**Post doc subject:** Modeling the uterine synchronization by means of the hydrodynamic-stretch activation mechanism

**Post doc Advisor:**
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**Context of the study:**
This project fits within the LABEX theme 3.1: Multi-level and multi-physical optimization of a set of complex systems. It concerns the development and the optimization of a multi-level (cellular, tissular, organ, whole body) and multiphysic (electrical, mechanical) model of the phenomenon regulating the uterine contractile efficiency. The central role of modeling and simulation on the analysis of biological or physiological process is now clearly established. Current research is moving towards the integration of different models, to analyze the complex interactions that govern these physiological systems. This integrative modeling approach is central to emerging disciplines such as Integrative Physiology. It is also the fundamental background of international research initiatives, such as the IUPS Physiome project [1] or, at the European level, the Virtual Physiological Human, that are moving towards the integration of models proposed for different functions (multiphysic, horizontal integration), at multiple scales (cell to organ and whole body, vertical integration) and with various levels of knowledge integration, in order to analyze the complex interactions that govern physiological systems. Most work has focused on the modeling of the electrical and mechanical activities of the heart and their regulation by the autonomic nervous system [2]. Few things have started for the modeling of the striated muscles, and nothing for the uterine muscle. Recent studies suggest that the uterine synchronization is a key factor for the efficiency of the uterine contraction [3]. During this project, we will focus our effort in modeling a new hypothesis, the hydrodynamic-stretch activation mechanism of uterine synchronization [4] that may be a better hypothesis than the electrical propagation, currently supported by most studies. This will be addressed in a system-based approach, through multiscale-multiphysic modeling [5] by coupling an existing multiscale electrical model of the uterine electrical activity to a new modeling of the mechanical properties of the uterine muscle, as well as of their complex interactions for the control of uterine contractile efficiency.

**Post doc description:**
This post doc will implement, from the existing multi-scale model, that simulates at the cell level the ionic dynamic phenomenon, the multi physic approach permitting to describe the hydrodynamic-stretch activation mechanism. This will need a co-simulation approach as well as the development of intensive parallel computing strategy to optimize the computational time and memory management. This model will need (figure 1): 1) a new model of the excitation/contraction phenomenon: different kinds of model already exist at the cellular level for different muscles (striated muscle, uterus, bladder….) linking the dynamic of the calcium (available from the existing model at the cellular level) to the force generated by a cell [6,7]. We will choose the most pertinent model for our multi physic approach (simulation of thousands of cells); 2) a new model for the generation of the intra-uterine pressure (IUP), from the force generated by all the active cells, by means of a simplified model of the uterine muscle (organ level: 3D mesh); 3) the computation of tissue stretching by the association of an elastic law to the uterine mesh elements (tissue level); 4) the definition of a law for the mechano/electric coupling permitting to generate the stimulation to other cells, based on their sensitivity to stretching.

The co-simulation will permit to run simultaneously the existing multiscale electrical model (generation of calcium dynamic and abdominal electrical activity) and the mechanical model (force and IUP generation, stretch computation), in order to simulate both electrical and mechanical activities in different hydrodynamic-stretch activation coupling. We will then compare the simulated signals to real signals recorded, with multiple sensors (multi-electrode grids), to validate our model.

This proposal is related to other Labex activities previously developed in our team: Jérémy Laforêt’s post-doc (2013), that permitted us to develop specific tools for the sensitivity analysis of the existing electrical model [8]; Mariam Al Harrach’s PhD thesis “Modeling of the surface EMG-Force relationship by data analysis of high resolution sensor network” (2013-2016). These projects share the same problematic: development/optimization of a co-simulated electro-mechanical model of muscles.

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Figure 1: Schematic presentation of the multiscale-multiphysic model of the hydrodynamic-stretch activation phenomenon. The rounded corner shapes represent the cellular level. The rectangular shapes represent the tissue/organ levels. The blue part represents the electrical model, the orange one the mechanical part.

Candidate’s profile:
- Experience in electrophysiological and/or mechanical modeling of physiological systems
- Computer and biomedical signal processing skills.

Documents required to apply:
Send to Catherine.marque@utc.fr
- Curriculum vitae
- Motivation letter
- At least two references and/or recommendation letters
- A statement of research experience and interests

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References: