Thesis subject: MechanIcal and electrical ModEling of the uTerIne Contraction (MIMETIC)

PhD Supervisors:

- Catherine MARQUE
  UMR CNRS 7338, BMBI laboratory, UTC
  +33 (0)3 44 23 45 71, Catherine.marque@.utc.fr
  Alain RASSINEUX
  UMR CNRS 7337, Roberval laboratory, UTC
  +33 (0)3 44 23 52 72, alain.rassineux@utc.fr

Context of the thesis:

The thesis is part of the project activities of the Laboratory of Excellence (LABEX) at the Université de Technologie de Compiègne (UTC) in France on the Control of Technological Systems of Systems (MS2T) (www.utc.fr/labexms2t). This project fits within the LABEX theme 3.1: **Multi-level and multi-physical optimization of a set of complex systems**. It is the continuation of the post-doctoral project of Maxime Yochum, that has been financed by the Labex, but with a new collaboration with the Roberval Laboratory and ANSYS company to develop the mechanical part of this uterine model.

PhD thesis description:

This thesis is part of a project which aim is to propose a tool for the **diagnosis** of pathological evolution of uterine contractility on a **model-aided approach**. 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**. This **multi-scale (cell to organ) multi-physic (electrical, mechanical) model** is based on a biophysical model, already developed by our team that will be improved during this project.

The work proposed in this thesis will concern the development and optimization of the **model of the mechanical contractile activity of the uterus** (in relation with its electrical activity, the electrohysterogram: EHG) in order to represent pathological evolution leading to preterm labor. We have already developed in our team, a biophysics multi-scale model of the genesis of the EHG, from uterine cell contractility, to the EHG recording on woman's abdomen[1] (Erasysbio+ project: http://www.erasysbio.net/index.php?index=268). This model also includes the diffusion of the electrical activity, classically proposed until now to explain the synchronization of the uterine activity during labor. Recent work permitted us to evidence that this electrical diffusion may not be sufficient to explain the efficiency of uterine contraction during labor. During this project, in order to test the new hypothesis, the **hydrodynamic-stretch activation mechanism of uterine synchronization**[2], that may be a better hypothesis than the electrical propagation alone currently supported by most studies, we will add to the electrical model, based on a **multi-physic approach,** the stretch activation mechanism of uterine synchronization (**mechanotransduction**). From the existing multi-scale model[3] that simulates the ionic dynamic at the cell level, the electrical diffusion and the excitation/contraction phenomenon, based on Burstyn's work[4], the implementation of this mechanotransduction mechanism will need: 1) the definition of a **realistic 3D mesh of the uterus** extracted from MRI imaging; 2) a model for the **generation of the intra-uterine pressure** (IUP), from the forces generated by all the active cells, based on the realistic mesh of the uterus and on **finite element modeling (FEM)** and **fluid-structure** interaction; 3) the computation of **tissue stretching** by the association of an elastic law to the uterine mesh elements; 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. This could be done by adding, to the electrical model at the cell level, stretch sensitive channels that have been evidenced yet on different kinds of cells.[5]

The implementation and use of this model requires a **co-simulation approach** as well as the development of intensive parallel computing strategy to optimize the computational time and memory management. This co-simulation will permit to run simultaneously the existing multi-scale electrical model (generation of action potentials and calcium dynamic, at the cell level, electrical diffusion at the tissue level, and abdominal electrical activity, whole body level) and the mechanical model (force and IUP generation, stretch computation), in order to **simulate both electrical and mechanical activities** with different hydrodynamic-stretch activation coupling. We will then compare the simulated signals to real signals (EHG, IUP) available in our lab from internal recordings of pregnant monkeys, to validate our model.
The develop model will finally permit to:

- Formalize and analyze the actual biological/physiological knowledge on the complex uterine system of systems concerned with preterm labor (PTL)
- Test new signal processing tools developed, or to be developed, to evidence the evolution of this system from its physiological to its pathological state, based on realistic simulated signals
- Develop a model aided diagnosis approach by using personalized models and identification process.

Cofunding or/and partnerships:
This work will be done in collaboration with the R&D center of ANSYS, specialized in numerical simulation (http://www.ansys.com/fr-FR), as co-financer of this thesis. ANSYS will foster and promote the creation of a startup to transfer the results of this research to clinical practice.

Links with other projects (submitted or already funded (Regional Council, ANR, Equipex etc), with a Labex Challenge Team:
An IUF project has been submitted by C. Marque related to the use of a multi-scale multi-physic model for the model-aided diagnosis of preterm labor.

Candidate's profile: Mechanics, biomechanics, numerical simulation

Documents required to apply:
Send to (adresse mail de l'encadrant qui sélectionnera les candidats)

- Curriculum vitae
- Motivation letter
- At least two references and/or recommendation letters
- A statement of research experience and interests

Location:
Laboratory BMBI, UMR CNRS 7338
Université de Technologie de Compiègne (UTC)
Centre de recherche de Royallieu
BP 20529 Rue Personne de Roberval
60205 Compiègne cedex –France

References:

1. Laforet J. et al. IEEE Trans Biomed Eng., 2011; 58(12): 3487-90.
2. Young RC. Ann N Y Acad Sci., 2007; 1101: 72–84.
3. Yochum, M., et al. Computers in Biology and Medicine, 77, 182-194, 2016.
4. Bursztyn L. et al. Am J Physiol Cell Physiol, 2007; 292(5): C1816-C1829.
5. Gilbert G. et al., Cardiovascular Research, 2014; 103: 313-23.

ANSYS France SAS (siège social) TEL : +33 (0)1 30 60 15 00
15 Place George Pompidou FAX : +33 (0)1 30 60 19 42
78180 Montigny le Bretonneux

ANSYS France SAS TEL : +33 (0)4 78 94 56 40
11 Avenue Albert Einstein FAX : +33 (0)4 72 82 31 55
69100 Villeurbanne

Catherine MARQUE
Laboratory BMBI, UMR CNRS 7338
Université de Technologie de Compiègne (UTC)
Centre de recherche de Royallieu
BP 20529 Rue Personne de Roberval
60205 Compiègne cedex –France

Villeurbanne, le 30 janvier 2017

Objet : Soutien de la thèse M2_ECU

La société ANSYS est le leader mondial des logiciels de simulation numérique avec plus de 3000 employés et un chiffre d'affaires annuel d'un milliard de dollars US.

La filiale ANSYS France SAS comprend 155 employés, dont 45 ingénieurs de développement et de recherche.

Le centre de recherche ANSYS de Lyon est en charge du développement des applications cliniques pour offrir aux cliniciens des logiciels de simulation 3D utiles en planning et per-opératoire.

Ce centre de recherches fort de ses 8 étudiants en thèse travaille en étroite collaboration avec les laboratoires académiques et centres hospitaliers.

La thèse proposée par le Professeur Catherine Marque sur la modélisation mécanique et électrique de la contraction utérine est en parfaite adéquation avec nos objectifs de recherche appliquée.

Nous soutenons totalement ce projet et considérons en priorité le financement complémentaire au Labex MS2T. Ce financement complémentaire couvrirait une partie des frais de salaire et d'encadrement.

Michel Rochette
Directeur de Recherche