IN PARTNERSHIP WITH:
Ecole Polytechnique

Activity Report 2017

Project-Team M3DISIM

Mathematical and Mechanical Modeling with Data Interaction in Simulations for Medicine

IN COLLABORATION WITH: Laboratoire de Mécanique des Solides

RESEARCH CENTER
Saclay - Île-de-France

THEME
Modeling and Control for Life Sciences

Table of contents

Project-Team M3DISIM

Creation of the Team: 2013 January 01, updated into Project-Team: 2016 June 01

Keywords:

Computer Science and Digital Science:

A6.1.1. - Continuous Modeling (PDE, ODE)
A6.1.2. - Stochastic Modeling (SPDE, SDE)
A6.1.4. - Multiscale modeling
A6.1.5. - Multiphysics modeling
A6.2.1. - Numerical analysis of PDE and ODE
A6.3.1. - Inverse problems
A6.3.2. - Data assimilation
A6.3.4. - Model reduction
A6.4.1. - Deterministic control
A6.4.3. - Observability and Controlability
A6.4.4. - Stability and Stabilization

Other Research Topics and Application Domains:

B1.1.10. - Mathematical biology
B2.2.1. - Cardiovascular and respiratory diseases
B2.6.2. - Cardiac imaging
B2.6.3. - Biological Imaging

1. Personnel

Research Scientists

Philippe Moireau [Team leader, Inria, Senior Researcher, HDR]
Radomir Chabiniok [Inria, Starting Research Position]
Dominique Chapelle [Inria, Senior Researcher, HDR]
Sébastien Imperiale [Inria, Researcher]

Faculty Members

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Martin Genet [Ecole polytechnique, Associate Professor]
Patrick Le Tallec [Ecole polytechnique, Professor, HDR]

Post-Doctoral Fellow

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PhD Students

Ezgi Berberoglu [ETH Zurich, PhD Student, from May 2017]
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Marija Gusseva [Inria, from Oct 2017]
Ustim Khristenko [Ecole polytechnique]
François Kimmig [Ecole polytechnique]
Arthur Le Gall [Assistance publique/Hôpitaux de Paris]
Cecile Patte [Inria, from Nov 2017]
Florent Wijanto [Ecole polytechnique]

Technical staff

Alexandre Laurin [Inria, until Jul 2017]

Interns

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Yasmine Thamri [Inria, from Mar 2017 until Jul 2017]
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Peter Baumgartner [Ecole polytechnique, from Sep 2017]
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Fabrice Vallee [Assistance publique/Hôpitaux de Paris, Researcher]
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Alexandre Laurin [Independent, from Oct 2017]
Hajer Methenni [CEA, from Oct 2017]

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 [4]. 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 [5].

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 [11]. 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

- Promotion of Jean-Marc Allain as a professor at Polytechnique.
- Patent submitted and accepted on heart and vessels modelling with data interaction ([40]).
- Submission of a IHU proposal, of 3 ERC proposals, 1 associated team proposal with UT Southwestern Medical Center Dallas
- Contract of collaboration with UT Southwestern Medical Center Dallas (Profs. G. Greil and T. Hussain)

6. New Software and Platforms

6.1. FELiScE

Finite Elements for Life SCiences and Engineering problems
KEYWORDS: Finite element modelling - Cardiac Electrophysiology - Cardiovascular and respiratory systems

FUNCTIONAL DESCRIPTION: FELiScE is a finite element code which the M3DISIM and REO project-teams have decided to jointly develop in order to build up on their respective experiences concerning finite element simulations. 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 respiratory and cardiovascular models considered in the two teams – namely involving fluid and solid mechanics, electrophysiology, and the various associated coupling phenomena. FELISCE is written in C++, and may be later released as an opensource library. FELiScE was registered in July 2014 at the Agence pour la Protection des Programmes under the Inter Deposit Digital Number IDDN.FR.001.350015.000.S.P.2014.000.10000.

- Participants: Axel Fourmont, Benoit Fabreges, Damiano Lombardi, Dominique Chapelle, Faisal Amlani, Irène Vignon-Clementel, Jean-Frédéric Gerbeau, Marina Vidrascu, Matteo Aletti, Miguel Angel Fernandez Varela, Mikel Landajuela Larma, Philippe Moireau and Sébastien Gilles
- Contact: Jean-Frédéric Gerbeau
- URL: http://felisce.gforge.inria.fr

6.2. HeartLab

KEYWORDS: Computational geometry - Image analysis - Cardiac - Health - Simulation
SCIENTIFIC DESCRIPTION: The heartLab software is a library designed to perform both simulation and estimation of the heart mechanical behavior (based on various types of measurements, e.g. images).

Also included are 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.
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- Participants: Radomir Chabiniok, Gautier Bureau, Martin Genet, Federica Caforio, Ustim Khristenko, 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 a free and 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.

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

6.4. CardiacLab

KEYWORDS: Cardiovascular and respiratory systems - Matlab - Real time

FUNCTIONAL DESCRIPTION: CardiacLab is a MATLAB toolbox allowing to perform “real-time” cardiac simulations using 0D models of the cardiovascular systems. Its modular development includes (1) a module integrating the mechanical dynamics of the cavity taking into account its particular geometry, (2) a module allowing to choose a micro-model of the cardiac contraction, (3) a module of phase management, (4) a circulation module based on Windkessel models or more advanced 1D flows models, and (5) a perfusion module. The objective of this code is threefold: (1) demonstrate to students, engineers, medical doctors, the interest of modeling in cardiac applications, (2) unify our original modeling developments with the possibility to evaluate them with previous team developments before integrating them into 3D complex formulations, and (3) explore some avenues pertaining to real-time simulat

- Participants: Sebastien Impériale, Martin Genet, Federica Caforio, Ustim Khristenko, Peter Baumgartner, Radomir Chabiniok, François Kimmig and Arthur Le Gall
- Contact: Philippe Moireau
- URL: https://gitlab.inria.fr/M3DISIM/CardiacLab

7. New Results

7.1. Mathematical and Mechanical Modeling

7.1.1. Modelling of collagen fibers elastic properties

Participants: Peter Baumgartner, Florent Wijanto, Jean-Marc Allain [correspondant], Matthieu Caruel [Univ. Paris-Est].

Our studies on collagen tissues have shown that the collagen fibers are able to elongate inelastically under stretch. In tendons, this effect has been attributed to the non-permanent cross-bridges that connect the different collagen fibrils (to assemble a fiber). This sliding effect appears experimentally to be reversible (at least partially) if the tissue is left long enough at its initial resting length. However, this sliding is classically included as an irreversible plastic response, or as a damage of the tissue. We are building a model based on a stochastic description of the binding and unbinding of the cross-bridges. This approach will enable us to have a microscopically based picture of the sliding, which will be able to explain some alterations in case of aging or pathologies of the tissue. At the moment, we have shown the importance of the density of cross-bridges in the cooperative response of the system. A publication is in preparation on the topic.

7.1.2. Multi-scale modeling of cardiac contraction

Participants: François Kimmig, Matthieu Caruel [Univ. Paris-Est], Dominique Chapelle [correspondant], Philippe Moireau.

This work aims at proposing a set of models of the muscular contraction targeting different scales in time and space and that can be used in the context of heart simulation. To this end, we developed so far two models using different approaches for the modeling of the force generating process at the molecular level called power stroke. First, we revised the standard chemo-mechanical models, which see the power stroke as a series of chemical states. Following the idea introduced by Truskinovsky and collaborators describing the power stroke as a continuum of mechanical states with the dynamics of the myosin head in the prescribed energy landscape governed by Langevin equations, we incorporated the attachment and detachment dynamics in the form of jump processes. In a second step, noting that the power stroke time scale is much shorter than that of heart contraction, we eliminated the power strokes dynamics and derived a two state – attached and detached – simplified model, each state being in fact associated with a statistical distribution of myosin head configurations. Both models have been integrated into our simulation framework CardiacLab, in order to benefit from the other modeling compartments available in the code, such as the geometrically reduced model of the heart left ventricle also developed in the team. These modeling elements will be confronted with experiments performed on cardiac muscle cells by collaborators in the team of Professor Lombardi at the University of Florence.

7.1.3. Mathematical and numerical modeling of shear waves propagation in the heart

Participants: Federica Caforio, Sébastien Imperiale [correspondant], Dominique Chapelle.

Shear acoustic waves remotely induced by the acoustic radiation force (ARF) of a focused ultrasound beam generated by piezoelectric sensors have been recently used in biomedical applications, e.g. in transient elastography techniques. By measuring the propagation velocity of generated shear waves in biological tissues, it is possible to locally assess biomechanical properties highly sensitive to structural changes corresponding to physiological and pathological processes. Recent experimental studies show the feasibility of applying transient elastography to the cardiac setting. In this context, the wave propagation induced by the ARF is superposed with the nonlinear mechanics associated with the heart deformation during the cardiac cycle. The aim of this work is to mathematically justify an original expression of the excitation induced by the ARF in nonlinear solids, based on energy considerations and asymptotic analysis. In soft media the propagation velocity of shear waves ($1 - -10\text{m.s}^{-1}$) is much smaller than the velocity of pressure waves (1500m.s^{-1}). The approach we propose consists in considering a family of problems parametrised by a small parameter ε related to the velocity ratio between the two wave propagation phenomena, the high frequency of the piezoelectric source term and the viscosity. In order to derive a simplified model for the expression of ARF, we investigate the limit behavior of the solution for $\varepsilon \to 0$. We show that the leading term of the expansion is related to the underlying nonlinear mechanics of the heart deformation, and the first two correction terms correspond to a fast-oscillating pressure wave excited by the probe, and an elastic field having as source term a nonlinear function of the first corrector. This field corresponds to the shear acoustic wave induced by the ARF.

7.1.4. Analysis and 2-scale convergence of a heterogeneous microscopic bidomain model

Participants: Sébastien Imperiale [correspondant], Annabelle Collin [Monc].

The aim of this work is to provide a complete mathematical analysis of the periodic homogenization procedure that leads to the macroscopic bidomain model in cardiac electrophysiology. We consider space-dependent and tensorial electric conductivities as well as space-dependent physiological and phenomenological non-linear ionic models. We provide the nondimensionalization of the bidomain equations and derive uniform estimates of the solutions. The homogenization procedure is done using 2-scale convergence theory which enables us to study the behavior of the non-linear ionic models in the homogenization process.

7.1.5. A reduced thoracic model for inverse problem solving in seismocardiography

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

Seismocardiography (SCG) is the study of low-frequency (< 60 Hz) vibrations of the thorax caused by the beating heart. Although it is assumed that SCG signals are caused by forces applied on the interior of the thorax by the heart, no comprehensive model exists to describe the parameters and relationships that govern the system. The main goal of this study is to describe in some detail the filter applied by the thorax on cardiac forces, taking into account its zone of contact with the heart as well as the zone of measurement, i.e. the location of the accelerometer on a participant's chest. A secondary goal is to identify the smallest set of parameters capable of reproducing the filter, reducing the model while retaining its capacity to lend itself to physiological interpretation. Finally, we described a method to use the reduced model to estimate cardiac forces from measured thoracic accelerations. The overall aim of the study is to develop numerical methods that can augment the existing SCG interpretations to include mechanical indices of the heart muscle, and do so in real time.

7.2. Numerical Methods

7.2.1. Numerical methods for computing cyclic steady states

Participants: Ustim Khristenko, Patrick Le Tallec [correspondant].

This work is focused on two techniques for fast computing of the steady cyclic states of evolution problems in non-linear mechanics with space-time periodicity conditions. This kind of problems can be faced in various applications, for instance in the rolling of a tyre with periodic sculptures as well as in a beating heart. Direct solvers for such problems are not very convenient, since they require the inversion of very large matrices. In order to avoid this, a cyclic solution is usually computed as an asymptotic limit of the associated initial value problem with prescribed initial data. However, when the relaxation time is high, convergence to the limit cycle can be very slow. The first technique considered is the Newton-Krylov method, looking for the unknown initial state that provides the space-time periodic solution. This initial state is defined by the space-time periodicity condition, solved with the Newton-Raphson technique. Since the associated Jacobian cannot be expressed explicitly, the method uses one of the matrix-free Krylov iterative solvers. Using information stored while computing the residual to solve the linear system makes its calculation time negligible with respect to the residual calculation time. The second method is the delayed feedback control: an observer-controller type modification of the standard evolution to the limit cycle by introducing a feedback control term, based on the periodicity error. The main result is the optimal form of the control term for a very general class of linear evolution problems, providing the fastest convergence to the cyclic solution. This control has also been adapted and tested for nonlinear problems. The methods discussed have been assessed using academic applications and they have also been implemented into the Michelin industrial code – applied to the rolling tyre model – as well as into the M3DISIM code for the cardiac contraction problem.

7.2.2. Solving isotropic elastodynamics using potentials

Participants: Sébastien Imperiale [correspondant], Jorge Albella.

This work has the potential to provide an original efficient method for the computations of elastic waves propagation in soft media (such as biological tissues), based on the property that pressure and shear waves decouple in isotropic media. Towards this direction, we considered the numerical solution of 2D elastodynamics isotropic equations using the decomposition of the displacement fields into potentials. This appears as a challenge for finite element methods, and we have addressed here the particular question of free boundary conditions. A stable (mixed) variational formulation of the evolution problem is proposed.

7.2.3. The Arlequin method for transient wave scattering by small obstacles

Participants: Sébastien Imperiale [correspondant], Jorge Albella.

In this work we extend the Arlequin method to overlapping domain decomposition technique for transient wave equation scattering by small obstacles. The main contribution of this work is to construct and analyze some variants of the Arlequin method from the continuous level to the fully discrete level. The constructed discretizations allow to solve wave propagation problems while using non-conforming and overlapping meshes for the background propagating medium and the surrounding of the obstacle, respectively. Hence we obtain a flexible and stable method in terms of the space discretization – an inf-sup condition is proven – while the stability of the time discretization is ensured by energy identities.

7.2.4. Construction of a fourth-order time scheme for dissipative wave equations

Participants: Sébastien Imperiale [correspondant], Juliette Chabassier [Magique-3d], Julien Diaz [Magique-3d].

This works deals with the construction of a fourth-order, energy preserving, explicit time discretization for dissipative linear wave equations. This discretization is obtained by replacing the inversion of a matrix – that comes naturally after using the technique of the Modified Equation on the second order Leap Frog scheme applied to dissipative linear wave equations – by an explicit approximation of its inverse. The stability of the scheme is studied first using an energy analysis, then an eigenvalue analysis. Numerical results in 1D illustrate the good behavior regarding space/time convergence and the efficiency of the newly derived scheme compared to more classical time discretizations. A loss of accuracy is observed for non-smooth profiles of dissipation, and we propose an extension of the method that fixes this issue. Finally, we assess the good performance of the scheme for a realistic dissipation phenomenon in Lorentz materials.

7.2.5. *Coupled variational formulations of linear elasticity and the DPG methodology*

Participant: Patrick Le Tallec [correspondant].

In this work, we develop a general approach akin to domain-decomposition methods to solve a single linear PDE, but where each subdomain of a partitioned domain is associated with a distinct variational formulation coming from a mutually well-posed family of so-called broken variational formulations of the original PDE. It can be exploited to solve challenging problems in a variety of physical scenarios where stability or a particular mode of convergence is desired in some part of the domain. The linear elasticity equations are solved in this work, but the approach can be applied to other equations as well. The broken variational formulations, which are essentially extensions of more standard formulations, are characterized by the presence of mesh-dependent broken test spaces and interface trial variables at the boundaries of the elements of the mesh. This allows necessary information to be naturally transmitted between adjacent subdomains, resulting in coupled variational formulations which are then proved to be globally well-posed. They are solved numerically using the DPG methodology, which is especially crafted to produce stable discretizations of broken formulations. Finally, expected convergence rates are verified in two different illustrative examples. This work has resulted in the publication [19].

7.2.6. *A discontinuous Galerkin approach for cardiac electrophysiology*

Participant: Radomir Chabiniok [correspondant].

Cardiac electrophysiology simulations are numerically challenging due to the propagation of a steep electrochemical wave front, and thus require discretizations with small mesh sizes to obtain accurate results. In this work – in collaboration with the Institute for Computational Mechanics, Technical University Munich and published in [21] – we present an approach based on the Hybridizable Discontinuous Galerkin method (HDG), which allows an efficient implementation of high-order discretizations into a computational framework. In particular using the advantage of the discontinuous function space, we present an efficient p-adaptive strategy for accurately tracking the wave front. HDG allows to reduce the overall degrees of freedom in the final linear system to those only on the element interfaces. Additionally, we propose a rule for a suitable integration accuracy for the ionic current term depending on the polynomial order and the cell model to handle high-order polynomials. Our results show that for the same number of degrees of freedom coarse high-order elements provide more accurate results than fine low-order elements. Introducing p-adaptivity further reduces computational costs while maintaining accuracy by restricting the use of high-order elements to resolve the wave front. For a patient-specific simulation of a cardiac cycle, p-adaptivity reduces the average number of degrees of freedom by 95% compared to the non-adaptive model. In addition to reducing computational costs, using coarse meshes with our p-adaptive high-order HDG method also simplifies practical aspects of mesh generation and postprocessing.

7.3. Inverse Problems

7.3.1. *Discrete-time optimal filtering or Mortensen observer discretization*

Participant: Philippe Moireau [correspondant].

In this work, we seek exact formulations of the optimal estimator and filter for a non-linear framework, as the Kalman filter is for a linear framework. The solution is well established with the Mortensen filter in a continuous-time setting, but we seek here its counterpart in a discrete-time context. We demonstrate that it is possible to pursue at the discrete-time level an exact dynamic programming strategy and we find an optimal estimator combining a prediction step using the model and a correction step using the data. This optimal estimator reduces to the discrete-time Kalman estimator when the operators are in fact linear. Furthermore, the strategy that consists of discretizing the least square criterion and then finding the exact estimator at the discrete level allows to determine a new time-scheme for the Mortensen filter which is proven to be consistent and unconditionally stable, with also a consistent and stable discretization of the underlying Hamilton-Jacobi-Bellman equation. This work has resulted in the publication [30].

7.3.2. An iterative method for identifying a stress-free state in image-based biomechanics

Participant: Martin Genet [correspondant].

Continued advances in computational power and methods have enabled image-based biomechanical modeling to become an important tool in basic science, diagnostic and therapeutic medicine, and medical device design. One of the many challenges of this approach, however, is identification of a stress-free reference configuration based on in vivo images of loaded and often prestrained or residually stressed soft tissues and organs. Fortunately, iterative methods have been proposed to solve this inverse problem, among them Sellier's method. This method is particularly appealing because it is easy to implement, converges reasonably fast, and can be coupled to nearly any finite element package. By means of several practical examples, however, we demonstrate that in its original formulation Sellier's method is not optimally fast and may not converge for problems with large deformations. Nevertheless, we can also show that a simple, inexpensive augmentation of Sellier's method based on Aitken's delta-squared process can not only ensure convergence but also significantly accelerate the method. This work has resulted in the publication [31].

7.3.3. A continuum finite strain formulation for finite element image correlation

Participant: Martin Genet [correspondant].

We propose a novel continuum finite strain formulation of the equilibrium gap principle – originally introduced in [Claire, Hild and Roux, 2004, Int. J. Num. Meth. Eng.] at the discrete level for linearized elasticity – used as a regularizer for finite element-based image correlation problems. Consistent linearization and finite element discretization is provided. The method is implemented using FEniCS & VTK, in a freely available Python library. The equilibrium gap constraint regularizes the image correlation problem, even in the presence of noise, and without affecting strain measurements.

7.3.4. Front shape similarity measure for Eikonal PDE data assimilation

Participants: Annabelle Collin [Monc], Philippe Moireau [correspondant].

We present a shape-oriented data assimilation strategy suitable for front-tracking problems through the example of wildfire. The concept of “front” is used to model, at regional scales, the burning area delimitation that moves and undergoes shape and topological changes under heterogeneous orography, biomass fuel and micrometeorology. The simulation-observation discrepancies are represented using a front shape similarity measure inspired from image processing and based on the Chan-Vese contour fitting functional. We show that consistent corrections of the front location and uncertain physical parameters can be obtained using this measure applied on a level-set fire growth model solving for an eikonal equation. This study involves a Luenberger observer for state estimation, including a topological gradient term to track multiple fronts, and a reduced-order Kalman filter for joint parameter estimation. We also highlight the need – prior to parameter estimation – for sensitivity analysis based on the same discrepancy measure, and for instance using polynomial chaos metamodels, to ensure that a meaningful inverse solution is achieved. The performance of the shape-oriented data assimilation strategy is assessed on a synthetic configuration subject to uncertainties in front initial position, near-surface wind magnitude and direction. The use of a robust front shape similarity measure paves the way toward the direct assimilation of infrared images and is a valuable asset in the perspective of data-driven wildfire modeling. This work has resulted in the publication [32].

7.3.5. The mechanism of monomer transfer between two distinct PrP oligomers

Participants: Aurora Armiento, Marie Doumic [Mamba], Philippe Moireau [correspondant].

In mammals, Prion pathology refers to a class of infectious neuropathologies whose mechanism is based on the self-perpetuation of structural information stored in the pathological conformer. The characterisation of the PrP folding landscape has revealed the existence of a plethora of pathways conducing to the formation of structurally different assemblies with different biological properties. However, the biochemical interconnection between these diverse assemblies remains unclear. The PrP oligomerisation process leads to the formation of neurotoxic and soluble assemblies called O1 oligomers with a high size heterodispersity. By combining the measurements in time of size distribution and average size with kinetic models and data assimilation, we revealed the existence of at least two structurally distinct sets of assemblies, termed Oa and Ob, forming O1 assemblies. We propose a kinetic model representing the main processes in prion aggregation pathway: polymerisation, depolymerisation, and disintegration. The two groups interact by exchanging monomers through a disintegration process that increases the size of Oa. Our observations suggest that PrP oligomers constitute a highly dynamic population. This work has resulted in the publication [14].

7.3.6. *Joint-state and parameters estimation using ROUKF for HIV mechanistic models*

Participants: Annabelle Collin [Monc], Philippe Moireau [correspondant], Mélanie Prague [Sism].

Various methods have been used in the statistical field to estimate parameters in mechanistic models. In particular, an approach based on penalised likelihood for the estimation of parameters in ordinary differential equations with non linear models on parameters (ODE-NLME) has proven successful. For instance, we consider the NIMROD program as a benchmark for estimation in these models. However, such an approach is time consuming. To circumvent this problem, we consider data assimilation approaches that historically arose in the context of geophysics. Here, we propose a Luenberger (also called nudging) state observer coupled with a parameter Kalman-based observer (RoUKF filter, also called SEIK filter) to perform a joint state and parameter estimation on a dataset composed of longitudinal observations of biomarkers for multiple patients. We compare these methods in terms of performances and computation time. We discuss how the concept of random effect can be modeled using Kalman-based filter and its limitations. We illustrate both methods in simulation and on two datasets (the ALBI ANRS 070 trial and the Aquitaine cohort observational data) using an HIV mechanistic model.

7.4. Experimental Assessments

7.4.1. *Microstructural interpretation of mouse skin mechanics from multiscale characterization*

Participant: Jean-Marc Allain [correspondant].

Skin is a complex, multi-layered organ, with important functions in the protection of the body. The dermis provides structural support to the epidermal barrier, and thus has attracted a large number of mechanical studies. As the dermis is made of a mixture of stiff fibres embedded in a soft non-fibrillar matrix, it is classically considered that its mechanical response is based on an initial alignment of the fibres, followed by the stretching of the aligned fibres. Using a recently developed set-up combining multiphoton microscopy with mechanical assay, we imaged the fibres network evolution during dermis stretching. These observations, combined with a wide set of mechanical tests, allowed us to challenge the classical microstructural interpretation of the mechanical properties of the dermis: we observed a continuous alignment of the collagen fibres along the stretching. All our results can be explained if each fibre contributes by a given stress to the global response. This plastic response is likely due to inner sliding inside each fibre. The non-linear mechanical response is due to structural effects of the fibres network in interaction with the surrounding non-linear matrix. This multiscale interpretation explains our results on genetically-modified mice with a simple alteration of the dermis microstructure. This work has resulted in the publication [27].

7.4.2. *Affine kinematics in planar fibrous connective tissues: an experimental investigation*

Participants: Jean-Sébastien Affagard, Jean-Marc Allain [correspondant].

The affine transformation hypothesis is usually adopted in order to link the tissue scale with the fibers scale in structural constitutive models of fibrous tissues. Thanks to the recent advances in imaging techniques, such as multiphoton microscopy, the microstructural behavior and kinematics of fibrous tissues can now be monitored at different stretching within the same sample. Therefore, the validity of the affine hypothesis can be investigated. In this study, the fiber reorientation predicted by the affine assumption is compared with experimental data obtained during mechanical tests on skin and liver capsule coupled with microstructural imaging using multiphoton microscopy. The values of local strains and the collagen fibers orientation measured at increasing loading levels are used to compute a theoretical estimation of the affine reorientation of collagen fibers. The experimentally measured reorientation of collagen fibers during loading could not be successfully reproduced with this simple affine model. It suggests that other phenomena occur in the stretching process of planar fibrous connective tissues, which should be included in structural constitutive modeling approaches. This work has resulted in the publication [22].

7.4.3. Improving the experimental protocol for the identification of skin mechanical behavior

Participants: Jean-Sébastien Affagard, Florent Wijanto, Jean-Marc Allain [correspondant].

Mechanical properties of the skin, the external organ of the human body, are important for many applications such as surgery or cosmetics. Due to the highly hierarchical structure of the tissue, it is interesting to develop microstructural models that have better predictability and should reduce the consequences of sample variability. However, these models generally include a quite large number of mechanical parameters. Therefore, complex assays are required to achieve a proper identification of the microstructural models. We investigated in this study the best experimental protocol to identify a nonlinear, anisotropic, model of skin behavior, namely, the Holzapfel law, using displacement field and force measurements. This was done through a sensitivity analysis of the different parameters. We determined first the optimal assay, which appears to be a biaxial test with an alternated loading: first a stretch in one direction, then in the perpendicular one, and so on. To further improve the quality of the assay, we also determined the optimal geometry. Interestingly, slightly asymmetric geometries are more adequate than symmetric ones, while being easier to realise. This work has resulted in the publication [13].

7.4.4. How aging impacts skin biomechanics: a multiscale study in mice

Participants: Jean-Sébastien Affagard, Jean-Marc Allain [correspondant].

Skin aging is a complex process that strongly affects the mechanical behavior of skin. This study aims at deciphering the relationship between age-related changes in dermis mechanical behavior and the underlying changes in dermis microstructure. To that end, we use multiphoton microscopy to monitor the reorganization of dermal collagen during mechanical traction assays in ex vivo skin from young and old mice. The simultaneous variations of a full set of mechanical and microstructural parameters are analyzed in the framework of a multiscale mechanical interpretation. They show consistent results for wild-type mice as well as for genetically-modified mice with modified collagen V synthesis. We mainly observe an increase of the tangent modulus and a lengthening of the heel region in old murine skin from all strains, which is attributed to two different origins that may act together: (i) increased cross-linking of collagen fibers and (ii) loss of water due to proteoglycans deterioration, which impedes inner sliding within these fibers. In contrast, the microstructure reorganization upon stretching shows no age-related difference, which can be attributed to opposite effects of the decrease of collagen content and of the increase of collagen cross-linking in old mice. This work has resulted in the publication [28].

7.4.5. Recent advances in studying single bacteria and biofilm mechanics

Participant: Jean-Marc Allain [correspondant].

Bacterial biofilms correspond to surface-associated bacterial communities embedded in hydrogel-like matrix, in which high cell density, reduced diffusion and physico-chemical heterogeneity play a protective role and induce novel behaviors. We made a summary of the recent advances on the understanding of how bacterial mechanical properties, from single cell to high-cell density community, determine biofilm three-dimensional growth and eventual dispersion, and we attempt to draw a parallel between these properties and the mechanical properties of other well-studied hydrogels and living systems. This work has resulted in the publication [18].

7.5. Clinical Applications

7.5.1. Assessment of atrioventricular valve regurgitation using cardiac modeling

Participants: Radomir Chabiniok [correspondant], Philippe Moireau, Dominique Chapelle.

In this work, we introduce the modeling of atrioventricular valve regurgitation in a spatially reduced-order biomechanical heart model. The model can be fast calibrated using non-invasive data of cardiac magnetic resonance imaging and provides an objective measure of contractile properties of the myocardium in the volume overloaded ventricle, for which the real systolic function may be masked by the significant level of the atrioventricular valve regurgitation. After demonstrating such diagnostic capabilities, we show the potential of modeling to address some clinical questions concerning possible therapeutic interventions for specific patients. The fast running of the model allows targeting specific questions of referring clinicians in a clinically acceptable time. The work was presented at the "Functional Imaging and Modeling of the Heart" conference (FIMH 2017, Toronto, Canada) and is included in the conference proceedings [35].

7.5.2. *Model for the dobutamine response in exercise-induced failure of the Fontan circulation*

Participants: Radomir Chabiniok [correspondant], Philippe Moireau, Dominique Chapelle.

Understanding physiological phenomena and mechanisms of failure in congenital heart diseases is often challenging due to the complex hemodynamics and high inter-patient variations in anatomy and function. Computational modeling techniques have the potential to greatly improve the understanding of these complex diseases and provide patient-specific clues on mechanisms of deterioration and impact of treatments. This work employs a reduced 0D biomechanical heart model coupled with venous return to capture various key pathophysiological phenomena observed in patients with completed Fontan circulation – a complex surgically established circulation used to palliate patients in whom only one of the two ventricles is functionally able to support the vascular system – with exercise-induced heart failure during dobutamine stress. The framework we propose is fast, efficient and well-suited to the type of pathology and available clinical data obtained by a combined cardiac catheterization and magnetic resonance imaging exam. We demonstrate that the outcomes of modeling are a valuable addition to the current clinical diagnostic investigations and explain patient-specific exercise hemodynamics, identify potential mechanisms of Fontan failure, and enable evaluation of a potential new therapy – selective heart rate modulation – in the treatment of patients with Fontan circulation. The paper is currently in preparation.

7.5.3. *Heart and vessels modeling with data interaction for monitoring anesthetized patients*

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

By using mathematical models of heart and vessels developed in the team, we aim at improving intra-operative cardio-vascular safety of anesthetized patients. The patient-specific models, calibrated by echocardiography images and fed by continuous monitoring of aortic arterial pressure and aortic cardiac outflow would allow us to: 1) diagnose pathophysiological modifications associated with changes in the cardio-vascular state; 2) predict the drug response of the patient before the administration of the vaso-active treatment.

7.5.4. *Intra-operative monitoring of cardiac afterload*

Participants: Arthur Le Gall, Fabrice Vallée [correspondant].

General anesthesia leads to alterations of the cardiovascular system. Intra-operative arterial hypotension is linked to post-operative complications, but using vasopressors to treat arterial hypotension has shown conflicting results. Vasopressors act mainly by elevating cardiac afterload, which could be deleterious in fragile patients, in case of excessive response. Moreover, differences among the most used vasopressors have been observed in vivo [34]. The choice of vasopressor could be important to improve our patients' care. Consequently, we proposed a tool (Velocity-Pressure Loops) to continuously quantify changes in cardiac afterload [33]. Although the first work involves invasive measurement of aortic blood pressure and cardiac outflow, consistent results have been observed when Velocity-Pressure Loops were obtained by a radial arterial catheter with a mathematical transform function [23]. Those findings allow the usage of the Velocity-Pressure Loop without addition of any invasive device.

7.5.5. *Review on extra-corporeal circulation*

Participant: Arthur Le Gall [correspondant].

This clinical review [26] aims at describing the issues of the management of extra-corporeal membrane oxygenation (ECMO) in the Intensive Care Unit (ICU). From pathophysiology to the description of the impact on mortality, this document shows a global picture of current clinical practices.

7.5.6. *On the importance of consistency in cardiac timings measurements*

Participants: Arthur Le Gall, Alexandre Laurin, Fabrice Vallee [correspondant].

With the contribution of Denis Chemla, professor of Cardiology at Bicêtre Hospital, we presented this work at the CinC conference in Rennes [36]. In this work, we emphasize the need for a consistent method to measure systolic period duration, which is related to cardiac afterload and could be used to quantify arterial pressure amplification phenomenon.

8. Bilateral Contracts and Grants with Industry

8.1. Bilateral Contracts with Industry

Technical contract with CEA-LIST on coupling strategies between subdomains for transient elastodynamics (8keuros)

Contract with the Sensome startup. Aims: feasibility of the measurement of blood clots mechanical properties. (1.6keuros)

9. Partnerships and Cooperations

9.1. National Initiatives

9.1.1. *ANR*

ANR METIS(ANR-13-BS09-0004-02). Title: “Mechanics of Tissues: multiscale structural approach of Ehlers-Danlos Syndrome”. Involved research groups: LMS (Ecole Polytechnique, CNRS, Mines ParisTech, PI: Jean-Marc ALLAIN), LOB - Optics and Biosciences Laboratory (Ecole Polytechnique, CNRS, INSERM), IGFL - Institut de Génétique Fonctionelle de Lyon (ENS Lyon, Université Lyon 1, CNRS, INRA). Total amount of the grant: 200k€ for the team. The METIS project is dedicated to the study of the biomechanics of connective tissues. Soft connective tissues such as skin, tendon or cornea are made of more than 90% of extracellular matrix proteins, fibrillar collagens being by far the predominant component. The rationale of this project is to understand the link between the microstructure of connective tissues and their macroscopic mechanical properties. To achieve this, observations of the fibrilar collagen will be done at different levels of stretch, while recording the mechanical properties. The consequences of change in the microstructure will also be explored through mutants mimicking the Ehler-Danlos syndrome, but also aging or wound-healing experiments. The project was completed on September 30th 2017 (4 years project).

9.1.2. *Other funding*

IPM-MS project (for Imagerie Polarimétrique de Mueller pour la réalisation d’un système original de caractérisation des propriétés mécaniques des Matériaux Structurés). 50k€ funded by the LABEX Lasips. This project, which involves the LPICM laboratory (Ecole Polytechnique, CNRS), the LMS (Ecole Polytechnique, CNRS, Mines ParisTech) and the Centre des Matériaux (Mines ParisTech), aims at developing an optical tool to study the link between the mechanical properties of a material and its hierarchical organization. Despite the development of new methods to observe the microstructure, one of the limitations is the number of observations that can be obtained on a given sample in a realistic experimental time. To overcome this difficulty, we are planning to use the Mueller polarimetry to obtain at a fast rate (a few frames per second, compared to a few frames per half-hour) relevant information on the local anisotropy of biological (heart, skin) and composite (short fibers composite) samples.

G. Bureau, software engineer in the team, is funded by an Inria Reo industrial contract with Kephalios, a startup working on innovative artificial valves devices.

9.2. European Initiatives

9.2.1. FP7 & H2020 Projects

9.2.1.1. VP2HF

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

Programm: FP7

Duration: October 2013 - March 2017

Coordinator: King's College London (UK)

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 aging 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.

9.3. International Initiatives

9.3.1. Inria International Partners

9.3.1.1. Informal International Partners

We have started a collaboration with the University of Texas Southwestern Medical Center in Dallas. A joint PhD student based at Inria and funded by UTSW is starting in October 2017. An associated team proposal has been submitted in October 2017.

9.4. International Research Visitors

9.4.1. Visits of International Scientists

9.4.1.1. PhD exchange program

J. Albella, PhD student at University of Santiago de Compostela, has spent 3 months in M3DISIM, working with S. Imperiale on numerical methods for elastodynamics wave propagation.

E. Bertoberoglu, PhD Student at ETH Zurich, has spent multiple weeks in M3DISIM to work with M. Genet on computational models of growth and remodeling of the heart, validated on MRI data acquired at ETH Zurich.

10. Dissemination

10.1. Promoting Scientific Activities

10.1.1. Scientific Events Organisation

10.1.1.1. General Chair, Scientific Chair

M. Genet, Session chair on Biomechanics at CSMA2017

M. Genet, Session chair on Software and Algorithms at FEniCS-2017

10.1.1.2. Member of the Organizing Committees

D. Chapelle, Member of the Paris-Saclay Biomechanical Seminar organizing committee

M. Genet, Member of the CSMA-2017 organizing committee

P. Le Tallec, Vice-president of the CSMA2017 (bi-annual national conference on computational structural mechanics) organizing committee

P. Moireau, Member of the organizing committee of the Inria-Saclay teams (Poems-M3disim-Defi) scientific computing seminar

10.1.2. Scientific Events Selection

10.1.2.1. Member of the Conference Program Committees

D. Chapelle, Member of the Conference Program Committee of FIMH 2017

M. Genet, Member of the Conference Program Committee of CSMA-2017

P. Le Tallec, Member of the Conference Program Committee of CSMA-2017

10.1.2.2. Reviewer

D. Chapelle, reviewer for FIMH 2017

M. Genet, reviewer for CSMA-2017

P. Le Tallec, reviewer for CSMA-2017

10.1.3. Journal

10.1.3.1. Member of the Editorial Boards

D. Chapelle, Member of the editorial board of journal *Computers & Structures*

D. Chapelle, Member of the editorial board of journal *ESAIM: M2AN*

10.1.3.2. Reviewer - Reviewing Activities

J.-M. Allain, reviewer for “Journal of the Mechanical Behavior of Biomedical Materials” and “Soft Matter journal”

R. Chabiniok, reviewer for “Journal of Computer Methods and Programs in Biomedicine”, “Computers and Structures” and “Journal of Cardiovascular Translational Research”

D. Chapelle, reviewer for “Biomechanics and Modeling in Mechanobiology”, “Computer Methods in Applied Mechanics and Engineering”, “Computers & Structures”

M. Genet, reviewer for “Acta Biomaterialia”

S. Imperiale, reviewer for “Journal of Computers and mathematics with application”, “Journal of Numerical Methods for Partial Differential Equations” “Journal of Methods and Algorithms for Scientific Computing section”, “Journal of Geophysics” and “Journal of Computational Physics”

P. Moireau, reviewer for “ANR” and “Bulletin of Mathematical Biology”

10.1.4. Invited Talks

D. Chapelle, invited seminars at Centrale-Supelec (Jan. 19th) and WIAS Berlin (Sept. 18th)

P. Moireau, “A discrete-time optimal filtering approach for nonlinear systems as a stable discretization of the Mortensen observer” , Workshop on Optimal Control of Dynamical Systems

10.1.5. Leadership within the Scientific Community

J.-M. Allain, Member of Society of Experimental Mechanics and of Biophysical Society

J.-M. Allain, Member of the Academic Council of Université Paris-Saclay, France

D. Chapelle, Head of Science of Inria Saclay-Ile-de-France, and member of the Inria Evaluation Committee

D. Chapelle, Member of the board of directors of the VPH Institute, and of the Avicenna Alliance

D. Chapelle, Member of the steering committee of the BioMedical Engineering Institute coordinated by Ecole Polytechnique

A. Le Gall, Chair of youth committee of SFAR (French Society of Anesthesia and Reanimation)

P. Le Tallec, Director of the LMS (Solid Mechanics Laboratory) Ecole Polytechnique

P. Le Tallec, President of the Mechanics department at University Paris Saclay

P. Moireau, Member of the steering committee of Department of Mathematics of Université Paris Saclay and Jacques Hadamard Foundation

10.1.6. Scientific Expertise

R. Chabiniok, Honorary medical consultant at Saint-Thomas hospital (King's College London)

S. Imperiale, Consultant for CEA (The French Alternative Energies and Atomic Energy Commission)

P. Le Tallec, Consultant for CEA

P. Le Tallec, Consultant for Michelin

P. Moireau, Reviewer for ANR

10.1.7. Research Administration

J.-M. Allain, Responsibility of the teaching experimental center (mechanics), at École Polytechnique

J.-M. Allain, Scientific Advisory Board, chair BioMecAM at ENSAM

J.-M. Allain, Responsible of the "Mechanics and Material for the bio" at the Fédération Francilienne de Mécanique

D. Chapelle, Head of Science of Inria Saclay-Ile-de-France, and member of the Inria Evaluation Committee

P. Le Tallec, Director of the LMS (Solid Mechanics Laboratory) Ecole Polytechnique

P. Le Tallec, in charge of 3rd year program in Mechanics and Energy at Ecole Polytechnique

P. Le Tallec, in charge of the André Citroën Chair

P. Le Tallec, in charge of the Mechanics department at University Paris Saclay

P. Le Tallec, President of the academic senate of the Ecole Polytechnique

10.2. Teaching - Supervision - Juries

10.2.1. Teaching

Bachelor: J.-M. Allain, "Introduction projects to physics", 15h, (L1), École Polytechnique, France

Bachelor: F. Caforio,"PEIP1 S2 M2 – Mathematical analysis in two and three dimensions, linear algebra in Rn", 22h, (L1), Polytech Paris-Sud, France

Bachelor: F. Caforio,"Math 255 – Differential calculus for physics (mathematical analysis in two and three dimensions)", 42h, (L2), Université Paris-Sud, France

Bachelor: M. Genet, "MEC435 – Modélisation et Simulation en Mécanique Industrielle", 32h, (L3), École Polytechnique, France

Bachelor: M. Genet,"MEC430 – Mécanique des Milieux Continus I", 32h, (L3), École Polytechnique, France

Bachelor: M. Genet, “MEC431 – Mécanique des Milieux Continus II”, 32h, (L3), École Polytechnique, France

Bachelor: S. Imperiale, “MA102 – Analyse pour les EDP”, 24h, (L3), ENSTA ParisTech, France

Bachelor: S. Imperiale, “MA104 – Analyse complexe”, 12h, (L3), ENSTA ParisTech, France

Bachelor: F. Kimmig, “Mathematical methods for physics”, 32h, (L1) level, École Polytechnique, France

Bachelor: F. Kimmig, “Introduction projects to physics”, 6h, (L1), École Polytechnique, France

Bachelor: F. Kimmig, “Modeling and simulation in industrial mechanics”, 32h, (L3), École Polytechnique, France

Bachelor: P. Le Tallec, “MEC 431 – Mécanique des Milieux Continus 2”, (L3), École Polytechnique, France

Bachelor: P. Le Tallec, “Continuum mechanics”, 32h, (L3), Shanghai ParisTech, China

Bachelor: P. Moireau, “MAP 411 – Approximation numérique et optimisation”, 32 h, (L3), Ecole Polytechnique, France

Master: P. Moireau, “MA103 – Introduction aux EDP et à la méthode des différences finies”, 14h, (L3), ENSTA ParisTech, France

Bachelor: F. Wijanto, “Modeling and simulation in industrial mechanics” 32 h, (L3), École Polytechnique, France

Master: J.-M. Allain, “conputational fluid dynamics”, 36h, (M1), Ecole Polytechnique, France

Master: J.-M. Allain, “Cellular Motility”, 32h, (M2), Ecole Polytechnique, France

Master: D. Chapelle: “Biomechanical Modeling of Active Tissues”, 33h, (M2), Université Paris-Saclay, France

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

Master: S. Imperiale, “Simnum – Programmation C++”, 18h, (M1), ENSTA ParisTech, France

Master: P. Le Tallec, “M4S – Numerical methods in non linear mechanics”,27h, (M2), École Polytechnique, France

Master: P. Le Tallec, “Nuclear Energy on Continuum Mechanics”,15h, (M2), INSTN, France

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

Master: P. Moireau, “Biomechanical Modeling of Active Tissues”, 12h, (M2), Université Paris-Saclay, France

Master: P. Moireau, “Méthodes et problèmes inverses en dynamique des populations”, 24h, (M2), UPMC, France

10.2.2. Supervision

PhD: Aurora Armiento, “Inverse problems and data assimilation methods applied to protein depolymerisation”, supervisors: M. Doumic and P. Moireau, Paris-Descartes University, defended Jan. 13th

PhD in progress: Ustim Khristenko, “Méthodes mathématiques et numériques pour la modélisation et le calcul des états établis cycliques en mécanique non-linéaire”, started Oct. 2014, supervised: P. Le Tallec

PhD in progress: Florent Wijanto, “Modélisation multi-échelle des fibres de collagènes”, started: Sept. 2015, supervisors: J.-M. Allain and M. Caruel

PhD in progress: Federica Caforio, “Modélisation mathématique et numérique de la propagation d’ondes élastique dans le coeur”, started: Nov. 2015, supervisors: D. Chapelle and S. Imperiale

PhD in progress: François Kimmig, “Multi-scale modeling of muscle contraction – From stochastic dynamics of molecular motors to continuum mechanics, in interaction with experimental assays”, started: Sept. 2016, supervisors: M. Caruel and D. Chapelle

PhD in progress: Arthur Le Gall, “Application of biomechanical heart modeling in hemodynamic monitoring of increased risk patients during anesthesia using clinical data”, started Nov. 2016, supervisors: D. Chapelle, E. Gayat (UP7 Paris Diderot) and R. Chabiniok

PhD in progress: Ezgi Berberoglu, “Image-guided Computational Cardiac Mechanics”, started: Jan. 2016 supervisors: Martin Genet and Sebastian Kozerke (ETH, Zurich, Switzerland)

PhD in progress: Cécile Patte, “Modélisation poro-mécanique multi-échelle du poumon, de la respiration au remodelage chronique associé à la fibrose pulmonaire”, started: Nov. 2017, supervisors: M. Genet and D. Chapelle

PhD in progress: Marija Gusseva, “Cardiac Biomechanical Modeling of Chronic Right Ventricular Loading”, started Dec. 2017, supervised: R. Chabiniok, D. Chapelle, T. Hussain (UTSW Medical Center Dallas)

10.2.3. Juries

D. Chapelle, Habilitation Jury of Marcela Szopos, Strasbourg University, President, Dec. 1st

P. Moireau, PhD Jury of Aurora Armiento, Paris-Descartes University, PhD Advisor, Jan. 13th

P. Moireau, PhD Jury of Chloé Audebert, Paris-6 University, Reviewer, Febr. 24th

P. Moireau, PhD Jury of Pauline Bernard, Paris-6 University, President, Nov. 20th

P. Moireau, PhD Jury of Roch Mollero, University of Nice-Sophia Antipolis, Dec. 19th

10.3. Popularization

J.-M. Allain, Jeudi de la Recherche de l’X: popularisation talk on research with medical application. June 2017

J.-M. Allain, 3 articles in popularisation journals (quotidien du médecin, le concours médical, biotech.info) by journalists

D. Chapelle, interview for “Usine Nouvelle”, Dec. 12th

A. Laurin, Inria Saclay inauguration demo and associated news article in “Le Parisien”, Jan. 2017

P. Moireau, Créteil district “Olympiades de Mathématiques” award ceremony, May 2017

R. Chabiniok, Review paper promoting Cardiovascular MRI particularly of congenital heart diseases for Czech and Slovak physicians [17]

A. Laurin, P. Moireau, D. Chapelle, demo at 50 ans de l’Inria, Nov. 7th and 8th

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^{o} 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^o 12 [*DOI :* 10.1142/S0218202512500406], http://hal.inria.fr/inria-00621052

[4] 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^o 2, pp. 189-211 [*DOI :* 10.1615/INTJMULTCOMPENG.2011002360], http://hal.inria.fr/hal-00678772

[5] 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

[6] B. LYNCH, S. BANCELIN, C. BONOD-BIDAUD, J.-B. GUEUSQUIN, F. RUGGIERO, M.-C. SCHANNE-KLEIN, J.-M. ALLAIN. *A novel microstructural interpretation for the biomechanics of mouse skin derived from multiscale characterization*, in "Acta Biomaterialia", 2017, vol. 50, pp. 302-311 [*DOI :* 10.1016/J.ACTBIO.2016.12.051], https://hal.archives-ouvertes.fr/hal-01531321

[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^o 6-8, pp. 659-677 [*DOI :* 10.1016/J.CMA.2007.08.021], http://hal.archives-ouvertes.fr/hal-00175623

[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^o 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] P. MOIREAU. *A Discrete-time Optimal Filtering Approach for Non-linear Systems as a Stable Discretization of the Mortensen Observer*, in "ESAIM: Control, Optimisation and Calculus of Variations", 2017, forthcoming, https://hal.inria.fr/hal-01671271

[11] 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^o 1, pp. 201-215 [*DOI :* 10.1016/J.MEDIA.2011.07.003], http://hal.inria.fr/inria-00616191

Publications of the year

Doctoral Dissertations and Habilitation Theses

[12] A. ARMIENTO. *Inverse problems and data assimilation methods applied to protein polymerisation*, Université Paris 7 - Diderot, January 2017, https://hal.inria.fr/tel-01447286

Articles in International Peer-Reviewed Journals

[13] J.-S. Affagard, F. Wijanto, J.-M. Allain. *Improving the experimental protocol for a more accurate identification of a given mechanical behavior in a single assay: application to skin*, in "Strain", August 2017 [*DOI :* 10.1111/str.12236], https://hal.archives-ouvertes.fr/hal-01570071

[14] A. Armiento, P. Moireau, D. Martin, N. Lepejova, M. Doumic, H. Rezaei. *The mechanism of monomer transfer between two structurally distinct PrP oligomers*, in "PLoS ONE", July 2017, vol. 12, n^{o} 7 [*DOI :* 10.1371/journal.pone.0180538], https://hal.archives-ouvertes.fr/hal-01574346

[15] L. Asner, M. Hadjicharalambous, R. Chabiniok, D. Peressutti, E. Sammut, J. Wong, G. Carr-White, R. Razavi, A. D. King, N. P. Smith, J. Lee, D. Nordsletten. *Patient-specific modeling for left ventricular mechanics using data-driven boundary energies*, in "Computer Methods in Applied Mechanics and Engineering", 2017, vol. 314, pp. 269-295 [*DOI :* 10.1016/j.cma.2016.08.002], https://hal.archives-ouvertes.fr/hal-01576770

[16] B. Burtschell, D. Chapelle, P. Moireau. *Effective and energy-preserving time discretization for a general nonlinear poromechanical formulation*, in "Computers and Structures", 2017, vol. 182, pp. 313-324 [*DOI :* 10.1016/j.compstruc.2016.10.022], https://hal.inria.fr/hal-01395508

[17] R. Chabiniok, L. Súkupová, D. Kautznerová, J. Tintěra. *Magnetic Resonance Imaging of the Heart and Large Vessels – Survey of methods and new perspectives*, in "Česká radiologie", November 2017, pp. 1-28, forthcoming, https://hal.archives-ouvertes.fr/hal-01667798

[18] C. Even, C. Marlière, J.-M. Ghigo, J.-M. Allain, A. Marcellan, E. Raspaud. *Recent advances in studying single bacteria and biofilm mechanics*, in "Advances in Colloid and Interface Science", 2017, 57 p. [*DOI :* 10.1016/j.cis.2017.07.026], https://hal.archives-ouvertes.fr/hal-01566801

[19] F. Fuentes, B. Keith, L. Demkowicz, P. Le Tallec. *Coupled variational formulations of linear elasticity and the DPG methodology*, in "Journal of Computational Physics", November 2017, vol. 348, pp. 715 - 731 [*DOI :* 10.1016/j.jcp.2017.07.051], https://hal.archives-ouvertes.fr/hal-01576307

[20] M. Hadjicharalambous, L. Asner, R. Chabiniok, E. Sammut, J. Wong, D. Peressutti, E. Kerfoot, A. D. King, J. Lee, R. Razavi, N. Smith, G. Carr-White, D. Nordsletten. *Non-invasive Model-Based Assessment of Passive Left-Ventricular Myocardial Stiffness in Healthy Subjects and in Patients with Non-ischemic Dilated Cardiomyopathy*, in "Annals of Biomedical Engineering", March 2017, vol. 45, n^{o} 3, pp. 605-618, https://hal.inria.fr/hal-01419936

[21] J. Hoermann, C. Bertoglio, M. Kronbichler, M. Pfaller, R. Chabiniok, W. Wall. *An adaptive Hybridizable Discontinuous Galerkin approach for cardiac electrophysiology*, in "International Journal for Numerical Methods in Biomedical Engineering", 2017, pp. 1 - 20, forthcoming, https://hal.archives-ouvertes.fr/hal-01672964

[22] C. Jayyosi, J.-S. Affagard, G. Ducourthial, C. Bonod-Bidaud, B. Lynch, S. Bancelin, F. Ruggiero, M.-C. Schanne-Klein, J.-M. Allain, K. Bruyère-Garnier, M. Coret. *Affine kinematics in planar fibrous connective tissues: an experimental investigation*, in "Biomechanics and Modeling in Mechanobiology", 2017, pp. 1–15 [*DOI :* 10.1007/s10237-017-0899-1], https://hal.archives-ouvertes.fr/hal-01529263

[23] J. JOACHIM, F. VALLÉE, J. MATEO, A. LE GALL, S. LENCK, S. MILLASSEAU, E. HOUDART, A. MEBAZAA, E. GAYAT. *Velocity–pressure loops for continuous assessment of ventricular afterload: influence of pressure measurement site*, in "Journal of Clinical Monitoring and Computing", November 2017, pp. 1-8, forthcoming [*DOI :* 10.1007/S10877-017-0082-3], https://hal.inria.fr/hal-01666355

[24] M. LANDAJUELA, M. VIDRASCU, D. CHAPELLE, M. A. FERNÁNDEZ. *Coupling schemes for the FSI forward prediction challenge: comparative study and validation*, in "International Journal for Numerical Methods in Biomedical Engineering", vol. 33, n^o 4, e02813 p. , 2017 [*DOI :* 10.1002/CNM.2813], https://hal.inria.fr/hal-01239931

[25] A. LAURIN, M. G. LLOYD, T. HACHIYA, M. SAITO, V. E. CLAYDON, A. BLABER. *New indices from microneurography to investigate the arterial baroreflex*, in "Physiological Reports", June 2017, vol. 5, n^o 12 [*DOI :* 10.14814/PHY2.13220], https://hal.inria.fr/hal-01555596

[26] A. LE GALL, A. FOLLIN, B. CHOLLEY, J. MANTZ, N. AISSAOUI, R. PIRRACCHIO. *Veno-Arterial-ECMO in the Intensive Care Unit:From Technical Aspects to Clinical Practice*, in "Anaesthesia Critical Care & Pain Medicine", October 2017, pp. 1-43 [*DOI :* 10.1016/J.ACCPM.2017.08.007], https://hal.inria.fr/hal-01629078

[27] B. LYNCH, S. BANCELIN, C. BONOD-BIDAUD, J.-B. GUEUSQUIN, F. RUGGIERO, M.-C. SCHANNE-KLEIN, J.-M. ALLAIN. *A novel microstructural interpretation for the biomechanics of mouse skin derived from multiscale characterization*, in "Acta Biomaterialia", 2017, vol. 50, pp. 302-311 [*DOI :* 10.1016/J.ACTBIO.2016.12.051], https://hal.archives-ouvertes.fr/hal-01531321

[28] B. LYNCH, C. BONOD-BIDAUD, G. DUCOURTHIAL, J.-S. AFFAGARD, S. BANCELIN, S. PSILODIMITRAKOPOULOS, F. RUGGIERO, J.-M. ALLAIN, M.-C. SCHANNE-KLEIN. *How aging impacts skin biomechanics: a multiscale study in mice*, in "Scientific Reports", December 2017, vol. 7, n^o 1 [*DOI :* 10.1038/S41598-017-13150-4], https://hal.archives-ouvertes.fr/hal-01667964

[29] N. MITROU, A. LAURIN, T. DICK, J. INSKIP. *A peak detection method for identifying phase in physiological signals*, in "Biomedical Signal Processing and Control", 2017, vol. 31, pp. 452 - 462 [*DOI :* 10.1016/J.BSPC.2016.07.001], https://hal.inria.fr/hal-01380875

[30] P. MOIREAU. *A Discrete-time Optimal Filtering Approach for Non-linear Systems as a Stable Discretization of the Mortensen Observer*, in "ESAIM: Control, Optimisation and Calculus of Variations", 2017, forthcoming, https://hal.inria.fr/hal-01671271

[31] M. K. RAUSCH, M. GENET, J. D. HUMPHREY. *An augmented iterative method for identifying a stress-free reference configuration in image-based biomechanical modeling*, in "Journal of Biomechanics", 2017, vol. 58, pp. 227 - 231 [*DOI :* 10.1016/J.JBIOMECH.2017.04.021], https://hal.archives-ouvertes.fr/hal-01571436

[32] M. ROCHOUX, A. COLLIN, C. ZHANG, A. TROUVÉ, D. LUCOR, P. MOIREAU. *Front shape similarity measure for shape-oriented sensitivity analysis and data assimilation for Eikonal equation*, in "ESAIM: Proceedings and Surveys", 2017, pp. 1-22, forthcoming, https://hal.inria.fr/hal-01625575

[33] F. VALLÉE, A. LE GALL, J. JOACHIM, O. PASSOUANT, J. MATEO, A. MARI, S. MILLASSEAU, A. MEBAZAA, E. GAYAT. *Beat-by-beat assessment of cardiac afterload using descending aortic velocity–pressure loop during general anesthesia: a pilot study*, in "Journal of Clinical Monitoring and Computing",

January 2017, vol. 113, n^{o} 5, pp. 727 - 735 [*DOI :* 10.1007/s10877-017-9982-5], https://hal.inria.fr/hal-01629079

[34] F. VALLÉE, O. PASSOUANT, A. LE GALL, J. JOACHIM, J. MATEO, A. MEBAZAA, E. GAYAT. *Norepinephrine reduces arterial compliance less than phenylephrine when treating general anesthesia-induced arterial hypotension*, in "Acta Anaesthesiologica Scandinavica Supplementum", July 2017, vol. 61, n^{o} 6, pp. 590 - 600 [*DOI :* 10.1111/AAS.12905], https://hal.inria.fr/hal-01666364

International Conferences with Proceedings

[35] R. CHABINIOK, P. MOIREAU, C. KIESEWETTER, T. HUSSAIN, R. RAZAVI, D. CHAPELLE. *Assessment of atrioventricular valve regurgitation using biomechanical cardiac modeling*, in "FIMH 2017 - 9th international conference on Functional Imaging and Modeling of the Heart", Toronto, Canada, LNCS - Lecture Notes in Computer Science, Springer, June 2017, vol. 10263, pp. 401-411, https://hal.archives-ouvertes.fr/hal-01505834

[36] A. LE GALL, A. LAURIN, F. VALLÉE, D. CHEMLA. *Comparison of Systolic Period Duration using Aortic Flow or Pressure Based Methods in Anesthetized Patients*, in "Computing in cardioogy", Rennes, France, September 2017, https://hal.inria.fr/hal-01580305

National Conferences with Proceedings

[37] M. PRAGUE, R. THIÉBAUT, P. MOIREAU, A. COLLIN. *Joint-state and parameters estimation using nudging and SEIK filters for HIV mechanistic models*, in "Journée de la statistique francaise", Avignon, France, June 2017, https://hal.inria.fr/hal-01579068

Conferences without Proceedings

[38] M. GENET, L. C. LEE, S. KOZERKE. *A continuum finite strain formulation of the equilibrium gap regularizer for finite element image correlation*, in "13e`me Colloque National en Calcul des Structures", Giens, France, May 2017, https://hal.archives-ouvertes.fr/hal-01661810

[39] M. GENET, L. C. LEE, S. KOZERKE. *Equilibrated Warping: Finite Element Image Correlation with Mechanical Regularization*, in "FEniCS'2017", Luxembourg, Luxembourg, June 2017, https://hal.archives-ouvertes.fr/hal-01661825

Patents and standards

[40] R. CHABINIOK, D. CHAPELLE, A. LE GALL, P. MOIREAU, F. VALLÉE. *Dispositif cardiaque*, 2017, n^{o} 1758006, https://hal.inria.fr/hal-01580331