



## Activity Report 2015

### **Team M3DISIM**

# Mathematical and Mechanical Modeling with Data Interaction in Simulations for Medicine

Inria teams are typically groups of researchers working on the definition of a common project, and objectives, with the goal to arrive at the creation of a project-team. Such project-teams may include other partners (universities or research institutions).

RESEARCH CENTER  
Saclay - Île-de-France

THEME  
Modeling and Control for Life Sciences



## Table of contents

<b>1. Members</b>	<b>1</b>
<b>2. Overall Objectives</b>	<b>2</b>
<b>3. Research Program</b>	<b>2</b>
3.1. Multi-scale modeling and coupling mechanisms for biomechanical systems, with mathematical and numerical analysis	2
3.2. Inverse problems with actual data – Fundamental formulation, mathematical analysis and applications	2
<b>4. Application Domains</b>	<b>3</b>
<b>5. Highlights of the Year</b>	<b>3</b>
<b>6. New Software and Platforms</b>	<b>3</b>
6.1. FELiScE	3
6.2. HeartLab	3
6.3. Verdandi	4
<b>7. New Results</b>	<b>4</b>
7.1. Modeling	4
7.1.1. Model-based analysis of continually measured signals of aortic pressure and flow	4
7.1.2. Thermodynamical framework for modeling chemical-mechanical coupling in muscle contraction – Formulation and validation	5
7.1.3. Biophysical modeling of seismocardiograms measurements	5
7.2. Numerical Analysis	5
7.2.1. Dirichlet-to-Neumann operator for diffraction problems in stratified anisotropic acoustic waveguides	5
7.2.2. Fourth-order energy-preserving locally implicit time discretization for linear wave equations	6
7.2.3. Numerical methods for poromechanics: Applications to cardiac perfusion	6
7.3. Model-Data Interaction	7
7.3.1. Displacement Reconstructions in Ultrasound Elastography	7
7.3.2. Recursive joint state and parameter estimation	7
7.3.3. Convergence of discrete-time Kalman filter estimate to continuous-time estimate	8
7.3.4. Observers for the wave equation in unbounded domains	8
7.3.5. A Luenberger observer for reaction-diffusion models with front position data	8
7.3.6. Identification of weakly coupled multiphysics problems. Application to the inverse problem of electrocardiography	9
7.3.7. Data assimilation of cine-MR images by a biophysical model	10
<b>8. Bilateral Contracts and Grants with Industry</b>	<b>10</b>
<b>9. Partnerships and Cooperations</b>	<b>10</b>
9.1. European Initiatives	10
9.1.1.1. VPH-Share	10
9.1.1.2. VP2HF	11
9.2. International Initiatives	11
9.3. International Research Visitors	11
<b>10. Dissemination</b>	<b>12</b>
10.1. Promoting Scientific Activities	12
10.1.1. Scientific events organisation	12
10.1.2. Scientific events selection	12
10.1.2.1. Member of the conference program committees	12
10.1.2.2. Reviewer	12
10.1.3. Journal	12
10.1.3.1. Member of the editorial boards	12

10.1.3.2. Reviewer - Reviewing activities	12
10.1.4. Invited talks	13
10.1.5. Leadership within the scientific community	13
10.2. Teaching - Supervision - Juries	13
10.2.1. Teaching	13
10.2.2. Supervision	13
10.2.3. Juries	14
10.3. Popularization	14
<b>11. Bibliography</b> .....	<b>14</b>

## Team M3DISIM

*Creation of the Team: 2013 January 01*

### Keywords:

#### **Computer Science and Digital Science:**

- 6.1.1. - Continuous Modeling (PDE, ODE)
- 6.1.2. - Stochastic Modeling (SPDE, SDE)
- 6.1.4. - Multiscale modeling
- 6.1.5. - Multiphysics modeling
- 6.2.1. - Numerical analysis of PDE and ODE
- 6.2.7. - High performance computing
- 6.3.1. - Inverse problems
- 6.3.2. - Data assimilation
- 6.3.4. - Model reduction
- 6.4.3. - Observability and Controlability
- 6.4.4. - Stability and Stabilization

#### **Other Research Topics and Application Domains:**

- 2.2.1. - Cardiovascular and respiratory diseases
- 2.6.2. - Cardiac imaging

## 1. Members

### **Research Scientists**

Dominique Chapelle [Team leader, Inria, Senior Researcher, HDR]  
Radomir Chabiniok [Inria, Starting Research position]  
Sébastien Imperiale [Inria, Researcher]  
Philippe Moireau [Inria, Researcher (Secondment from Corps des Mines)]  
Fabrice Vallée [AP/HP, from Jun 2015 (50% part-time)]

### **Engineers**

Gautier Bureau [Inria]  
Sébastien Gilles [Inria]

### **PhD Students**

Bruno Burtschell [Inria, granted by FP7 VPH-SHARE project]  
Federica Caforio [Inria, from Nov 2015]

### **Post-Doctoral Fellows**

Atte Aalto [Inria]  
Alexandre Laurin [Inria]  
Antoine Tonnoir [Inria]

### **Administrative Assistant**

Hélène Kutniak [Inria]

### **Others**

Annabelle Collin [INP BORDEAUX]  
Gabriel Valdes Alonzo [Inria, intern from Pontificia Univ. Católica de Chile, until Mar 2015]  
Matthieu Caruel [Univ. Paris XII]

Arthur Le Gall [AP/HP, from May 2015]

## 2. Overall Objectives

### 2.1. Overall Objectives

The research carried out in the M3DISIM team has a rather global methodological perspective oriented towards biomechanics, encompassing mathematical modeling and analysis, inverse problems arising from model-data coupling, and the formulation and analysis of effective and reliable numerical procedures adapted to this overall program. We are also very keen on demonstrating the effectiveness and relevance of these methods in actual applications, usually by proof-of-concept studies carried out within various collaborations.

## 3. Research Program

### 3.1. Multi-scale modeling and coupling mechanisms for biomechanical systems, with mathematical and numerical analysis

Over the past decade, we have laid out the foundations of a multi-scale 3D model of the cardiac mechanical contraction responding to electrical activation. Several collaborations have been crucial in this enterprise, see below references. By integrating this formulation with adapted numerical methods, we are now able to represent the whole organ behavior in interaction with the blood during complete heart beats. This subject was our first achievement to combine a deep understanding of the underlying physics and physiology and our constant concern of proposing well-posed mathematical formulations and adequate numerical discretizations. In fact, we have shown that our model satisfies the essential thermo-mechanical laws, and in particular the energy balance, and proposed compatible numerical schemes that – in consequence – can be rigorously analyzed, see [5]. In the same spirit, we have recently formulated a poromechanical model adapted to the blood perfusion in the heart, hence precisely taking into account the large deformation of the mechanical medium, the fluid inertia and moving domain, and so that the energy balance between fluid and solid is fulfilled from the model construction to its discretization, see [6].

### 3.2. Inverse problems with actual data – Fundamental formulation, mathematical analysis and applications

A major challenge in the context of biomechanical modeling – and more generally in modeling for life sciences – lies in using the large amount of data available on the system to circumvent the lack of absolute modeling ground truth, since every system considered is in fact patient-specific, with possibly non-standard conditions associated with a disease. We have already developed original strategies for solving this particular type of inverse problems by adopting the observer stand-point. The idea we proposed consists in incorporating to the classical discretization of the mechanical system an estimator filter that can use the data to improve the quality of the global approximation, and concurrently identify some uncertain parameters possibly related to a diseased state of the patient, see [7], [8], [9]. Therefore, our strategy leads to a coupled model-data system solved similarly to a usual PDE-based model, with a computational cost directly comparable to classical Galerkin approximations. We have already worked on the formulation, the mathematical and numerical analysis of the resulting system – see [3] – and the demonstration of the capabilities of this approach in the context of identification of constitutive parameters for a heart model with real data, including medical imaging, see [1].

## 4. Application Domains

### 4.1. Clinical applications

After several validation steps – based on clinical and experimental data – we have reached the point of having validated the heart model in a pre-clinical context where we have combined direct and inverse modeling in order to bring predictive answers on specific patient states. For example, we have demonstrated the predictive ability of our model to set up pacemaker devices for a specific patient in cardiac resynchronization therapies, see [10]. We have also used our parametric estimation procedure to provide a quantitative characterization of an infarct in a clinical experiment performed with pigs, see [1].

## 5. Highlights of the Year

### 5.1. Highlights of the Year

#### 5.1.1. Awards

A. Collin (who did her PhD in the team) received the SMAI-GAMNI award 2015 for Best PhD thesis and the ECCOMAS PhD award 2015.

A. Aalto received the award for the best doctoral thesis in Aalto University School of Science during 2014.

## 6. New Software and Platforms

### 6.1. FELiScE

Finite Elements for Life Sciences and Engineering problems

KEYWORDS: Health - Cardiac - Finite elements - Cardiac Electrophysiology

FUNCTIONAL DESCRIPTION

FELISCE – standing for “Finite Elements for Life Sciences and Engineering” – is a new finite element code. One specific objective of this code is to provide in a unified software environment all the state-of-the-art tools needed to perform simulations of the complex cardiovascular models considered in the teams M3DISIM and REO – namely, involving fluid and solid mechanics, electrophysiology, and the various associated coupling phenomena.

In FELISCE we have prepared a branch called HappyHeart, which aims at providing a user-friendly interface able to deal efficiently with complex cardiovascular simulations. Started in 2013, the code is already quite large (about 55,000 lines of code in almost 700 different files) and its core is about to be complete. It includes among others full HPC functionalities, high-order finite elements, physics coupling and topology capabilities. Our purpose will then be to use the library to implement the sophisticated cardiovascular models of the team and couple them with Verdandi (data assimilation library) to provide patient-specific simulations.

- Participants: Dominique Chapelle, Miguel Angel Fernandez Varela, Jean-Frédéric Gerbeau, Philippe Moireau, Marina Vidrascu, Sébastien Gilles, Sébastien Impériale and Gautier Bureau
- Contact: Sébastien Gilles
- URL: <http://felisce.gforge.inria.fr>

### 6.2. HeartLab

KEYWORDS: Simulation - Health - Cardiac - Image analysis - Computational geometry

SCIENTIFIC DESCRIPTION

The heartLab software is a library written in (64-bit compatible) Matlab and C (mex functions), designed to perform both simulation and estimation (based on various types of measurements, e.g. images) of the heart mechanical behavior. Started in 2006, it is already quite large (about 60,000 lines), and is used within various collaborations.

#### FUNCTIONAL DESCRIPTION

The code relies on OpenFEM – to which the team has previously contributed, see <http://www.openfem.net> – for the finite element computations, and the implementation was performed with a particular concern for modularity, since modeling and estimation use the same finite element operators. This modularity also allows to couple the code with other FEM solvers, such as LifeV and Mistral developed in the Reo team-project. In particular, we are now able to include perfusion and electrical coupling with LifeV using PVM, and fluid-structure interaction using Mistral.

We also included geometric data and tools in the code to define cardiac anatomical models compatible with the simulation requirements in terms of mesh quality, fiber direction data defined within each element, and the referencing necessary for handling boundary conditions and estimation, in particular. These geometries are analytical or come from computerized tomography (CT) or magnetic resonance (MR) image data of humans or animals.

We incorporated numerous non-linear data assimilation observation operators based on medical imaging post-processing to be able to now perform estimation with a large variety of medical imaging modalities. And recently we have worked on generalized micro-macro cardiac law using stochastic formulations.

- Participants: Radomir Chabiniok, Dominique Chapelle and Philippe Moireau
- Contact: Philippe Moireau
- URL: <https://raweb.inria.fr/rapportsactivite/RA2013/m3disim/uid14.html>

## 6.3. Verdandi

KEYWORDS: HPC - Model - Software Components - Partial differential equation

#### FUNCTIONAL DESCRIPTION

Verdandi is an open-source (LGPL) library for data assimilation. It includes various such methods for coupling one or several numerical models and observational data. Mainly targeted at large systems arising from the discretization of partial differential equations, the library is devised as generic, which allows for applications in a wide range of problems (biology and medicine, environment, image processing, etc.). Verdandi also includes tools to ease the application of data assimilation, in particular in the management of observations or for a priori uncertainty quantification. Implemented in C++, the library may be used with models implemented in Fortran, C, C++ or Python. Moreover, a Matlab module called VerdandinMatlab is developed in the team for pedagogical and test purposes.

- Participants: Nicolas Claude, Vivien Mallet, Dominique Chapelle, Philippe Moireau, Aurora Armiento and Gautier Bureau
- Contact: Vivien Mallet
- URL: <http://verdandi.gforge.inria.fr/>

## 7. New Results

### 7.1. Modeling

#### 7.1.1. Model-based analysis of continually measured signals of aortic pressure and flow

**Participants:** Radomir Chabiniok, Dominique Chapelle [correspondant], Arthur Le Gall, Philippe Moireau, Fabrice Vallée.



We have started an application of reduced-order cardiac modeling in identifying relevant functional properties and state of heart from clinical records obtained during long-term (minutes-hours) monitoring of patients. Those are obtained either from anesthetized or intensive care patients by Fabrice Vallée, medical doctor in the department of anesthesia and intensive care at Lariboisière Hospital, Paris, who has joined the M3DISIM team in November 2015. The collaboration was initiated already in February 2015, and together with Fabrice we supervised the master's internship of Arthur Le Gall (medical doctor in his last year of specialization residency training). The internship took place at Lariboisière Hospital and in our lab at Inria Saclay (50:50%, period of April-September 2015). First published results are expected in 2016, when also a master's internship of a second student of Fabrice Vallée is scheduled. In addition, we intend to start a PhD on this topic in late 2016.

### **7.1.2. Thermodynamical framework for modeling chemical-mechanical coupling in muscle contraction – Formulation and validation**

**Participants:** Matthieu Caruel, Dominique Chapelle [correspondant], Philippe Moireau.

Muscle contraction occurs at the nanoscale of a hierarchical multi-scale structure with the attachment of so-called cross-bridges within sarcomeres, namely, the creation of chemical bonds between myosin heads and specific sites on actin filaments. A cross-bridge in itself can be seen as a special chemical entity having internal mechanical variables – or degrees of freedom – pertaining to the actual geometric configuration, which implies that the free energy of the cross-bridge – whether in an attached or unattached state – must be made dependent on these internal variables (T.L. Hill, *Free Energy Transduction And Biochemical Cycle Kinetics*, Dover, 2004). This provides a thermodynamical basis for modeling the complex interplay of chemical and mechanical phenomena at the sarcomere level. Within this framework we propose a muscle model with two mechanical variables associated with a cross-bridge. For the action of individual cross-bridges occurring at the nanometer scale, the energy provided by the Langevin thermostat cannot be neglected, and we therefore propose to endow the internal mechanical variables with stochastic dynamics. Important motivations for this modeling choice include the ability to represent (i) the so-called power-stroke phenomenon and (ii) short-time responses of a muscle, e.g. to load steps. Our approach allows for systematic treatment of the model energetics, and in particular one goal of the proposed description is to investigate the potential benefit in mechanical efficiency with systems including – in addition to chemically-induced transformations – thermally-induced conformational changes such as the power-stroke.

### **7.1.3. Biophysical modeling of seismocardiograms measurements**

**Participants:** Alexandre Laurin, Sébastien Imperiale [correspondant], Philippe Moireau, Dominique Chapelle.

We are developing models of various levels of complexity to represent seismocardiograms (SCG) that record mechanical thoracic vibrations induced by the beating heart. Our model combines a complete heartbeat model with a mechanical model of the thorax. The coupling is ensured by a unilateral contact modeling the non-penetration between the beating heart and the thoracic chest. In parallel, we are fine-tuning signal processing algorithms to identify the relevant characteristics of SCG and creating an iPhone application that is capable of acquiring the signal with its standard sensors. The application is also developed to integrate a simplified version of the cardio-thoracic model.

## **7.2. Numerical Analysis**

### **7.2.1. Dirichlet-to-Neumann operator for diffraction problems in stratified anisotropic acoustic waveguides**

**Participants:** Antoine Tonnoir [correspondant], Sonia Fliss [Poems team], Anne-Sophie Bonnet-Ben Dhia [Poems team].

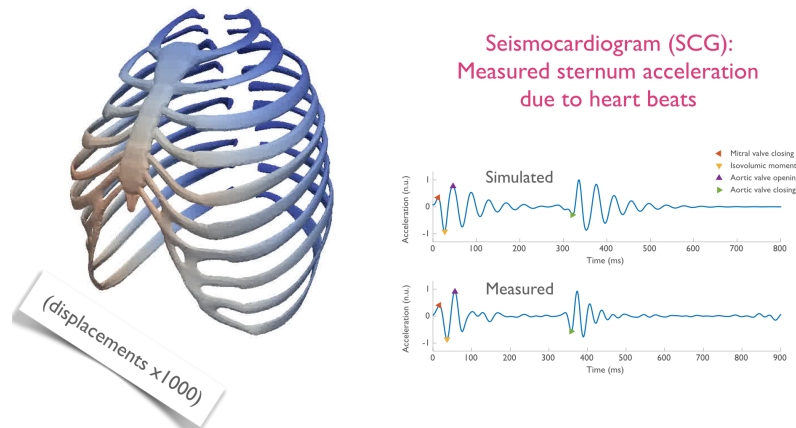


Figure 1. Model-based synthetic SCG compared to a measured SCG.

In this work, we are interested in the construction of a Dirichlet-to-Neumann operator for the diffraction problem in stratified anisotropic acoustic waveguides. The key idea consists in using an adapted change of coordinates that allows to recover the completeness and the orthogonality of the modes on “deformed” cross-sections of the waveguide. Thus, we can properly define the diffraction problem and construct transparent boundary conditions to reformulate this problem in a bounded domain. Using classical arguments we easily prove the well-posedness. The method has also been implemented in a C++ code and has been validated.

### 7.2.2. Fourth-order energy-preserving locally implicit time discretization for linear wave equations

**Participants:** Sébastien Imperiale [correspondant], Juliette Chabassier [MAGIQUE-3D team].

In collaboration with Juliette Chabassier, we have constructed a family of fourth-order implicit-explicit time schemes for linear wave equations. Our application is the simulation of elastic waves propagation in a locally stiff medium. The domain of propagation is decomposed into several regions where different fourth-order time discretization are used, chosen among a family of implicit (for the stiff regions) or explicit fourth-order schemes. The coupling is based on a Lagrangian formulation on the boundaries between several non-conforming meshes of the regions. A global discrete energy is shown to be preserved and leads to global fourth-order consistency in time. Numerical results in 1D and 2D illustrate the good behavior of the schemes and their potential for the efficient simulation of realistic highly heterogeneous media for which using an explicit scheme everywhere can be extremely penalizing. Accuracy up to fourth-order reduces the numerical dispersion inherent to implicit methods used with a large time step, and makes this family of schemes attractive compared to second-order accurate methods.

### 7.2.3. Numerical methods for poromechanics: Applications to cardiac perfusion

**Participants:** Bruno Burtshell, Dominique Chapelle [correspondant], Philippe Moireau.

We have previously formulated a rather general modeling framework of poromechanics – formulations that combine solid and fluid components to represent the behavior of a porous medium – to take into account large deformations and rapid fluid flows, see [6]. This allows to consider, in particular, the application of blood perfusion within the cardiac tissue, which features these specific complex phenomena, out of the scope of classical poromechanical models. One of our major objectives now, within the PhD of Bruno Burtshell, is to propose and analyse some associated relevant numerical schemes.

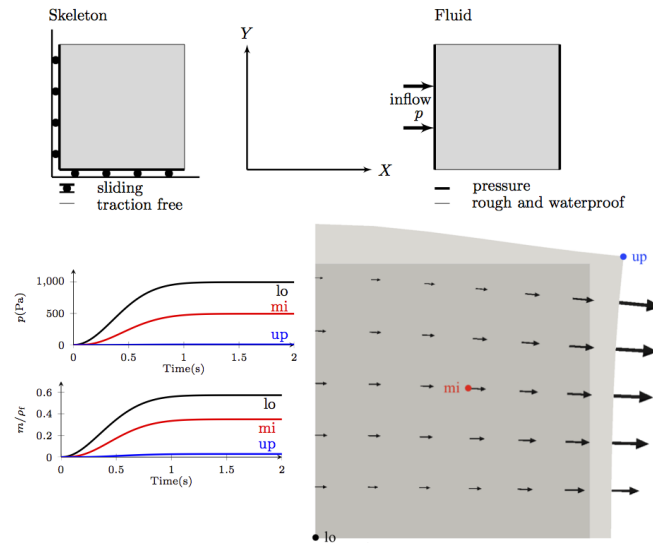


Figure 2. Swelling of a porous sample. On the left, fluid pressure and mass at three points in time during the swelling test. On the right, the fluid velocity field vector at the steady state in the deformed configuration.

Some existing algorithms of fluid-structure interaction, with which our poromechanics formulations feature deep similarities, have been implemented – in FreeFEM++, both in axisymmetric configuration and in 3D – and compared. Their numerical and theoretical analysis – consistency, convergence – has been performed. Then, the adaptation of these algorithms to our poromechanics formulations enabled us to propose a time discretisation well-fitted to our framework, and to present its energy stability analysis. Spatial discretizations issues have also been specifically addressed, based on a complete analysis performed on a linearized problem, in order to guarantee pressure stability – via the selection of adequate inf-sup-compatible discretization spaces – including when the solid constituent is nearly or fully incompressible. Implementation and detailed numerical validations of these schemes have been performed. Integration into FELISCE (“HappyHeart” module) in 3D, and into a reduced model of cardiac cycle to take into account myocardium perfusion, are ongoing work.

## 7.3. Model-Data Interaction

### 7.3.1. Displacement Reconstructions in Ultrasound Elastography

**Participant:** Sébastien Imperiale.

In collaboration with Guillaume Bal (Columbia University, New York, USA), we have considered the reconstruction of internal elastic displacements from ultrasound measurements, which finds applications in the medical imaging modality called elastography. By appropriate interferometry and windowed Fourier transforms of the ultrasound measurements, we have proposed a reconstruction procedure of the vectorial structure of spatially varying elastic displacements in biological tissues. This provides a modeling and generalization of scalar reconstruction procedures routinely used in elastography. The proposed algorithm has been justified using a single scattering approximation and local asymptotic analysis. Its validity has been assessed by numerical simulations.

### 7.3.2. Recursive joint state and parameter estimation

**Participants:** Atte Aalto, Philippe Moireau [correspondant].

We propose a method for estimating the parameters of a linear dynamical system from noisy measurements over a given, finite time, interval. For this purpose we develop a recursive modification of the joint state and parameter estimation method proposed in [7]. As the time interval is fixed, any errors in the initial state of the system may cause a significant error in the parameter estimate. Therefore, the parameter estimator is complemented by the so called back and forth nudging (BFN) method for estimating the system's initial state. The proposed strategy can also be regarded as a hybrid least squares optimization method for minimizing the quadratic discrepancy between the measured and simulated outputs over the set of all possible initial states and system parameters.

The optimality of the BFN method with colocated feedback has been considered as well. We have shown that in the case when the system's dynamics are governed by a skew-adjoint generator, the initial state estimate given by the BFN method converges to the minimizer of the quadratic output discrepancy – provided that the observer gains are chosen suitably. If the system's generator is essentially skew-adjoint and dissipative, a certain modification of the feedback operator is required in order to obtain such convergence.

### 7.3.3. *Convergence of discrete-time Kalman filter estimate to continuous-time estimate*

**Participant:** Atte Aalto [correspondant].

The Kalman(-Bucy) filter gives the optimal (minimum variance) solution to the state estimation problem for linear systems with Gaussian initial state, and white input and output noise processes. The implementation of the discrete-time Kalman filter is straightforward as it is readily formulated in an algorithmic manner. Thus, it may be tempting to use the discrete-time filter on the time-sampled continuous-time system. We study the convergence of the state estimate obtained from the discrete-time Kalman filter to the continuous-time estimate as the temporal discretization is refined. The convergence follows from the martingale convergence theorem, but surprisingly, no results exist on the rate of convergence. We derive convergence rate estimates for the discrete-time estimate under a number of different sets of assumptions starting from finite-dimensional systems and infinite-dimensional systems with bounded output operators and then proceeding to systems with unbounded output operators and systems with analytic semigroups. The proofs are based on applying the discrete-time Kalman filter on a dense, numerable subset of the time interval of interest, and bounding the change in the state estimate as the new data points are being added. These bounds, in turn, are based on smoothness estimates of the noise-free output.

### 7.3.4. *Observers for the wave equation in unbounded domains*

**Participants:** Sébastien Imperiale, Philippe Moireau [correspondant], Antoine Tonnoir, Sonia Fliss [Poems team], Karim Ramdani [Sphinx team].

We are interested in the reconstruction of initial data for the wave equation problem in unbounded domains using an observer strategy. A major advantage of this method for problems set in bounded domains is the exponential convergence of the algorithm of reconstruction. In our case, the specificity is the unboundedness of the domain which requires to bound it with artificial boundaries for numerical computations. To avoid spurious reflections due to these artificial boundaries, we consider transparent boundary conditions. The difficulty then is to adapt the classical observers technique to this case. Indeed, after enough time, the outgoing waves have left the computational domain and the related information is in some sense “lost”.

First results have been obtained for the 1D case: the theoretical proof of the (exponential) convergence of the algorithm has been done, and the method has been numerically validated. We are currently working on the extension to the 2D case, which raises new difficulties. In particular, the construction of the transparent boundary condition is not obvious and implies a non-local operator in both time and space. Due to this non-local operator, the theoretical analysis of the convergence of the method is then much more difficult.

### 7.3.5. *A Luenberger observer for reaction-diffusion models with front position data*

**Participants:** Dominique Chapelle, Annabelle Collin, Philippe Moireau [correspondant].

We propose a Luenberger observer for reaction-diffusion models with propagating front features, and for data associated with the location of the front over time. Such models are considered in various application fields, such as electrophysiology, wild-land fire propagation and tumor growth modeling. Drawing our inspiration from image processing methods by considering a data similarity measure of Mumford-Shah type, we start by proposing an observer for the eikonal-curvature equation that can be derived from the reaction-diffusion model by an asymptotic expansion. We then carry over this observer to the underlying reaction-diffusion equation by an “inverse asymptotic analysis”, and we show that the associated correction in the dynamics has a stabilizing effect for the linearized estimation error. We also discuss the extension to joint state-parameter estimation by using the earlier-proposed ROUKF strategy. We published a first work [17] where the observer feedback is derived from the shape-derivative of the data similarity measure. Then, in [21], in order to improve the observer formulation, we followed a strategy of increasing importance in shape optimization or “level-set”-based image segmentation by complementing the required shape derivatives, used to modify the shape contours, by a topological derivative that represents the sensitivity of the similarity measure when removing a small part of the domain. Both results are illustrated with test problems pertaining to electrophysiology modeling, including with a realistic model of cardiac atria. Our numerical trials show that state estimation is directly very effective with the proposed Luenberger observer.

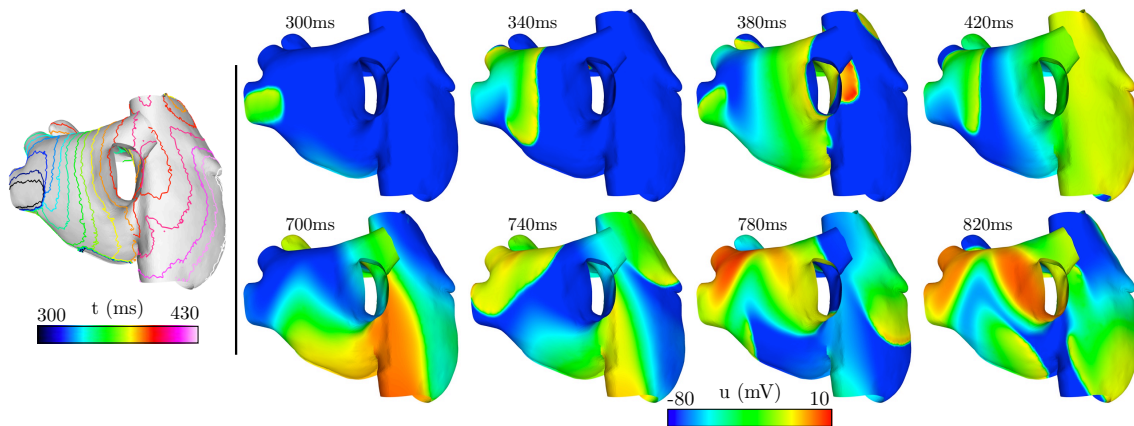


Figure 3. Atrial fibrillation: synthetic front data with noise (left, note that only the first times of passage after the onset of fibrillation are displayed, for the sake of clarity), and corresponding observer solutions (right)

### 7.3.6. Identification of weakly coupled multiphysics problems. Application to the inverse problem of electrocardiography

**Participants:** Cesare Corrado [Reo team], Jean-Frédéric Gerbeau [Reo team], Philippe Moireau [correspondant].

This work addresses the inverse problem of electrocardiography from a new perspective, by combining electrical and mechanical measurements. Our strategy relies on the definition of a model of the electromechanical contraction which is registered on ECG data, but also on measured mechanical displacements of the heart tissue typically extracted from medical images. In this respect, we establish in this work the convergence of a sequential estimator which combines for such coupled problems various state-of-the-art sequential data assimilation methods in a unified consistent and efficient framework. Indeed, we aggregate a Luenberger observer for the mechanical state and a Reduced-Order Unscented Kalman Filter applied on the parameters to be identified and a POD projection of the electrical state. Then, using synthetic data we show the benefits of our approach for the estimation of the electrical state of the ventricles along the heart beat, compared with more classical

strategies that only consider an electrophysiological model with ECG measurements. Our numerical results actually show that the mechanical measurements improve the identifiability of the electrical problem, allowing to reconstruct the electrical state of the coupled system more precisely. Therefore, this work is intended to be a first proof of concept, with theoretical justifications and numerical investigations, of the advantage of using available multi-modal observations for the estimation and identification of an electromechanical model of the heart.

### **7.3.7. Data assimilation of cine-MR images by a biophysical model**

**Participants:** Radomir Chabiniok, Dominique Chapelle [correspondant], Alexandra Groth, Philippe Moireau, Juergen Weese.

Within the European project VP2HF, we participated in extending the image segmentation tool developed by Philips Hamburg (Alexandra Groth, Jürgen Weese) to process clinically routine cine-MR images for creating anatomical models of heart. Secondly, together with A. Groth and J. Weese we defined a discrepancy operator – between a biomechanical heart model and cine-MR images – that does not require segmenting MR images prior to data assimilation. Initial results of the state estimation using this discrepancy operator were presented at the 2nd VP2HF evaluation meeting (December 2015), and extending these results into a journal paper is a joint objective of the M3DISIM team and of Philips Hamburg.

## **8. Bilateral Contracts and Grants with Industry**

### **8.1. Bilateral Contracts with Industry**

We have signed a collaboration agreement with Clinique Pasteur (Toulouse), the 3rd private hospital in France in global activity and the 1st in cardiology, in particular with the motivation of performing research oriented towards the perspective of developing connected applications for the monitoring of cardiac pathologies.

## **9. Partnerships and Cooperations**

### **9.1. European Initiatives**

#### **9.1.1. FP7 & H2020 Projects**

##### *9.1.1.1. VPH-Share*

Title: Virtual Physiological Human: Sharing for Healthcare – A Research Environment

Programm: FP7

Duration: March 2011 - May 2015

Coordinator: Univ. Sheffield (UK)

Other partners: Cyfronet (Cracow), University College London, Istituto Ortopedico Rizzoli (Bologna), NHS, IBM Israel, Univ. Auckland, Agència d'Informació, Avaluació i Qualitat en Salut (Barcelona), Biocomputing Competence Centre (Milano), Universitat Pompeu Fabra (Barcelona), Philips Research, TUE (Eindhoven), Sheffield Teaching Hospitals, Atos Origin (Madrid), the Open University (UK), Univ. Vienna, King's College London, Empirica (Bonn), Fundació Clínic (Barcelona), Univ. Amsterdam

See also: <http://vph-share.org/>

Inria contact: Dominique Chapelle

Abstract: VPH-Share (concluded in May 2015) aimed at developing the organisational fabric (the infostructure) and integrating the optimised services to expose and share data and knowledge, to jointly develop multiscale models for the composition of new VPH workflows, and to facilitate collaborations within the VPH community. Within this project, the M3DISIM team was in charge of developing some high-performance data assimilation software tools.

#### 9.1.1.2. VP2HF

Title: Computer model derived indices for optimal patient-specific treatment selection and planning in Heart Failure

Programm: FP7

Duration: October 2013 - September 2016

Coordinator: King's College London (UK)

See also: <http://vp2hf.eu/>

Inria contact: Dominique Chapelle

Abstract: Heart failure (HF) is one of the major health issues in Europe affecting 6 million patients and growing substantially because of the ageing population and improving survival following myocardial infarction. The poor short to medium term prognosis of these patients means that treatments such as cardiac re-synchronisation therapy and mitral valve repair can have substantial impact. However, these therapies are ineffective in up to 50% of the treated patients and involve significant morbidity and substantial cost. The primary aim of VP2HF is to bring together image and data processing tools with statistical and integrated biophysical models mainly developed in previous VPH projects, into a single clinical workflow to improve therapy selection and treatment optimisation in HF.

## 9.2. International Initiatives

### 9.2.1. Participation In other International Programs

M3DISIM is the leading representative of Inria within the “Living Heart Project”, a research network coordinated by Dassault-Systèmes to foster collaborations on cardiac modeling between various academic and industrial partners.

## 9.3. International Research Visitors

### 9.3.1. Visits of International Scientists

#### 9.3.1.1. Internships

**Alexandre Laurin**

[Simon Fraser Univ., Canada]

**Sébastien Imperiale**

[correspondant]

**Philippe Moireau**

**Dominique Chapelle**

**Gabriel Valdes Alonzo**

[Pontificia Univ. Católica de Chile]

**Radomir Chabiniok**

[correspondant]

**Dominique Chapelle**

A. Laurin's doctoral internship (2 months) has taken place in the context of an ongoing collaboration between the Aerospace Physiology lab (Simon Fraser University, Vancouver, Canada) and Inria (M3DISIM and Reo teams), with the objective of initiating the modelling of seismocardiography (SCG) measurements. SCG consists in measuring displacements of the sternum and ribs generated by a heart beat using accelerometers placed on the thorax. In this context, linear elastodynamics equations are applicable to account for the transient propagation of motion from the heart to the sternum via the highly heterogeneous underlying materials (cartilage and bone). Specific care has been taken to solve the aforementioned equation in a realistic 3D geometry including the complete thoracic cage. Fully coupled simulations (beating heart with thorax deformation) are planned at the final stage of this modelling work. Following the completion of his PhD, A. Laurin has joined the team for a post-doc, which provides the setting for continuing and extending this work.

G. Valdes (Master's student at Pontificia Univ. Católica de Chile) has been awarded a Conicyt funding for a 3 months internship within our team. He has worked on a simplified dynamical model of venous return, allowing to account for the evolution of the preload – the pressure that induces the filling of the heart – under the effect of variations of cardiac output. This is crucial for simulating sequences of heartbeats in transient regimes, and one major motivation for this was to initiate the modeling of the dynamics of heart failure.

## 10. Dissemination

### 10.1. Promoting Scientific Activities

#### 10.1.1. Scientific events organisation

##### 10.1.1.1. Member of the organizing committees

Philippe Moireau

- Member of the CEMRACS-2016 organizing committee
- P. Le Tallec's 60th Birthday conference

#### 10.1.2. Scientific events selection

##### 10.1.2.1. Member of the conference program committees

Dominique Chapelle

- Program committee of conference "Functional Imaging and Modeling of the Heart 2015"

##### 10.1.2.2. Reviewer

Dominique Chapelle

- Reviewer for conference "Functional Imaging and Modeling of the Heart 2015"

#### 10.1.3. Journal

##### 10.1.3.1. Member of the editorial boards

Dominique Chapelle

- Member of the editorial board of journal *Computers & Structures*
- Member of the editorial board of journal *ESAIM: M2AN*

##### 10.1.3.2. Reviewer - Reviewing activities

The members of the team reviewed numerous papers:

- D. Chapelle: *Computers & Structures*, *CMAME*, *IJNME*, *BMMB*, etc.
- P. Moireau: *Computers in Biology and Medicine*, *ESAIM: COCV*, *ESAIM: M2AN*
- S. Imperiale: *ESAIM: M2AN*, et *Waves in Random and Complex Media*
- A. Aalto: *International Journal of Control*



### 10.1.4. Invited talks

Philippe Moireau

- “Mechanisms of observers and observers in mechanics”, P. Le Tallec’s 60th Birthday conference, Ecole Polytechnique, France

Dominique Chapelle

- Invited lecturer at International Workshop on Electroactivity of Biological Systems (Orsay Univ., November 18-19 2015)
- Seminar at CERMICS (Ecole des Ponts ParisTech, Nov. 10)

### 10.1.5. Leadership within the scientific community

Dominique Chapelle

- Member of the Academic Senate of FCS Paris-Saclay
- Member of the board of directors of the VPH Institute

## 10.2. Teaching - Supervision - Juries

### 10.2.1. Teaching

Bachelor: S. Imperiale, “MA102 – Analyse pour les EDP”, 12h, (L3), ENSTA ParisTech, France

Bachelor: S. Imperiale, “MA104 – Analyse complexe”, 8h, (L3), ENSTA ParisTech, France

Master: S. Imperiale, “MA2610 Calcul Scientifique – Mécanique des solides”, 6h, (M1), Central/Supélec, France

Master: P. Moireau, “MA103 – Introduction aux EDP et à leur approximation numérique”, 14h, (L3), ENSTA ParisTech, France

Master: P. Moireau, “MAP-Ann1 – La méthode des éléments finis”, 21h, (M1), ENSTA ParisTech, France

Master: P. Moireau, “MAP 411 – Approximation numérique et optimisation”, (M1), Ecole Polytechnique, France

Master: D. Chapelle, “Biomechanical Modeling of Active Tissues”, 18h, (M2), Université Paris-Saclay, France

Master: P. Moireau, “Biomechanical Modeling of Active Tissues”, 17h, (M2), Université Paris-Saclay, France

Master: P. Moireau, “Méthodes et Problèmes inverses en dynamique des populations”, 6h, (M2), UPMC, France

Master: D. Chapelle, lecture on biomechanical modeling in Master BME, 3h, (M2), Paris 5 and ParisTech

#### E-learning

Mooc: Contributor: Main teacher Emmanuel De Langre, Title: Fundamentals of Fluid-Solid Interactions, 6 weeks long, Coursera, Ecole Polytechnique, About 2000 students, Level M1

Pedagogical resources: B. Burtschell, Poromechanical modelling and application to the myocardium perfusion, video

### 10.2.2. Supervision

PhD in progress: Bruno Burtschell. Title: Poromechanical modelling and application to the myocardium perfusion. Started: October 2013. Supervisors: Dominique Chapelle and Philippe Moireau.

PhD in progress: Aurora Armiento <sup>1</sup>. Title: Inverse problems for depolymerization models. Started: October 2013. Supervisors: Marie Doumic <sup>2</sup> and Philippe Moireau.

PhD in progress: Federica Caforio, Mathematical and numerical modelling of elastic waves propagation in the heart. Started: November 2015. Supervisors: Sébastien Imperiale, Dominique Chapelle.

PhD in progress: Geoffrey Beck, Mathematical modelling of electrical cables network. Started: September 2012. Supervisors: Patrick Joly <sup>3</sup>, Sébastien Imperiale.

<sup>1</sup>Mamba Team

<sup>2</sup>Mamba Team

### 10.2.3. Juries

- D. Chapelle was the chairman of the PhD jury of Fang Yao (Ecole Polytechnique, Nov. 25)
- D. Chapelle and P. Moireau have actively participated in the recruitment of an Ecole Polytechnique assistant professor intended to join the team (soon to become a joint team between LMS / Ecole Polytechnique and Inria). The selection process led to the recruitment of Martin Genet.

## 10.3. Popularization

D. Chapelle, Febr. 9th, article in "Le Figaro": "A quoi sert de modéliser le fonctionnement du cœur ?"

P. Moireau, May 20th 2015, keynote entitled "The heart forecasting" at Créteil District Academy "Olympiade de Mathématiques" award ceremony.

# 11. Bibliography

## Major publications by the team in recent years

- [1] R. CHABINIOK, P. MOIREAU, P.-F. LESAULT, A. RAHMOUNI, J.-F. DEUX, D. CHAPELLE. *Estimation of tissue contractility from cardiac cine-MRI using a biomechanical heart model*, in "Biomechanics and Modeling in Mechanobiology", 2012, vol. 11, n<sup>o</sup> 5, pp. 609-630 [DOI : 10.1007/s10237-011-0337-8], <http://hal.inria.fr/hal-00654541>
- [2] D. CHAPELLE, K. BATHE. *The Finite Element Analysis of Shells - Fundamentals - Second Edition*, Computational Fluid and Solid Mechanics, Springer, 2011, 410 p. [DOI : 10.1007/978-3-642-16408-8], <http://hal.inria.fr/hal-00654533>
- [3] D. CHAPELLE, N. CÎNDEA, P. MOIREAU. *Improving convergence in numerical analysis using observers - The wave-like equation case*, in "Mathematical Models and Methods in Applied Sciences", 2012, vol. 22, n<sup>o</sup> 12 [DOI : 10.1142/S0218202512500406], <http://hal.inria.fr/inria-00621052>
- [4] D. CHAPELLE, M. FRAGU, V. MALLET, P. MOIREAU. *Fundamental principles of data assimilation underlying the Verdandi library: applications to biophysical model personalization within euHeart*, in "Medical & Biological Engineering & Computing", 2013, vol. 51, pp. 1221–1233 [DOI : 10.1007/s11517-012-0969-6], <https://hal.inria.fr/hal-00760887>
- [5] D. CHAPELLE, P. LE TALLEC, P. MOIREAU, M. SORINE. *An energy-preserving muscle tissue model: formulation and compatible discretizations*, in "International Journal for Multiscale Computational Engineering", 2012, vol. 10, n<sup>o</sup> 2, pp. 189-211 [DOI : 10.1615/INTJMULTCOMPENG.2011002360], <http://hal.inria.fr/hal-00678772>
- [6] D. CHAPELLE, P. MOIREAU. *General coupling of porous flows and hyperelastic formulations – From thermodynamics principles to energy balance and compatible time schemes*, in "European Journal of Mechanics - B/Fluids", 2014, vol. 46, pp. 82-96, Updated version of previously published research report [DOI : 10.1016/J.EUROMECHFLU.2014.02.009], <https://hal.inria.fr/inria-00520612>
- [7] P. MOIREAU, D. CHAPELLE, P. LE TALLEC. *Joint state and parameter estimation for distributed mechanical systems*, in "Computer Methods in Applied Mechanics and Engineering", 2008, vol. 197, n<sup>o</sup> 6-8, pp. 659-677 [DOI : 10.1016/J.CMA.2007.08.021], <http://hal.archives-ouvertes.fr/hal-00175623>

<sup>3</sup>Poems Team

- [8] P. MOIREAU, D. CHAPELLE, P. LE TALLEC. *Filtering for distributed mechanical systems using position measurements: perspectives in medical imaging*, in "Inverse Problems", 2009, vol. 25, n<sup>o</sup> 3, 035010 [DOI : 10.1088/0266-5611/25/3/035010], <http://hal.archives-ouvertes.fr/hal-00358914>
- [9] P. MOIREAU, D. CHAPELLE. *Reduced-order Unscented Kalman Filtering with application to parameter identification in large-dimensional systems*, in "ESAIM - Control Optimisation and Calculus of Variations", 2010, Published online - See also erratum DOI:10.1051/cocv/2011001 [DOI : 10.1051/cocv/2010006], <http://hal.inria.fr/inria-00550104>
- [10] M. SERMESANT, R. CHABINIOK, P. CHINCHAPATNAM, T. MANSI, F. BILLET, P. MOIREAU, J.-M. PEYRAT, K. C. WONG, J. RELAN, K. S. RHODE, M. GINKS, P. LAMBIASE, H. DELINGETTE, M. SORINE, C. A. RINALDI, D. CHAPELLE, R. RAZAVI, N. AYACHE. *Patient-Specific Electromechanical Models of the Heart for Prediction of the Acute Effects of Pacing in CRT: a First Validation*, in "Medical Image Analysis", January 2012, vol. 16, n<sup>o</sup> 1, pp. 201-215 [DOI : 10.1016/J.MEDIA.2011.07.003], <http://hal.inria.fr/inria-00616191>

## Publications of the year

### Articles in International Peer-Reviewed Journals

- [11] L. ASNER, M. HADJICHARALAMBOUS, R. CHABINIOK, D. PERESUTTI, E. SAMMUT, J. WONG, G. CARR-WHITE, P. CHOWIENCYK, J. LEE, A. D. KING, N. P. SMITH, R. RAZAVI, D. NORDSLETTEN. *Estimation of passive and active properties in the human heart using 3D tagged MRI*, in "Biomechanics and Modeling in Mechanobiology", November 2015 [DOI : 10.1007/s10237-015-0748-z], <https://hal.archives-ouvertes.fr/hal-01254900>
- [12] G. BAL, S. IMPERIALE. *Displacement Reconstructions in Ultrasound Elastography*, in "SIAM Journal on Imaging Sciences", 2015, vol. 8, n<sup>o</sup> 2, pp. 1070-1089 [DOI : 10.1137/140988504], <https://hal.inria.fr/hal-01188761>
- [13] A.-C. BOULANGER, P. MOIREAU, B. PERTHAME, J. SAINTE-MARIE. *Data Assimilation for hyperbolic conservation laws. A Luenberger observer approach based on a kinetic description*, in "Communications in Mathematical Sciences", March 2015, vol. 13, n<sup>o</sup> 3, pp. 587 – 622 [DOI : 10.4310/CMS.2015.v13.n3.a1], <https://hal.archives-ouvertes.fr/hal-00924559>
- [14] M. CARUEL, J.-M. ALLAIN, L. TRUSKINOVSKY. *Mechanics of collective unfolding*, in "Journal of the Mechanics and Physics of Solids", 2015, vol. 76, pp. 237 - 259 [DOI : 10.1016/J.JMPS.2014.11.010], <https://hal.archives-ouvertes.fr/hal-01100823>
- [15] J. CHABASSIER, S. IMPERIALE. *Fourth order energy-preserving locally implicit time discretization for linear wave equations*, in "International Journal for Numerical Methods in Engineering", 2015 [DOI : 10.1002/NME.5130], <https://hal.inria.fr/hal-01222072>
- [16] N. CINDEA, A. IMPERIALE, P. MOIREAU. *Data assimilation of time under-sampled measurements using observers, the wave-like equation example*, in "ESAIM - Control Optimisation and Calculus of Variations", 2015, 35 p. [DOI : 10.1051/COCV/2014042], <https://hal.inria.fr/hal-01054551>
- [17] A. COLLIN, D. CHAPELLE, P. MOIREAU. *A Luenberger observer for reaction-diffusion models with front position data*, in "Journal of Computational Physics", August 2015, vol. 300, 20 p. [DOI : 10.1016/J.JCP.2015.07.044], <https://hal.inria.fr/hal-01111675>

- [18] C. CORRADO, J.-F. GERBEAU, P. MOIREAU. *Identification of weakly coupled multiphysics problems. Application to the inverse problem of electrocardiography*, in "Journal of Computational Physics", February 2015, vol. 283, pp. 271–298 [DOI : 10.1016/J.JCP.2014.11.041], <https://hal.inria.fr/hal-01091751>
- [19] M. HADJICHARALAMBOUS, R. CHABINIOK, L. ASNER, E. SAMMUT, J. WONG, G. CARR-WHITE, J. LEE, R. RAZAVI, N. SMITH, D. NORDSLETTEN. *Analysis of passive cardiac constitutive laws for parameter estimation using 3D tagged MRI*, in "Biomechanics and Modeling in Mechanobiology", August 2015, vol. 14, n<sup>o</sup> 4, pp. 807-828 [DOI : 10.1007/s10237-014-0638-9], <https://hal.archives-ouvertes.fr/hal-01254911>

### International Conferences with Proceedings

- [20] D. CHAPELLE, A. FELDER, R. CHABINIOK, A. GUELICH, J.-F. DEUX, T. DAMY. *Patient-Specific Biomechanical Modeling of Cardiac Amyloidosis – A Case Study*, in "Functional Imaging and Modeling of the Heart 2015", Maastricht, Netherlands, H. VAN ASSEN, P. BOVENDEERD, T. DELHAAS (editors), Lecture Notes in Computer Science, Springer, June 2015, vol. 9126, pp. 295-303 [DOI : 10.1007/978-3-319-20309-6\_34], <https://hal.inria.fr/hal-01174913>
- [21] A. COLLIN, D. CHAPELLE, P. MOIREAU. *Sequential State Estimation for Electrophysiology Models with Front Level-Set Data Using Topological Gradient Derivations*, in "Functional Imaging and Modeling of the Heart 2015", Maastricht, Netherlands, H. VAN ASSEN, P. BOVENDEERD, T. DELHAAS (editors), Lecture Notes in Computer Science, Springer, June 2015, vol. 9126, pp. 402-411 [DOI : 10.1007/978-3-319-20309-6\_46], <https://hal.inria.fr/hal-01174916>

### Conferences without Proceedings

- [22] R. CHABINIOK, E. SAMMUT, M. HADJICHARALAMBOUS, L. ASNER, D. NORDSLETTEN, R. RAZAVI, N. SMITH. *Steps Towards Quantification of the Cardiological Stress Exam*, in "Functional Imaging and Modeling of Heart", Maastricht, Netherlands, LNCS, June 2015, vol. 9126, pp. 12-20 [DOI : 10.1007/978-3-319-20309-6\_2], <https://hal.archives-ouvertes.fr/hal-01254914>

### Research Reports

- [23] M. LANDAJUELA, M. VIDRASCU, D. CHAPELLE, M. A. FERNÁNDEZ. *Coupling schemes for the FSI forward prediction challenge: comparative study and validation*, Inria, December 2015, n<sup>o</sup> RR-8824, <https://hal.inria.fr/hal-01239931>

### Other Publications

- [24] A. AALTO. *Convergence of discrete-time Kalman filter estimate to continuous-time estimate for systems with unbounded observation*, December 2015, working paper or preprint, <https://hal.inria.fr/hal-01236950>
- [25] A. AALTO. *Output error minimizing back and forth nudging method for initial state recovery*, October 2015, working paper or preprint, <https://hal.inria.fr/hal-01216075>
- [26] A. ARMIENTO, M. DOUMIC, P. MOIREAU, H. REZAEI. *Estimation from Moments Measurements for Amyloid Degradation*, December 2015, working paper or preprint, <https://hal.archives-ouvertes.fr/hal-01248255>
- [27] E. SCHENONE, A. COLLIN, J.-F. GERBEAU. *Numerical simulation of electrocardiograms for full cardiac cycles in healthy and pathological conditions*, August 2015, In press (in International Journal for Numerical Methods in Biomedical Engineering) [DOI : 10.1002/CNM.2744], <https://hal.inria.fr/hal-01184744>