the origin of bone density evolution for medical applications such as surgery, repair, prosthesis, and orthopedic. The subject is integrated within the Materials, multiscale and Biomechanics team as well as Fluid Mechanics team on the modeling and simulation of local phenomena for bone mechanotransduction, and the development of a homogenized model that will provide a better understanding of the existing links between the microscopic and macroscopic scales.

A theoretical numerical model for bone regeneration is currently under development within the team that accounts for the links between the mechanical behavior, through the applied external forces, and the mechanosensitive cell responses and activation through the existing molecular exchanges within the structure.

The PhD objectoves are multiple : (i) Develop a theoretical numerical model of bone mechanotransduction closer to reality integrating the mechanical and induced biological effects, (ii) Identify and quantify the most influencing factors of this mechanotransduction through local numerical study of fluid-structure interactions and diffusion, and develop with our external collaborators experimental tools and methods to measure these biological parameters at the origin of bone density evolution, (iii) Link through the homogenization techniques the local phenomena with experimental observations of bone kinetics done at the macroscopic scale.

Subject description

The development of predictive models for bone regeneration based on the Mecanostat principal by Frost [1] has been active for many years, but to be efficient, these models need integration of appropriate theories accounting for the mechano-physiological phenomena according at the microstructural scale of the material. Numerous works have tried to reach this objective, but without being able to integrate all the phenomena at play. Recently, new models have appeared [2-10] trying to link these phenomena. However, numerous difficulties remain to be solved in the comprehension of the mechanotransduction process at the origin of this evolution, that also depends on the vascular growth and cell nutriment availability [11,12].

To obtain a better prediction of bone density evolution, other sources influencing the global mechanobiological stimulus definition, must be integrated. Some experimental studies have already shown that oxygen and glucose disponibility have an important impact [13,14] on cell survival after implantation. These effects must be accounted for in a coupled model using adapted homogenization tools. Preliminary studies enabled the extraction of the existing links between mechanics and biology through cell migration and, oxygen and glucose disposal [15-18]. Nevertheless, the exact mechanotransduction communication through the lacuna-canalicular network remains unknown.

The PhD work will focus more specifically, through the definition of the internal microstructural distribution of bone canalicular network, on a fluid-structure interaction model. This model will represent, at the microscopic scale, the flow and diffusion of biological fluids within their environment. This step will, in the same time, enable to identify the local important parameters of the mechanotransduction process. Once this step done, A micro-macro homogenization will be undertaken, to reproduce, as a function of the specific bone microstructure, the transport phenomena and existing biological communications. Three scales need to be linked : (i) the cellular and lacunocanalicular scale source of the cell to cell communications, (ii) the osteon scale, base component of bone, and (iii) the macroscopic scale where bone density becomes homogeneous. Each scale change requires its own homogenization process. The micro-meso homogenization will be done using statistical homogenization (in collaboration with Tehran University), and the meso-macro homogenization will be done with Mori-Tanaka or Generalized Mori-Tanaka methods.

The existing collaborations with the Institut de Biomécanique Humaine George Charpak (ENSAM Paris Tech), L'aquila, La Sapienza University (Rome), Technical Universit Warsaw, and Tehran University for the theoretical modeling, and laboratoire de bioingénierie ostéo-articulaire (B2OA, Paris 7) and LEM3 Laboratory (Nancy) for cell experiments enable to reach the goals of this work with validation of this new model. The proposed subject requires good knowledge of theoretical mechanics, physics and numeric. Ideally the candidate will possess good background in applied mathematics and numerical physics/mechanics. Some experimental knowledge will be appreciated.

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