RESEARCH CENTRE

Saclay - Île-de-France

IN PARTNERSHIP WITH:

Ecole Polytechnique

2020

ACTIVITY REPORT

Project-Team

M3DISIM

Mathematical and Mechanical Modeling with Data Interaction in Simulations for Medicine

DOMAIN

Digital Health, Biology and Earth

THEME

Modeling and Control for Life Sciences

Contents

Project-Team M3DISIM

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

Keywords

Computer sciences and digital sciences

A6.1.1. – Continuous Modeling (PDE, ODE)

A6.1.2. – Stochastic Modeling

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

A6.4.6. – Optimal control

A6.5.1. – Solid mechanics

A6.5.2. – Fluid mechanics

A6.5.4. – Waves

A9.2. – Machine learning

Other research topics and application domains

B1.1.3. – Developmental biology

B1.1.8. – Mathematical biology

B1.1.9. – Biomechanics and anatomy

B2.2.1. – Cardiovascular and respiratory diseases

B2.6.2. – Cardiac imaging

B2.6.3. – Biological Imaging

1 Team members, visitors, external collaborators

Research Scientists

- Philippe Moireau [Team leader, Inria, Senior Researcher, HDR]
- Radomir Chabiniok [Inria, Advanced Research Position, until Nov 2020]
- Dominique Chapelle [Inria, Senior Researcher, HDR]
- Frédérique Clément [Inria, Senior Researcher, until July 2020, HDR]
- Sébastien Imperiale [Inria, Researcher]

Faculty Members

- Jean-Marc Allain [École polytechnique, Associate Professor, HDR]
- Martin Genet [École polytechnique, Associate Professor]
- Patrick Le Tallec [École polytechnique, Professor, HDR]

PhD Students

- Nicolas Adam [École polytechnique, until Sep 2020]
- Guillaume Ballif [Inria, until Jun 2020]
- Mathieu Barré [Inria, from Oct 2020]
- Ezgi Berberoglu [Institut fédérale de technologie Zurich - Suisse]
- Andre Dalmora [CEA, from Oct 2020]
- Tiphaine Delaunay [Inria, from Oct 2020]
- Chloe Giraudet [École polytechnique]
- Marija Gusseva [Inria]
- Jona Joachim [Assistance publique/Hôpitaux de Paris]
- Arthur Le Gall [Assistance publique/Hôpitaux de Paris]
- Jessica Manganotti [Inria]
- Mahdi Manoochehrtayebi [Institut Polytechnique de Paris, from Nov 2020]
- Cecile Patte [Inria]
- Nicole Tueni [École polytechnique]
- Vincenzo Zarra [École polytechnique, from Aug 2020]

Technical Staff

- Jerome Diaz [Inria, Engineer]
- François Kimmig [Inria, Engineer]

Interns and Apprentices

- Felipe Alvarez Barrientos [École polytechnique, until Mar 2020]
- Mathieu Barré [Inria, from Apr 2020 until Sep 2020]
- Tiphaine Delaunay [Inria, from Mar 2020 until Aug 2020]
- Mahdi Manoochehrtayebi [École polytechnique, from Mar 2020 until Aug 2020]
- Matthieu Melennec [Inria, from Jun 2020 until Jul 2020]

Administrative Assistant

- Bahar Carabetta [Inria]

Visiting Scientists

- Andre Dalmora [CEA, Sep 2020]
- Giulia Merlini [École polytechnique, from Oct 2020]
- Francesco Regazzoni [Politecnico di Milano, until Feb 2020]
- Vincent Sounthakith [Assistance publique/Hôpitaux de Paris, from Nov 2020]

External Collaborators

- Matthieu Caruel [Univ Paris-Val de Marne]
- Radomir Chabiniok [University of Texas Southwestern Medical Center Dallas - USA, from Dec 2020]
- Didier Lucor [CNRS]
- Fabrice Vallée [Assistance publique/Hôpitaux de Paris]
- Maya de Buhan [CNRS]

2 Overall objectives

The research carried out in the MΞDISIM 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 [6]. In the same spirit, we have 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 [7].

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. 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 [5] – 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 [3].

4 Application domains

As already emphasized in the team's objectives, we consider experimental studies and clinical applications as crucial, both for motivating our new modeling endeavors, and to validate the global modeling simulation chain, via the numerical simulation and inverse problems (for data-based estimation).

For instance, the translation of the modeling and data assimilation techniques developed in our team into cardiac clinical applications is pursued in two main directions: 1. Cardiac modeling for monitoring purposes in anesthesia and critical care medicine 2. Cardiac modeling in heart diseases. Concerning the clinical applications of lung modeling and data interaction, the team works for a better understanding of pulmonary fibrosis and with recent new research about COVID pulmonary infections. Another example is the clinical relevance of our modeling and characterization of the biomechanical behavior of the cornea.

Beyond medical applications, our general methods have applications in many industrial fields. For instance, our expertise in wave propagation and associated inverse problems have potential applications in non-destructive testing of structure.

5 Highlights of the year

5.1 Awards

Cécile Patte, PhD student in the team is one of the laureates of the "For Women and Science" prize from the L'Oréal Foundation and UNESCO. This award aims to develop the visibility of women in science based on the quality of their scientific project and their ability to transmit their passion for science. Maria Gusseva, PhD student in the team received a student poster award and the Medtronic young professionals lightning-round competition award at the VPH2020 Conference.

5.2 Conference VPH2020

The 2020 edition was organized by Inria, in particular the MΞDISIM team (in collaboration with AP-HP, Ecole Polytechnique, INSA Lyon, Sorbonne Université) in partnership with the VPH Institute and EIT

Health France. This edition was held online (in the context of the COVID-19 pandemic), with a special day on modeling and simulations for COVID-related applications on August 24th, followed by satellite workshops on August 25th, before the conference per se on August 26th - 28th 2020. Unlike many conferences organized online in a "Plan B" mode during the pandemic (with most presentations prerecorded) we decided to make full use of modern videoconferencing tools to provide a 100% live experience, with all features of a real conference preserved (poster sessions, satellite events, roundtables…). This edition was a great success with more than 600 participants (whereas VPH conferences usually gather around 200 participants), and enthusiastic feedback.

5.3 COVID missions

PréLiFa Project: The aim of this project, led by D. Chapelle at the request of AP-HP during the first national lockdown period, was to alleviate the "black hole" effect caused by the particular situation of Covid-19 patients, for whom families risked receiving no news (or very little) of their loved ones during their entire stay in intensive care, because the patients themselves are generally not in a condition to give news, and access to hospitals is not authorized for families in the Covid context. The idea was to set up an IT platform, named PréLiFa (Préservation du Lien aux Familles), allowing all the healthcare staff (doctors, nurses, nursing aides, physiotherapists, etc.) to send messages to the patients' families in a very simple way, directly "at the bedside" of each patient. It therefore seemed obvious to associate Nicolas Anciaux and the PETRUS project-team, who for their part have an expertise in the management of secure health data, as well as a long-standing collaboration with the Hippocad company. P. Moireau also participated in the back-office team coordinated by Céline Grandmont (Inria-Paris). During its two months of intensive operation, the PréLiFa system served about 150 Covid patients in 3 AP-HP hospitals (Lariboisière, Saint-Louis and Beaujon), with about 750 accounts created for healthcare staff to provide regular news to families, and the ability to follow patients transferred to remote hospitals.

GestEpid Project The GestEpid project, led by by the Sistm project-team (Inria Bordeaux-Sud Ouest) specialized in data sciences, is concerned with the progression of the COVID-19 epidemic in France and more particularly in Nouvelle-Aquitaine. The objective of the project is to quantify the impact of sanitary containment and decontainment measures using dynamic model methods. P. Moireau, in close collaboration with A. Collin (Monc project-team),worked in this project to propose Kalman-based monitoring strategies of the epidemic, in particular the estimation of the containment and decontainment impact on the system dynamics.

6 New software and platforms

The team benefited from the support of the experimentation and development service (SED), Inria Saclay-Ile-de-France. Indeed, Sébastien Gilles is part-time working in the team on MoReFEM and is the main contributor of the library. Moreover, Laurent Steff is part-time working in the team on AKILLES and is the main developer of the library.

6.1 New software

6.1.1 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

Release Contributions: Addition of a mechanical formulation expressed analytically as a function of displacements

URL: https://gitlab.inria.fr/M3DISIM/CardiacLab

Authors: Philippe Moireau, Dominique Chapelle, François Kimmig, Jérôme Diaz, Sebastien Impériale

Contacts: Philippe Moireau, Dominique Chapelle

Participants: Philippe Moireau, Dominique Chapelle, François Kimmig, Jérôme Diaz, Sebastien Impériale, Martin Genet, Federica Caforio, Radomir Chabiniok, Arthur Le Gall, Matthieu Caruel, Jessica Manganotti

6.1.2 HeartLab

Keywords: Computational geometry, Image analysis, Cardiac, Health, Simulation

Functional 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.

URL: https://raweb.inria.fr/rapportsactivite/RA2013/m3disim/uid14.html

Contact: Philippe Moireau

Participants: Radomir Chabiniok, Gautier Bureau, Martin Genet, Federica Caforio, Ustim Khristenko, Dominique Chapelle, Philippe Moireau

6.1.3 MoReFEM

Name: Modeling Research with the Finite Element Method

Keywords: HPC, Multiphysics modelling, Data assimilation

Functional Description: MoReFEM is a HPC finite element library for simulating multiphysics evolution problems like the ones encounter in cardiac modeling (electrophysiology, structure and fluid mechanics, transport-diffusion, wave equations)

URL: https://gitlab.inria.fr/MoReFEM

Contacts: Philippe Moireau, Sébastien Gilles, Dominique Chapelle

Participants: Sébastien Gilles, Jérôme Diaz, Patrick Le Tallec, Philippe Moireau, Dominique Chapelle, Chloe Giraudet, Giulia Merlini

6.1.4 AKILLES

Name: Agnostic Kalman Inference parraLLEl Strategies.

Keywords: Kalman filter, Data assimilation

Functional Description: This library concerns sequential data assimilation algorithms and more particularly of the Uscented Kalman Filter type (Normal, Reduced, Transformed etc.). The principle is to communicate the sigma-points representing the model instances via a message exchange library (here ZeroMQ). Thus each particle calculates in parallel with the others, and the core of the algorithm in C ++ can cooperate with models written in any language.

Contact: Philippe Moireau

Participants: Laurent Steff, Sébastien Gilles, Philippe Moireau

6.1.5 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.

URL: `http://verdandi.gforge.inria.fr/`

Authors: Vivien Mallet, Dominique Chapelle, Gautier Bureau, Nicolas Claude, Philippe Moireau

Contacts: Vivien Mallet, Dominique Chapelle, Philippe Moireau

Participants: Dominique Chapelle, Gautier Bureau, Nicolas Claude, Philippe Moireau, Vivien Mallet

7 New results

7.1 Mathematical and Mechanical Modeling

7.1.1 Calcium and plasma membrane force-gated ion channels behind development

Participants Jean-Marc Allain.

During development, tissues are submitted to large variations of compression and tension forces. The roles of the cell wall, the cytoskeleton, the turgor pressure and the cell geometry during this process have received due attention. In contrast, apart from its role in the establishment of turgor pressure, the involvement of the plasma membrane as a transducer of mechanical forces during development has been scarcely studied. Force-gated (FG) or Mechanosensitive (MS) ion channels embedded in the bilayer represent 'per se' archetypal mechanosensors able to directly and instantaneously transduce membrane forces into electrical and calcium signals. We are working on how their fine-tuning, combined with their ability to detect micro-curvature and local membrane tension, allows FG channels to transduce mechanical cues into developmental signals.

7.1.2 Upscaling of elastic network models

Participants Patrick Le Tallec.

The purpose of this work [19] is to present a general upscaling strategy for deriving macroscopic constitutive laws for rubberlike materials from the knowledge of the network distribution and a mechanical description of the individual chains and of their free energy. The microscopic configuration is described by the position of the crosslinks and is not obtained by an affine assumption but by minimizing the corresponding free energy on stochastic large representative volume elements with adequate boundary conditions. This general framework is then approximated by using a microsphere (directional) description of the network. It is presented in a global setting and is extended in order to handle situations with tube-like constraints and stress-induced crystallization.

7.1.3 Upscaling of nonlinear multiscale structures

Participants Patrick Le Tallec.

Predicting the long term evolution of the fuel assemblies inside a nuclear reactor is crucial for operational and safety purposes. Under the combined actions of hydraulic forces and neutron fluxes, they are subjected to significant bows and severe contact relaxation at the interface between the fixation grids and the fuel tubes. One must take into account around 200 fuel assemblies, each of them being faced with irradiation induced and thermal creeping, contact and friction at the tens of thousands connectors inside each fuel assembly, and displacement depending hydraulic forces. All these effects depend on the position and history of the assembly inside the core. To be accurate, a complete finite element model of a single assembly would require close to one million degrees of freedom. Our objective is to upscale such a model keeping fewer than one hundred history dependent coefficients to describe its geometrical, physical and mechanical state during its evolution. Our strategy is based on the Non linear Transformation Field Analysis that we extend to structural problems where the representative volume element is a fuel assembly subjected to viscous creeping, contact and friction.

7.1.4 Hierarchical modeling of force generation in cardiac muscle

Participants François Kimmig *(correspondant)*, Matthieu Caruel.

Performing physiologically relevant simulations of the beating heart in clinical context requires to develop detailed models of the microscale force generation process. These models however may reveal difficult to implement in practice due to their high computational costs and complex calibration. In this work, we propose a hierarchy of three interconnected muscle contraction models – from the more refined to the more simplified – that are rigorously and systematically related with each other, offering a way to select, for a specific application, the model that yields a good trade-off between physiological fidelity, computational cost and calibration complexity. The three models families are compared to the same set of experimental data to systematically assess what physiological indicators can be reproduced or not and how these indicators constrain the model parameters. Finally, we discuss the applicability of these models for heart simulation. *The work has been published in [22].*

7.1.5 Coupling reduced-order blood flow and cardiac models through energy-consistent strategies: modeling and discretization

Participants Jessica Manganotti, Francois Kimmig, Sebastien Imperiale *(correspondant)*, Philippe Moireau.

In this work we provide a novel energy-consistent formulation for the classical 1D formulation of blood flow in an arterial segment. The resulting reformulation is shown to be suitable for the coupling with a lumped (0D) model of the heart that incorporates a reduced formulation of the actin-myosin interaction. The coupling being consistent with energy balances, we provide a complete heart-circulation model compatible with thermodynamics, hence numerically stable and physiologically informative. These latter two properties are verified by numerical experiments.

7.1.6 Asymptotic modelling of Skin-effects in coaxial cables

Participants Sebastien Imperiale *(correspondant)*, Patrick Joly *(Poems)*.

In this work we tackle the modeling of non-perfectly conducting thin coaxial cables. From the non-dimensionnalised 3D Maxwells equations, we derive, by asymptotic analysis with respect to the (small) transverse dimension of the cable, a simplified effective 1D model and an effective reconstruction procedure of the electric and magnetic fields. The derived effective model involves a fractional time derivative that accounts for the so-called skin effects in highly conducting regions. *The work has been published in [15].*

7.1.7 Mathematical modelling of Acoustic Radiation Force in transient shear wave elastography in the heart

Participants Sebastien Imperiale.

The aim of this work is to provide a mathematical model and analysis of the excitation and the resulting shear wave propagation in Acoustic Radiation Force (ARF)-based shear wave cardiac elastography. Our approach is based on asymptotic analysis; more precisely, it consists in considering a family of problems, parametrised by a small parameter inversely proportional to the excitation frequency of the probes, the viscosity and the velocity of pressure wave propagation. We derive a simplified model for the expression of the ARF by investigating the limit behaviour of the solution when the small parameter goes to zero. By formal asymptotic analysis - an asymptotic expansion of the solution is used - and energy analysis of the nonlinear elastodynamic problem, we show that the leading-order term of the expansion is solution of the underlying, incompressible, nonlinear cardiac mechanics. Subsequently, two corrector terms are derived. The first is a fast-oscillating pressure wave generated by the probes, solution of a Helmholtz equation at every time. The second corrector term consists in an elastic field with prescribed divergence, having a function of the first corrector as a source term. This field corresponds to the shear acoustic wave induced by the ARF. We also confirm that, in cardiac mechanics, the presence of viscosity in the model is essential to derive an expression of the shear wave propagation from the ARF, and that this phenomenon is related to the nonlinearity of the partial differential equation. *The work has been published in M2AN, [17].*

7.1.8 A poromechanical model of the lungs

Participants Cécile Patte, Martin Genet *(correspondant)*, Dominique Chapelle.

Lung vital function of providing oxygen to the body is dependent on the mechanical behavior of pulmonary tissue. During air inhalation, lung inflation is allowed by the pulmonary tissue, which is highly compliant and porous. The driving forces of breathing involve a complex environment, with diaphragm, pleura, rib cage and intercostal muscles. We developed a poromechanical model of the lungs during breathing, adapted from a general poromechanics theory by the formulation of lung-specific assumptions. Our model includes physiological boundary conditions and a hyperelastic potential reproducing the volume response of the pulmonary mixture to a change of pressure. A strategy is established to estimate the unloaded, reference configuration with a particular focus on ensuring a positive porosity, since this issue occurs for large deformation problems. Finally we emphasize through several illustrations the relevance of our model and its possible clinical applications. This paper will be finalized and submitted very soon.

7.2 Numerical Methods

7.2.1 Numerical Analysis of a Method for Solving 2D Linear Isotropic Elastodynamics with Free Boundary Condition using Potentials and Finite Elements

Participants Sebastien Imperiale *(correspondant)*, Patrick Joly *(Poems)*.

When solving 2D linear elastodynamic equations in homogeneous isotropic media, a Helmholtz decomposition of the displacement field decouples the equations into two scalar wave equations that only interact at the boundary. It is then natural to look for numerical schemes that independently solve the scalar equations and couple the solutions at the boundary. The case of rigid boundary conditions was already treated by the participants and – in a previous work – the case of free surface boundary conditions was proven to be unstable if a straightforward approach is used. Then an adequate functional framework as well as a time-domain mixed formulation to circumvent these issues was presented. In this work we propose a subsequent discretised formulation. We provide the complete stability analysis of the corresponding numerical scheme. Numerical results that illustrate the theory are also shown. *The work has been accepted in Mathematics of Computation, [13].*

7.2.2 Multipatch isogeometric analysis for complex structures

Participants Patrick Le Tallec *(correspondant)*, Nicolas Adam.

This work [12] introduces, analyzes and validates isogeometric mortar methods for the solution of thick shells problems which are set on a multipatch geometry. A particular attention has been devoted to the introduction of a proper formulation of the coupling conditions, with a particular interest on augmented Lagrangian formulations, on the choice and validation of mortar spaces, and on the derivation of adequate integration rules. The relevance of the proposed approach is assessed numerically on various significative examples.

7.2.3 Mathematical analysis of a penalization strategy for incompressible elastodynamics

Participants Sebastien Imperiale.

This work addresses the mathematical analysis – by means of asymptotic analysis – of a penalisation strategy for the full discretisation of elastic wave propagation problems in quasi- incompressible media that has been recently developed by the authors. We provide a convergence analysis of the solution to the continuous version of the penalised problem towards its formal limit when the penalisation parameter tends to infinity. Moreover, as a fundamental intermediate step we provide an asymptotic analysis of the convergence of solutions to quasi-incompressible problems towards solutions to purely incompressible problems when the incompressibility parameter tends to infinity. Finally, we further detail the regularity assumptions required to guarantee that the mentioned convergence holds. *The work has been published in Asymptotic Analysis, [16].*

7.3 Inverse Problems

7.3.1 Flow recovery from distal pressure in linearized hemodynamics: An optimal control approach

Participants Jessica Manganotti, Sebastien Imperiale *(correspondant)*, Philippe Moireau.

In this work we derive a reliable (i.e. stable and accurate) inverse problem strategy for the reconstruction of the blood flow in the ascending aorta – an important physiological marker – from measurements of pressure in a distal location of the arterial tree (i.e. the descending aorta). The method we develop is based on a 4D-Var approach applied to a reduced one-dimensional model of the aorta. More precisely, we minimize the sum of two contributions: first, the discrepancy between the measurements and a simulated state, second, the error with respect to a periodic state. Assuming that physical parameters are known, the proposed methodology is fully analyzed in a linearized framework, including stability with respect to noise and well-posedness.

7.3.2 Sequential data assimilation for mechanical systems with complex image data: application to tagged-MRI in cardiac mechanics

Participants Dominique Chapelle, Philippe Moireau *(correspondant)*.

Tagged Magnetic Resonance images (tagged-MRI) are generally considered to be the gold standard of medical imaging in cardiology. By imaging spatially-modulated magnetizations of the deforming tissue, indeed, this modality enables an assessment of intra-myocardial deformations over the heart cycle. The objective of the present work in collaboration with A. Imperiale (former member of the team and now CEA-List) is to incorporate the most valuable information contained in tagged-MRI in a data assimilation framework, in order to perform joint state-parameter estimation for a complete biomechanical model of the heart. This type of estimation is the second major step, after initial anatomical personalization, for obtaining a genuinely patient-specific model that integrates the individual characteristics of the patient, an essential prerequisite for benefitting from the model predictive capabilities. Here, we focus our attention on proposing adequate means of quantitatively comparing the cardiac model with various types of data that can be extracted from tagged-MRI after an initial image processing step, namely, 3D displacements fields, deforming tag planes or grids, or apparent 2D displacements. This quantitative comparison called discrepancy measure is then used to feed a sequential data assimilation procedure. In the state estimation stage of this procedure, we also propose a new algorithm based on the prediction correction paradigm, which provides increased flexibility and effectiveness in the solution process. The complete estimation chain is eventually assessed with synthetic data, produced by running a realistic model simulation representing an infarcted heart characterized by increased stiffness and reduced contractility in a given region of the myocardium. From this simulation we extract the 3D displacements, tag planes and grids, and apparent 2D displacements, and we assess the estimation with each corresponding discrepancy measure. We demonstrate that – via regional estimation of the above parameters – the data assimilation procedure allows to quantitatively estimate the biophysical parameters with good accuracy, thus simultaneously providing the location of the infarct and characterizing its seriousness. This shows great potential for combining a biomechanical heart model with tagged-MRI in order to extract valuable new indices in clinical diagnosis. *This work has been published in [21]* .

7.3.3 Signed-Distance Function Based Non-Rigid Registration of Image Sequences with Varying Image Intensity

Participants Radomir Chabiniok.

In this work we deal with non-rigid registration of the image series acquired by the Modified Look-Locker Inversion Recovery (MOLLI) magnetic resonance imaging sequence, which is used for a pixel-wise estimation of T_1 relaxation time. The spatial registration of the images within the series is necessary to compensate the patient's imperfect breath-holding. The evolution of intensities and a large variation of the image contrast within the MOLLI image series, together with the myocardium of the left ventricle (the object of interest) typically not being the most distinct object in the scene, makes the registration challenging. We propose a method for locally adjusted optical flow-based registration of multimodal images, which uses the segmentation of the object of interest and its representation by the signed-distance function. This work describes all steps of the proposed OF^{dist} method and their implementation. The OF^{dist} method is then compared to the performance of a standard mutual information maximization-based registration method, applied either to the original image (MIM) or to the signed-distance function (MIM^{dist}). Several experiments with synthetic and real MOLLI images are carried out. On synthetic images with a single object, MIM performed the best, while OF^{dist} and MIM^{dist} provided better results on synthetic images with more than one object and on real images. When applied to the signed-distance function of two objects of interest, MIM^{dist} provided a larger registration error (but more homogeneously distributed) compared to OF^{dist}. For the real MOLLI image sequence with the left ventricle pre-segmented using a level-set method, the proposed OF^{dist} registration performed the best, as demonstrated visually and by measuring the increase of mutual information in the object of interest and its neighborhood. *This collaborative work (Czech Technical University, Institute of Clinical and Experimental Medicine in Prague and Inria) was published in Discrete and Continuous Dynamical Systems [28]. The work represents a part of the objectives of and is supported by the Inria-UTSW Associated Team TOFMOD.*

7.3.4 A flexible framework for sequential estimation of model parameters in computational hemodynamics

Participants Philippe Moireau.

A major challenge in constructing three dimensional patient specific hemodynamic models is the calibration of model parameters to match patient data in flow, pressure, wall motion, etc. acquired in the clinic. Current workflows are manual and time-consuming. This work resulting from a long collaboration between Philippe Moireau and Alberto Figueroa's group (University of Michigan) presents a flexible computational framework for model parameter estimation in cardiovascular flows that relies on the following fundamental contributions: (i) A Reduced-Order Unscented Kalman Filter (ROUKF) model for data assimilation for wall material and simple lumped parameter network (LPN) boundary condition model parameters; (ii) A constrained least squares augmentation (ROUKF-CLS) for more complex LPNs; (iii) A "Netlist" implementation, supporting easy filtering of parameters in such complex LPNs. The ROUKF algorithm is demonstrated using non-invasive patient-specific data on anatomy, flow and pressure from a healthy volunteer. The ROUKF-CLS algorithm is demonstrated using synthetic data on a coronary LPN. The methods described in this paper have been implemented as part of the CRIMSON hemodynamics software package.

7.3.5 Estimation for dynamical systems using a population-based Kalman filter

Participants Annabelle Collin *(Monc)*, Melanie Prague *(Sistm)*, Philippe Moireau *(correspondant)*.

Many methods exist to identify parameters of dynamical systems. Unfortunately, in addition to the classical measurement noise and under-sampling drawbacks, mean and variance priors of the estimated parameters can be very vague. These difficulties can lead the estimation procedure to underfitting. In clinical studies, a circumvention consists in using the fact that multiple independent patients are observed as proposed by nonlinear mixed-effect models. However, these very effective approaches can turn to be time-consuming or even intractable when the model complexity increases. Here, we propose an alternative strategy of controlled complexity. We first formulate a population least square estimator and its associated Kalman-based filter, hence defining a robust large population sequential estimator. Then, to reduce and control the computational complexity, we propose a reduced-order version of this population Kalman filter based on a clustering technique applied to the observations. Using simulated pharmacokinetics data or the theophylline pharmacokinetics data and more recent COVID French data, we compare the proposed approach with literature methods. We show that using the population filter improves the estimation performance compared to the classical and fast patient-by-patient Kalman filter, and leads to estimation results comparable to state-of-the-art population-based approaches. Then, the reduced-order version allows to drastically reduce the computational time for equivalent estimation and prediction.

7.3.6 Combining data assimilation and machine learning to build data-driven models for unknown long time dynamics – Applications in cardiovascular modeling

Participants Francesco Regazzoni, Dominique Chapelle, Philippe Moireau *(correspondant)*.

We propose a method to discover differential equations describing the long-term dynamics of phenomena featuring a multiscale behavior in time, starting from measurements taken at the fast-scale. Our methodology is based on a synergetic combination of Data Assimilation (DA), used to estimate the parameters associated with the known fast-scale dynamics, and Machine Learning (ML), used to infer the laws underlying the slow-scale dynamics. Specifically, by exploiting the scale sep- aration between the fast and the slow dynamics, we propose a decoupling of time scales that allows to drastically lower the computational burden. Then, we propose a ML algorithm that learns a parametric mathematical model from a collection of time series coming from the phenomenon to be modeled. Moreover, we study the interpretability of the data-driven models obtained within the black-box learning framework proposed in this paper. In particular, we show that every model can be rewritten in infinitely many different equivalent ways, thus making intrinsically ill- posed the problem of learning a parametric differential equation starting from time series. Hence, we propose a strategy that allows to select a unique representative model in each equivalence class, thus enhancing the interpretability of the results. We demonstrate the effectiveness and noise-robustness of the proposed methods through several test cases, in which we reconstruct several differential models starting from time series generated through the models themselves. Finally, we show the results obtained for a test case in the cardiovascular modeling context, which sheds light on a promising field of application of the proposed methods. This manuscript was submitted to IJNMBE.

7.4 Experimental Assessments

7.4.1 Ultrasounds could be considered as a future tool for probing growing bone properties

Participants Jean-Marc Allain.

Juvenile bone growth is well described (physiologically and anatomically) but there is still a lack of knowledge on intrinsic material properties. Our collaborators and us have already published, on different samples, several studies on the assessment of intrinsic material properties of juvenile bone compared to material properties of adult bone. The purpose of this study was finally to combine different experimental modalities available (ultrasonic measurement, micro-Computed Tomography analysis, mechanical compression tests and biochemical measurements) applied on small cubic bone samples in order to gain insight into the multiparametric evaluation of bone quality. Differences were found between juvenile and adult groups in terms of architectural parameters (Porosity Separation), Tissue Mineral Density (TMD), diagonal stiffness coefficients (C33, C44, c55, c66) and ratio between immature and mature cross-links (CX). Diagonal stiffness coefficients are more representative of the microstructural and biochemical parameters of child bone than of adult bone. We also found that the compression modulus E was highly correlated with several microstructure parameters and CX in children group while it was not at all correlated in the adult group. Similar results were found for the CX which was linked to several microstructure parameters (TMD and E) only in the juvenile group. To our knowledge, this is the first time that, on the same sample, ultrasonic measurements have been combined with the assessment of mechanical and biochemical properties. It appears that ultrasonic measurements can provide relevant indicators of child bone quality (microstructural and biochemical parameters) which is promising for clinical applications, since B-mode ultrasound is the preferred first-line modality over other more constraining imaging modalities (radiation, parent–child accessibility and access to the patient's bed) for pediatric patients.

7.4.2 Microstructural deformation observed by Mueller polarimetry during traction assay on myocardium samples

Participants Nicole Tueni, Martin Genet, Jean-Marc Allain *(correspondant)*.

Despite recent advances, the myocardial microstructure remains imperfectly understood. In particular, bundles of cardiomyocytes have been observed but their three-dimensional organisation remains debated and the associated mechanical consequences unknown. One of the major challenges remains to perform multiscale observations of the mechanical response of the heart wall. For this purpose, in this study, a full-field Mueller polarimetric imager (MPI) was combined, for the first time, with an in-situ traction device. The full-field MPI enables to obtain a macroscopic image of the explored tissue, while providing detailed information about its structure at the microscopic scale. Specifically it exploits the polarization of the light to determine various biophysical quantities related to the tissue scattering or anisotropy properties. Combined with a mechanical traction device, the full-field MPI allows to measure the evolution of such biophysical quantities during tissue stretch. We observe separation lines in the tissue, which are associated with a fast variation of the fiber orientation, and have the size of cardiomyocyte bundles. Thus, we hypothesize that these lines are the perimysium, the collagen layer surrounding these bundles. During mechanical traction, we observe two mechanisms simultaneously. On the one hand, the azimuth shows an affine behavior, meaning the orientation changes according to the tissue deformation, and showing coherence in the tissue. On the other hand, the separation lines appear to be resistant in shear and compression but weak against traction, with gaps forming in the tissue. *The work has been published in [29].*

7.4.3 Multi-scale Patient-Specific Modeling of the Human Cornea

Participants Chloé Giraudet, Jean-Marc Allain *(correspondant)*, Patrick Le Tallec.

In this study, we are developping a patient-specific model, implemented in the homemade finite element code (MoReFEM), in order to help better understand the consequences of laser surgery in the cornea. The patient-specific geometry of the cornea is extracted from clinical Optical Coherence Tomography images to construct the mesh. Collagen fiber images (X-rays or Second Harmonic Generation microscopy) are used to extract micro-structural data, which are injected in a microsphere based mechanical model to consider the effect of fiber orientation on the mechanical response of the cornea. The model parameters are then identified through experimental inflation tests. Finally, the optical power is calculated to determine the cornea ability to converge light rays in the eye, and thus ensure its proper functioning. The final objective of this work is to mimic in the finite element code changes in the cornea due to laser surgery, both from a macroscopic (via geometry) and microscopic (via the structure of collagen fibers) point of view. Thus, the mechanical behaviour and refractive power of the cornea after surgery can be anticipated.

7.5 Clinical Applications

7.5.1 Estimation of regional pulmonary compliance in IPF based on personalized lung poromechanical modeling

Participants Cécile Patte, Dominique Chapelle, Martin Genet *(correspondant)*.

Pulmonary function is tightly linked to the lung mechanical behavior, especially large deformation during breathing. Interstitial Lung Diseases, such as Idiopathic Pulmonary Fibrosis (IPF), have an impact on the pulmonary mechanics and consequently alter lung function. However, IPF remains poorly understood, poorly diagnosed and poorly treated. Currently, the mechanical impact of such diseases is assessed by pressure-volume curves, giving only global information. We developed a poromechanical model of the lung that can be personalized to a patient based on routine clinical data. The personalization pipeline uses clinical data, mainly CT-images at two time steps and involves the formulation of an inverse problem to estimate the material behavior. Regional effective compliances are estimated for one control subject and three patients, allowing to quantify the IPF-induced tissue stiffening. The rescaled compliances and compliance ratios, where the first order impact of the porosity has been removed, are also estimated. This personalized model could be used in the clinic as an objective and quantitative tool for IPF diagnosis. An article corresponding to this work has been just submitted to the Annals of Biomedical Engineering.

7.5.2 Three-dimensional biventricular strains in pulmonary arterial hypertension patients using hyperelastic warping

Participants Martin Genet.

Background and Objective. Evaluation of biventricular function is an essential component of clinical management in pulmonary arterial hypertension (PAH). This study aims to examine the utility of biventricular strains derived from a model-to-image registration technique in PAH patients in comparison to age- and gender-matched normal controls. Methods. A three-dimensional (3D) model was reconstructed from cine short- and long-axis cardiac magnetic resonance (CMR) images and subsequently partitioned into right ventricle (RV), left ventricle (LV) and septum. The hyperelastic warping method was used to register the meshed biventricular finite element model throughout the cardiac cycle and obtain the corresponding biventricular circumferential, longitudinal and radial strains. Results. Intra- and inter-observer reproducibility of biventricular strains was excellent with all intra-class correlation coefficients > 0.84. 3D biventricular longitudinal, circumferential and radial strains for RV, LV and septum were significantly decreased in PAH patients compared with controls. Receiver operating characteristic (ROC) analysis showed that the 3D biventricular strains were better early markers (Area under the ROC curve = 0.96 for RV longitudinal strain) of ventricular dysfunction than conventional parameters such as two-dimensional strains and ejection fraction. Conclusions. Our highly reproducible methodology holds potential for extending CMR imaging to characterize 3D biventricular strains, eventually leading to deeper understanding of biventricular mechanics in PAH. *The work has been published, [30].*

7.5.3 AnaestAssist project

Participants François Kimmig *(correspondant)*, Dominique Chapelle, Philippe Moireau.

Unstable hemodynamics during general anaesthesia increases the risk of cardiac, renal and brain disfunctions during the postoperative period, thus leading to a higher level of morbidity and mortality. To improve the patient's condition, learned societies therefore recommend monitoring the hemodynamics of the patient and having treatment strategies with quantitative objectives based on this monitoring. Currently, medical doctors have at their disposal some physiological signals (ECG, blood pressure) displayed on their monitor, and must rely on established practices and their experience to act in case of a dangerous drift.

The AnaestAssist project proposes to develop an augmented monitoring tool for anaesthesia. The proposed technology will introduce into the monitoring loop a predictive biophysical model, simulated in real time, and fed by the routinely measured physiological signals. The model will be personalised for the patient creating a digital avatar of the patient's cardiovascular system. With this digital avatar, physiological information that can cannot be measured or that can only be obtained with highly invasive methods will be computed in real time and treatment recommendations will be made. Our system will thus provide a much more complete vision of the patient's cardiovascular state and allow more informed and faster decisions. Eventually, the effects of drugs will be included in the model, which will enable (through predictive modelling) adapted action recommendations, or even a real-time automatic drug administration loop. Our technology is expected to allow the medical staff to deliver a better treatment to the patient, to improve the patient condition through a reduction of the risks related to general anaesthesia and a wiser exposition to drugs, and to reduce the costs for the healthcare system due to a lower rate of complications and shorter stays of the patients at the hospital.

The AnaestAssist project is intended to lead to a startup creation in the coming years.

7.5.4 Dobutamine stress testing in patients with Fontan circulation augmented by biomechanical modeling

Participants Philippe Moireau, Dominique Chapelle, Radomir Chabiniok *(correspondant)*.

Understanding (patho)physiological phenomena and mechanisms of failure in patients with Fontan circulation — a surgically established circulation for patients born with a functionally single ventricle — remains challenging due to the complex hemodynamics and high inter-patient variations in anatomy and function. In this work, we present a biomechanical model of the heart and circulation to augment the diagnostic evaluation of Fontan patients with early-stage heart failure. The proposed framework employs a reduced-order model of heart coupled with a simplified circulation including venous return, creating a closed-loop system. We deploy this framework to augment the information from data obtained during combined cardiac catheterization and magnetic resonance exams (XMR), performed at rest and during dobutamine stress in 9 children with Fontan circulation and 2 biventricular controls. We demonstrate that our modeling framework enables patient-specific investigation of myocardial stiffness, contractility at rest, contractile reserve during stress and changes in vascular resistance. Hereby, the model allows to identify key factors underlying the pathophysiological response to stress in these patients. In addition, the rapid personalization of the model to patient data and fast simulation of cardiac cycles makes our framework directly applicable in a clinical workflow. We conclude that the proposed modeling framework is a valuable addition to the current clinical diagnostic XMR exam that helps to explain patient-specific stress hemodynamics and can identify potential mechanisms of failure in patients with Fontan circulation.

The work was published in the PLOS One Journal [27]. The work represents a part of the objectives of and is supported by the Inria-UTSW Associated Team TOFMOD.

7.5.5 Investigation of phase contrast magnetic resonance imaging underestimation of turbulent flow through the aortic valve phantom: Experimental and computational study by using lattice Boltzmann method

Participants Radomir Chabiniok.

Objective The accuracy of phase-contrast magnetic resonance imaging (PC-MRI) measurement is investigated using a computational fluid dynamics (CFD) model with the objective to determine the magnitude of the flow underestimation due to turbulence behind a narrowed valve in a phantom experiment.
Materials and Methods An acrylic stationary flow phantom is used with three insertable plates mimicking aortic valvular stenoses of varying degrees. Positive and negative horizontal fluxes are measured at equidistant slices using standard PC-MRI sequences by 1.5T and 3T systems. The CFD model is based on the 3D lattice Boltzmann method (LBM). The experimental and simulated data are compared using the Bland-Altman-derived limits of agreement. Based on the LBM results, the turbulence is quantified and confronted with the level of flow underestimation.
Results Matching results of PC-MRI flow were obtained for valves up to moderate stenosis on both field strengths. The flow magnitude through a severely stenotic valve was underestimated due to signal void in the regions of turbulent flow behind the valve, consistently with the level of quantified turbulence intensity.
Discussion Flow measured by PC-MRI is affected by noise and turbulence. LBM can simulate turbulent flow efficiently and accurately, it has therefore the potential to improve clinical interpretation of PC-MRI. *This collaborative work (Czech Technical University, Institute of Clinical and Experimental Medicine in Prague and Inria) was published in Magnetic resonance materials in physics, biology and medicine (MAGMA) [20]. The work represents a part of objectives and is supported by the Inria-UTSW Associated Team TOFMOD.*

7.5.6 Estimation of left ventricular pressure-volume loop using hemodynamic monitoring augmented by a patient-specific biomechanical model. An observational study

Participants Arthur Le Gall, Fabrice Valée, Dominique Chapelle, Radomir Chabiniok *(correspondant)*.

Background During general anaesthesia, direct analysis of the arterial pressure or aortic flow waveforms may be confusing in complex haemodynamic situations. Patient-specific biomechanical modelling allows to simulate Pressure-Volume (PV) loops and obtain functional indicators of the cardiovascular (CV) system, such as ventricular-arterial coupling (Vva), cardiac efficiency (CE) or myocardial contractility. It therefore augments the information obtained by monitoring and could help in medical decision-making.
Methods Patients undergoing GA for neuroradiological procedure were included in this prospective observational study. A biomechanical model of heart and vasculature specific to each patient was built using transthoracic echocardiography and aortic pressure and flow signals. If intraoperative hypotension (IOH) appeared, diluted noradrenaline (NOR) was administered and the model readjusted.
Results The model was calibrated for 29 (64%) normotensive and for 16 (36%) hypotensive patients before and after NOR administration. The simulated mean aortic pressure (MAP) and stroke volume (SV) were equivalent to the measurements (Percentage Error: 6% for MAP and 18% for SV) in all 45 datasets at baseline. After NOR administration, the percentage of concordance with 10% exclusion zone between measurement and simulation was > 95% for both MAP and SV. The modelling results showed a decreased Vva (0.64±0.37 vs 0.88±0.43; p=0.039), and an increased CE (0.8±0.1 vs 0.73±0.11; p=0.042) in hypotensive as compared with normotensive patients. After NOR administration, Vva increased by 92±101%, CE decreased by 13±11% (p<0.001 for both) and contractility increased by 14±11% (p=0.002).
Conclusions The numerical models built for individual patients were applied to estimate patients' PV loops and functional indicators of CV system during haemodynamic alterations and during restoration by NOR. This study demonstrates the feasibility of patient-specific cardiovascular modelling using clinical data readily available during GA and paves the way for model-augmented haemodynamic monitoring at operating theatres and intensive care units. *The work was published in the PLOS One journal [23]. The work represents a part of the objectives of and is supported by the Inria-UTSW Associated Team TOFMOD.*

7.5.7 Patient Data and Biomechanical Modeling Used to Assess the Response to Pulmonary Valve Replacement

Participants Maria Gusseva, Dominique Chapelle, Radomir Chabiniok *(correspondant).*

Objectives Clinical data obtained from cardiovascular magnetic resonance imaging (CMR) and catheterization in a cohort of tetralogy of Fallot patients after complete repair (rTOF) were combined with a biomechanical model to characterize the right ventricle response to pulmonary valve replacement (PVR), and to assess comparative influences of residual right ventricular outflow tract obstruction (RVOTO) and pulmonary regurgitation on ventricular health.
Methods 20 rTOF patients who underwent percutaneous PVR and CMR were included in this study. Biomechanical models specific to individual patients and physiology (pre- and post-PVR) were created and utilized to estimate the RV myocardial contractility. Secondly, the models were validated by post-PVR changes of RV end-diastolic volume (EDV) and effective flow in pulmonary artery (Q_{eff}).
Results RV contractility pre-PVR (65 ± 17 kPa, mean ± SD) was increased in rTOF patients in comparison to normal RV (39-45 kPa) ($p<0.05$). The contractility decreased significantly in all patients post-PVR ($p<0.05$). Patients with predominantly RVOTO demonstrated greater reduction in contractility (median decrease 35%) post PVR than those with predominant pulmonary regurgitation (median decrease 12%). The model simulated changes of EDV and Q_{eff} post-PVR in line with published data.
Conclusions This work combines clinical data and biomechanical modeling to give an insight into RV health. Individualized modeling allows us to predict the RV response to PVR. Initial data suggest that residual RVOTO imposes greater ventricular work than isolated pulmonary regurgitation.

8 Bilateral contracts and grants with industry

8.1 Bilateral contracts with industry

- Technical contract with CEA-LIST on the modelling of rough interfaces in the context of wave scattering (10k€).

9 Partnerships and cooperations

9.1 International initiatives

9.1.1 Inria associate team not involved in an IIL

ToFMod associated team

Title: *Predictive modeling for tetralogy of Fallot patients*

Duration: 2018 - *2020*

Coordinator: Radomir Chabiniok

Partners:
- *Pediatric–Radiology*, UT Southwestern Medical Center, Dallas,Texas (United States)

Inria contact: Radomir Chabiniok

Summary: This collaboration aims at addressing a crucial issue in cardiology of congenital heart diseases, namely, the optimal timing of pulmonary valve replacement (PVR) in patients with surgically repaired tetralogy of Fallot (ToF) prone to chronic pulmonary regurgitation or right ventricular outflow tract stenosis. Our strategy consists in exploiting the predictive power of biomechanical modeling to shed light in the decision process. We will start by a detailed proof-of-concept study, based on datasets that will be acquired in patients indicated for percutaneous PVR, prior to the procedure, and in the follow-up at 3 and 12 months post-PVR. These datasets will be first used to calibrate the Inria MΞDISIM patient-specific heart model simulating a cardiac cycle (at each follow-up time point) to access the myocardial properties – namely, the active contractility and passive stiffness. The instantaneous tissue properties will be statistically analyzed and compared with the level of reverse remodeling – i.e. the positive outcome of PVR. Secondly, the data at each time point will be used to calibrate and further develop the models of long-term tissue remodeling created by the MΞDISIM researchers. It is only by combining such invaluable longitudinal data with biomechanical modeling expertise that progress can be achieved in the above objectives, indeed.

9.2 National initiatives

9.2.1 ANR

- **ANR JCJC LungManyScale**, M. Genet, P. Moireau, D. Chapelle, M. Manoochehrtayebi (383 k€) – The lungs' architecture and function are well characterized; however, many fundamental questions remain (e.g., there is no quantitative link between tissue- and organ-level material responses), which represent real health challenges (e.g., Idiopathic Pulmonary Fibrosis is a poorly understood disease, for which a mechanical vicious cycle has been hypothesized, but not demonstrated). The general objective of this project is twofold: (i) scientifically, to better understand pulmonary mechanics, from the alveola to the organ in health and disease; (ii) clinically, to improve diagnosis and prognosis of patients through personalized computational modeling. More precisely, This project aims at developing a many-scale model of the pulmonary biomechanics, linked by computational nonlinear homogenization. The model will integrate the experimental and clinical data produced by partners, through an estimation pipeline that will represent augmented diagnosis and prognosis tools for the clinicians.

- **ANR ODISSE**, P. Moireau, S. Imperiale, T. Delaunay (154 k€) – Motivated by some recent developments from two different fields of research, that is, observer design for finite-dimensional systems and inverse problems analysis for some PDE systems, the ODISSE project aims at developing rigorous methodological tools for the design of estimating algorithms for infinite-dimensional systems arising from hyperbolic PDE systems.

- **ANR SIMR**, P. Moireau, D. Chapelle, J. Diaz, M. Genet (97 k€) SIMR is a multi-disciplinary project seeking a better understanding of the biophysical mechanisms involved in mitral valve (MV) regurgitation diseases, to improve decision-making in patients by helping to determine the optimal timing for surgery. This project aims at facing this major issue with the following main two objectives: (1) Evaluate the biophysical consequences of MV repair and (2) Design numerical tools, for cardiac hemodynamics, fluid-structure interaction and myocardium biomechanics to provide an in silico counterpart of the in vivo data obtained by tension measurement and imaging.

- **ANR AAP RA-COVID-19 SILICOVILUNG**, M. Genet, (55k€) It is currently impossible to predict the evolution of severe COVID19-induced lung pathologies, in particular towards pulmonary fibrosis. A patient-specific model of lungs at 2-3 months after the acute stage will be used to seek mechanical indicators that may be valuable to predict the lung state after one year.

9.2.2 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), J.M. Allain (50k€ funded by the LABEX Lasips) – This project, which involves the LPICM laboratory (Ecole Polytechnique, CNRS), 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.

9.3 Regional initiatives

9.3.1 Appel SESAME IDF

The team is involved in the SACHEMS project: Structural Health Monitoring (SHM) consists of integrating sensors into a high-stakes structure (aircraft, nuclear power plant, wind turbine, etc.) to monitor its state of health in real time and thus anticipate maintenance operations. The project entitled "SACHEMS" ("SAClay High-end Equipment for the Monitoring of Structures") as it was accepted in 2019 under the SESAME call of the Ile-de-France region aims to create a federative platform for research and innovation allowing the development of complete SHM systems, and to deploy them on the application cases provided by industrial end-users. This platform brings together both academic teams and industrial end-users. It offers to the public laboratories involved the possibility of carrying out research in close collaboration with industrial partners.

9.3.2 Regional LABEX

M. Barré has received a PhD fellowship from Labex Mathématiques Hadamard (LMH), Saclay, Ile-de-France.

10 Dissemination

10.1 Promoting scientific activities

10.1.1 Scientific events: organisation

General chair, scientific chair

- D. Chapelle: co-chair of the VPH2020 organizing committee (24–28 August, online, 600+ participants)
- R. Chabiniok & T. Hussain: organizer of a 1-day TOFMOD workshop as a satellite event of Virtual Physiological Human Conference VPH2020 (14 international speakers and >50 participants)

Member of the organizing committees

- P. Moireau, organizing committee of VPH2020 Conference (24–28 August, online, 600+ participants)
- R. Chabiniok, co-organizer of of 1-week international doctoral school on “Modelling of biomaterials” (in charge of cardiovascular program)

10.1.2 Journal

Member of the editorial boards

- D. Chapelle, member of the editorial board of journal *Computer and Structures*
- D. Chapelle, member of the editorial board of journal *ESAIM: M2AN*
- P. Le Tallec, member of the editorial board of journal *Computer Methods in Applied Mechanics and Engineering*
- P. Le Tallec, member of the editorial board of journal *Computer and Structures*

Reviewer - reviewing activities

- R. Chabiniok, reviewer for “Cardiovascular Engineering and Technology”
- J.M. Allain, reviewer for “Acta Biomateriala”, “Journal of the Mechanical Behavior of Biomedical Materials” (twice), “Proceedings of the Institution of Mechanical Engineers, Part H: Journal of Engineering in Medicine”, and “Scientific Reports”
- M. Genet, reviewer for the “Journal of the Mechanical Behavior of Biomedical Materials”
- S. Imperiale, reviewer for “SIAM SISC”, “Mathematics of computations”, “International Journal of Numerical Analysis and Modeling”, “Journal of computational physics”, “Mathematics in Engineering”, “SIAM JSC”
- P. Le Tallec, reviewer for “Methods in Applied Mech and Engineering” and “International Journal of Numerical Methods in Engineering”.
- P. Moireau, reviewer for “Computers & Mathematics with Applications”, “Vietnam Journal of Mathematics”, “Biomechanics and Modeling in Mechanobiology”, “International Journal for Numerical Methods in Biomedical Engineering”

10.1.3 Invited talks

- J.M. Allain, invited presentation at “Eladyn-bio” (11/12/2020, online)
- R. Chabiniok, invited talk (February, 10) at International doctoral school on “Modelling of biomaterials”, Kacov, Czech Republic
- D. Chapelle, invited lecture at “1ère Rencontre entre Experts TIC & Santé [Cap Digital x Medicen x Systematic]” (27/02/2020, Délégation Générale du Québéc, Paris)
- D. Chapelle, invited lecture at “Conférence NAFEMS France 2020” (26/11/2020, online)
- D. Chapelle, invited lecturer for CISM Webinar“Computational Biomechanics - Advanced Models and Methods” (02/12/2020, online)
- M. Gusseva, invited talk at TOFMOD workshop at VPH2020 Paris (25/08/2020 online)
- P. Moireau, invited seminar at Politecnico di Milano (17/02/2020, Milano, Italy)
- P. Moireau, invited lecture at “Workshop on Mathematical issues of complex systems in biology and medecine” (26/02/2020, Luminy, France)
- P. Moireau, invited lecture at “Teratec forum” (13/10/2020, online)
- P. Moireau with A. Collin and M. Prague, invited presentation at Webinar Infectious Disease Outbreaks (27/01/2021,online)

10.1.4 Leadership within the scientific community

- J. M. Allain, Member of the Société de Biomécanique, and Member of the European Society of Biomechanics.
- J.M. Allain, Scientific Advisory Board, chair BioMecAM
- D. Chapelle, Member of the board of directors of the VPH Institute
- D. Chapelle, Member of the Scientific Advisory Board of ENS Paris-Saclay
- D. Chapelle, Member of the steering committees of the EUR BERTIP PhD track, and of the Biomedical Engineering Seed Grants Program (Institut Polytechnique de Paris)

- M. Genet, Member of the Francophone Biomechanics Society
- P. Moireau, Member of the steering committee of Department of Mathematics of Institut Polytechnique de Paris
- P. Moireau, Member of the steering committee of Department of Mathematics of Institut Polytechnique de Paris
- P. Moireau, Member of the “Commission scientifique et technique” of Corps des Mines

10.1.5 Scientific expertise

- R. Chabiniok, Reviewer for Domain Applied and Engineering Sciences (NWO Domain TTW), Netherlands Organisation for Scientific Research
- Chabiniok, Reviewer for Swiss National Science Foundation
- D. Chapelle, Member of the Inria DR2 selection committee, and of the Inria-Saclay CRCN selection committee
- P. Moireau, Member of the ANR Comité 46: “Modèle numérique, simulations, applications”
- P. Moireau, Member of the LJLL UPMC Sorbonne Université, MCF (assistant professor) admission jury

10.1.6 Research administration

- J.M. Allain, Responsible of the axis “mécanique et matériaux pour le bio” at the Fédération Francilienne de Mécanique.
- R. Chabiniok, PI of transatlantic associated team TOFMOD between Inria and UT Southwestern Medical Center Dallas, coordinating actions of main TOFMOD actors (Inria, UTSW) and associated members (King’s College London, Institute for Clinical and Experimental Medicine in Prague, Czech Technical University in Prague and others)
- D. Chapelle, Head of Science of Inria Saclay-Ile-de-France, and member of the Inria Evaluation Committee
- D. Chapelle, Head of the joint APHP-Inria laboratory “Daniel Bernoulli” (since Nov. 2020)
- M. Genet, Responsible of the teaching assistants of Ecole Polytechnique’s mechanic department
- S. Imperiale, Vice-president of the CDT-Inria Saclay (Commission d’aide au Développement Technologique)
- P. Le Tallec, Dean of the bachelor program at Ecole Polytechnique
- P. Moireau, Member of the LMS board of direction

10.2 Teaching - Supervision - Juries

10.2.1 Teaching

- Bachelor: J. Manganotti, “Bachelor Intro”, 4h, (L1), École Polytechnique, France
- Bachelor: J. Manganotti, “Mathematical methods for Physics I”, 30h, (L1), École Polytechnique, France
- Bachelor: J. Manganotti, “Classical Mechanics”, 15h, (L2), École Polytechnique, France
- Bachelor: J.-M. Allain, Academic advisor for mechanics at the Bachelor program Ecole Polytechnique, France

- Bachelor: J.-M. Allain, Supervision of the introductory projects in physics, 15h, B1, Ecole Polytechnique, France
- Bachelor: J.-M. Allain, “Classical mechanics”, 24h, B2, Ecole Polytechnique, France
- Bachelor: J.-M. Allain, “Advanced labwork”, 12h, B3, Ecole Polytechnique, France
- Bachelor: S. Imperiale, “MA102 – Analyse pour les EDP”, 24h, B3, ENSTA ParisTech, France
- Bachelor: P. Le Tallec , “Mécanique des Milieux Continus 2. ”, 24h, L3, École Polytechnique, France
- Bachelor: P. Le Tallec , “Mechanics of Continuous Media and Structure. ”, 24h, Y4, Shanghai Jiao Tong Elite Institute of Technology, China
- Master: J.-M. Allain, “Statistical mechanics: application to cell motility”, 20h, M2, Ecole Polytechnique, France
- Master: D. Chapelle & P. Moireau, “Biomechanical Modeling of Active Tissues”, 40h, M2, Université Paris-Saclay, France
- Master: M. Genet, “Numerical methods in (solid) mechanics”, 54h, (M1), École Polytechnique, France
- Master: M. Genet & P. Moireau, “Model-Data interaction in mechanics”, 40h, (M1), École Polytechnique, France
- Master: S. Imperiale, “Techniques de discr‘’etisation avancées pour les problèmes d’évolutions”, 18h, M2, Université Paris-Saclay, France
- Master: P. Le Tallec, “Solid and Continuum Mechanics”, 12h, M1, Master of Nuclear Energy, Université Paris-Saclay, France
- Master: P. Moireau, “AMS305 – Complétion de données et identification dans les problèmes gouvernés par des équations aux dérivées partielles”, 16h, M2, Université Paris-Saclay, France

10.2.2 Supervision

- L2: M. Melennec, “Validation of a biophysical cardiovascular system model calibration algorithm”, July-August 2020, supervisors: F. Kimmig, École polytechnique.
- Master 1: F. Álvarez-Barrientos (Pontificia Universidad Católica de Chile), “Pulmonary micromechanics”, 12/2019-02/2020, supervisor: M. Genet
- Master 2: T. Delaunay, April-Sept. 2020, “Stratégies d’assimilation de données par observateurs pour les équations d’ondes”, supervisors: S. Imperiale and P. Moireau, INSA-Rouen
- Master 2: M. Barré, “Analysis and approximation of a linearized poromechanics model”, April-Sept. 2020, supervisors: C. Grandmont (Inria Commedia) and P. Moireau, Ensta
- Master 2: M. Manoochehrtayebi, “Parameter identification for lung modelling”, April-Sept. 2020, supervisors: M. Genet,m Ecole Polytechnique
- PhD in progress: J. Manganotti, “Energy preserving cardiac circulation models”, started October 2019, supervisors: S. Imperiale and P. Moireau,
- PhD in progress: N. Tueni, “Multiscale properties of the passive cardiac muscle”, started January 2018, supervisors: J.M. Allain and M. Genet
- PhD in progress: C. Giraudet, “Cornea biomechanics”, started October 2018; supervisors: J.M. Allain and P. Le Tallec

- PhD in progress: E. Berberoglu (ETHZ, Switzerland), “Image Guided Computational Cardiac Mechanics”, started February 2017, supervisors: M. Genet and S. Kozerke (ETHZ, Switzerland)
- PhD in progress: M. Gusseva, “Cardiac Biomechanical Modeling for Chronic Ventricular Loading”, started in December 2017, supervisors: R. Chabiniok, D. Chapelle, T. Hussain
- PhD in progress: A. Le Gall, “Cardiac modelling for monitoring purposes during general anaesthesia and at Intensive Care Unit”, supervisors: R. Chabiniok, D. Chapelle, E. Gayat, started in November 2016
- PhD in progress: C. Patte, “Lung multiscale poromechanical modeling: from breathing to pulmonary fibrosis-induced chronic remodeling”, supervisors: M. Genet and D. Chapelle, started November 2017, defended in December 2020
- PhD in progress: J. Joachim “Développement d’une nouvelle méthode d’administration automatisée des médicaments utilisés chez les patients sous anesthésie générale basée sur un monitorage totalement non-invasif”, started September 2018, supervisor: E. Gayat
- PhD in progress: T. Delaunay, “Adaptative observers for propagative systems and associated discretization: formulation and analysis”, started October 2020, supervisors: P. Moireau and S. Imperiale
- PhD in progress: A. Dalmora, “Modélisation et estimation par assimilation de données de la précontrainte dans le contrôle non-destructif”, started September 2020, supervisors: P. Moireau, S. Imperiale and A. Imperiale (CEA List),
- PhD : Nicolas Adam, “Méthodes isogéométrique multipatch pour des coques épaisses non linéaires avec contact”, started September 2020, supervisor: P. Le Tallec
- PhD in progress: Vincenzo Zarra, “Simulation thermomécanique des procédés de fabrication additive par des méthodes Galerkin discontinues de haut ordre couplées à des algorithmes d’interface immergée”, started August 2020, supervisor: P. Le Tallec
- PhD in progress: Bertrand Leturcq, “Réductions de modèles thermomécaniques non-linéaires pour l’évaluation des déformations du cœur de réacteur”, started November 2017 supervisor: P. Le Tallec
- PhD in progress: M. Manoochertayebi, “Manyscale modeling of lung poromechanics”, started November 2020, supervisors: M. Genet, A. Bel-Brunon (INSA-Lyon) and D. Chapelle
- PhD in progress: M.Barré, “Mathematical framework for biological tissue perfusion modeling and simulation”, started october 2020, supervisors: C. Grandmont (Inria Commedia) and P. Moireau

10.2.3 Juries

- J.M Allain, PhD Jury of S. Cazayus, Université Paris-Saclay, PhD Advisor M. Lenz, February 25th
- J.M Allain, PhD Jury of M. Fraulob (referee and president), Université Paris-Est, PhD Advisor G. Haiat, October 14
- J.M Allain, PhD Jury of N. Petitjean, Université Montpellier, PhD Advisor P. Royer, December 18th
- R. Chabiniok, PhD Jury of J. I. Colorado Cervantes, Unversity Paris-Est and University Roma Tre, PhD Advisor Vittorio Sansalone and Luciano Teresi, December 16th
- P. Moireau, PhD Jury (Reviewer) of F. Regazzoni, Politecnico di Milano, February 18th

10.3 Popularization

10.3.1 Articles and contents

- D. Chapelle, interview in Sciences et Avenir Magazine for article on digital twins in medical applications, Dec 2020
- D. Chapelle, M. Genet, P. Moireau, Article “La modélisation mécanique en cardiologie : vers le patient virtuel” in Ecole Polytechnique vulgarization journal “La Jaune et la Rouge”, Feb 2020
- C. Patte, interview in Polytechnique Insights on digital avatars for lung diseases, Dec 2020

10.3.2 Interventions

- J. Manganotti presented “modélisation cardiovasculaire: problèmes de coeur?” at "Chiche": presentation of the work of a researcher in numerical science to secondary school and high school students. October 06th, December 11th
- M. Barré, conference speaker at the regional mathematical olympiad awards ceremony (Créteil Academy). October 14th
- P. Moireau, presented “La météo du coeur” at Ecole Polytechnique "learning platform GEN361", June 10th

11 Scientific production

11.1 Major publications

[1] J. Albella Martínez, S. Imperiale, P. Joly and J. Rodríguez. ‘Solving 2D linear isotropic elastodynamics by means of scalar potentials: a new challenge for finite elements’. In: *Journal of Scientific Computing* (2018). DOI: 10.1007/s10915-018-0768-9. URL: https://hal.inria.fr/hal-01803536.

[2] M. Caruel, P. Moireau and D. Chapelle. ‘Stochastic modeling of chemical-mechanical coupling in striated muscles’. In: *Biomechanics and Modeling in Mechanobiology* (2018). DOI: 10.1007/s10237-018-1102-z. URL: https://hal.inria.fr/hal-01928279.

[3] R. Chabiniok, P. Moireau, P.-F. Lesault, A. Rahmouni, J.-F. Deux and D. Chapelle. ‘Estimation of tissue contractility from cardiac cine-MRI using a biomechanical heart model’. English. In: *Biomechanics and Modeling in Mechanobiology* 11.5 (2012), pp. 609–630. DOI: 10.1007/s10237-011-0337-8. URL: http://hal.inria.fr/hal-00654541.

[4] D. Chapelle and K. Bathe. *The Finite Element Analysis of Shells - Fundamentals - Second Edition*. English. Computational Fluid and Solid Mechanics. Springer, 2011, p. 410. DOI: 10.1007/978-3-642-16408-8. URL: http://hal.inria.fr/hal-00654533.

[5] D. Chapelle, N. Cîndea and P. Moireau. ‘Improving convergence in numerical analysis using observers - The wave-like equation case’. English. In: *Mathematical Models and Methods in Applied Sciences* 22.12 (2012). DOI: 10.1142/S0218202512500406. URL: http://hal.inria.fr/inria-00621052.

[6] D. Chapelle, P. Le Tallec, P. Moireau and M. Sorine. ‘An energy-preserving muscle tissue model: formulation and compatible discretizations’. English. In: *International Journal for Multiscale Computational Engineering* 10.2 (2012), pp. 189–211. DOI: 10.1615/IntJMultCompEng.2011002360. URL: http://hal.inria.fr/hal-00678772.

[7] D. Chapelle and 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* 46 (2014). Updated version of previously published research report, pp. 82–96. DOI: 10.1016/j.euromechflu.2014.02.009. URL: https://hal.inria.fr/inria-00520612.

[8] A. Collin and S. Imperiale. 'Mathematical analysis and 2-scale convergence of a heterogeneous microscopic bidomain model'. In: *Mathematical Models and Methods in Applied Sciences* (2018). URL: https://hal.inria.fr/hal-01759914.

[9] B. Lynch, S. Bancelin, C. Bonod-Bidaud, J.-B. Gueusquin, F. Ruggiero, M.-C. Schanne-Klein and J.-M. Allain. 'A novel microstructural interpretation for the biomechanics of mouse skin derived from multiscale characterization'. In: *Acta Biomaterialia* 50 (2017), pp. 302–311. DOI: 10.1016/j.actbio.2016.12.051. URL: https://hal.archives-ouvertes.fr/hal-01531321.

[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). URL: 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 and N. Ayache. 'Patient-Specific Electromechanical Models of the Heart for Prediction of the Acute Effects of Pacing in CRT: a First Validation'. English. In: *Medical Image Analysis* 16.1 (2012), pp. 201–215. DOI: 10.1016/j.media.2011.07.003. URL: http://hal.inria.fr/inria-00616191.

11.2 Publications of the year

International journals

[12] N. Adam, P. Le Tallec and M. Zarroug. 'Multipatch isogeometric mortar methods for thick shells'. In: *Computer Methods in Applied Mechanics and Engineering* 372 (1st Dec. 2020), p. 113403. DOI: 10.1016/j.cma.2020.113403. URL: https://hal.archives-ouvertes.fr/hal-03088221.

[13] J. Albella Martínez, S. Imperiale, P. Joly and J. Rodríguez. 'Numerical Analysis of a Method for Solving 2D Linear Isotropic Elastodynamics with Free Boundary Condition using Potentials and Finite Elements'. In: *Mathematics of Computation* (2021). DOI: 10.1007/s10915-018-0768-9. URL: https://hal.inria.fr/hal-02345808.

[14] C. J. Arthurs, N. Xiao, P. Moireau, T. Schaeffter and A. A. Figueroa. 'A flexible framework for sequential estimation of model parameters in computational hemodynamics'. In: *Advanced Modeling and Simulation in Engineering Sciences* 7 (Dec. 2020). DOI: 10.1186/s40323-020-00186-x. URL: https://hal.inria.fr/hal-03113107.

[15] G. Beck, S. Imperiale and P. Joly. 'Asymptotic modelling of Skin-effects in coaxial cables'. In: *SN Partial Differential Equations and Applications* (Oct. 2020). URL: https://hal.inria.fr/hal-02512156.

[16] F. Caforio and S. Imperiale. 'Mathematical analysis of a penalization strategy for incompressible elastodynamics'. In: *Asymptotic Analysis* (2020). URL: https://hal.inria.fr/hal-02389286.

[17] F. Caforio and S. Imperiale. 'Mathematical modelling of Acoustic Radiation Force in transient shear wave elastography in the heart'. In: *ESAIM: Mathematical Modelling and Numerical Analysis* (2020). URL: https://hal.inria.fr/hal-01992069.

[18] F. Clément, F. Robin and R. Yvinec. 'Stochastic nonlinear model for somatic cell population dynamics during ovarian follicle activation'. In: *Journal of Mathematical Biology* 82.12 (2021). URL: https://hal.inria.fr/hal-02057983.

[19] J. Diani and P. Le Tallec. 'Variational upscaling for modeling state of strain-dependent behavior and stress-induced crystallization in rubber-like materials'. In: *Continuum Mechanics and Thermodynamics* (26th Nov. 2020). DOI: 10.1007/s00161-020-00954-5. URL: https://hal.archives-ouvertes.fr/hal-03088208.

[20] R. Fučík, R. Galabov, P. Pauš, P. Eichler, J. Klinkovský, R. Straka, J. Tintěra and R. Chabiniok. 'Investigation of phase-contrast magnetic resonance imaging underestimation of turbulent flow through the aortic valve phantom: Experimental and computational study using lattice Boltzmann method'. In: *Magnetic Resonance Materials in Physics, Biology and Medicine* 33.5 (27th Feb. 2020), pp. 649–662. URL: https://hal.inria.fr/hal-02470588.

[21] A. Imperiale, D. Chapelle and P. Moireau. 'Sequential data assimilation for mechanical systems with complex image data: application to tagged-MRI in cardiac mechanics'. In: *Advanced Modeling and Simulation in Engineering Sciences* 8 (9th Jan. 2021). DOI: 10.1186/s40323-020-00179-w. URL: https://hal.inria.fr/hal-03113109.

[22] F. Kimmig and M. Caruel. 'Hierarchical modeling of force generation in cardiac muscle'. In: *Biomechanics and Modeling in Mechanobiology* (2020). DOI: 10.1007/s10237-020-01357-w. URL: https://hal.archives-ouvertes.fr/hal-02570784.

[23] A. Le Gall, F. Vallée, K. Pushparajah, T. Hussain, A. Mebazaa, D. Chapelle, E. Gayat and R. Chabiniok. 'Monitoring of cardiovascular physiology augmented by a patient-specific biomechanical model during general anesthesia. A proof of concept study'. In: *PLoS ONE* (14th May 2020). DOI: 10.1371/journal.pone.0232830. URL: https://hal.inria.fr/hal-02561128.

[24] E. Lefevre, C. Baron, E. Gineyts, Y. Bala, H. Gharbi, J.-M. Allain, P. Lasaygues, M. Pithioux and H. Follet. 'Ultrasounds could be considered as a future tool for probing growing bone properties'. In: *Scientific Reports* 10.1 (Sept. 2020). DOI: 10.1038/s41598-020-72776-z. URL: https://hal.archives-ouvertes.fr/hal-03064686.

[25] Z. Ma, H. Maitournam and P. Le Tallec. 'An energy-based strategy for fatigue analysis in presence of general multi-axial time varying loadings'. In: *International Journal of Fatigue* 132 (Mar. 2020), p. 105367. DOI: 10.1016/j.ijfatigue.2019.105367. URL: https://hal.archives-ouvertes.fr/hal-02421856.

[26] H. Mella, J. Mura, H. Wang, M. D. Taylor, R. Chabiniok, J. Tintera, J. Sotelo and S. Uribe. 'HARP-I: A Harmonic Phase Interpolation Method for the Estimation of Motion from Tagged MR Images'. In: *IEEE Transactions on Medical Imaging* (2021). URL: https://hal.inria.fr/hal-03112239.

[27] B. Ruijsink, K. Zugaj, J. Wong, K. Pushparajah, T. Hussain, P. Moireau, R. Razavi, D. Chapelle and R. Chabiniok. 'Dobutamine stress testing in patients with Fontan circulation augmented by biomechanical modeling'. In: *PLoS ONE* (21st Feb. 2020). DOI: 10.1371/journal.pone.0229015. URL: https://hal.inria.fr/hal-02470571.

[28] K. Škardová, T. Oberhuber, J. Tintěra and R. Chabiniok. 'Signed-distance function based non-rigid registration of image series with varying image intensity'. In: *Discrete and Continuous Dynamical Systems - Series S* 14.3 (2021), pp. 1145–1160. DOI: 10.3934/xx.xx.xx.xx. URL: https://hal.inria.fr/hal-02514998.

[29] N. Tueni, J. Vizet, M. Genet, A. Pierangelo and J.-M. Allain. 'Microstructural deformation observed by Mueller polarimetry during traction assay on myocardium samples'. In: *Scientific Reports* 10 (2020), p. 20531. DOI: 10.1038/s41598-020-76820-w. URL: https://hal.archives-ouvertes.fr/hal-03036179.

[30] H. Zou, S. Leng, C. Xi, X. Zhao, A. S. Koh, F. Gao, J. Le Tan, R.-S. Y. Tan, J. C. Allen, L. C. Lee, M. Genet and L. Zhong. 'Three-dimensional biventricular strains in pulmonary arterial hypertension patients using hyperelastic warping'. In: *Computer Methods and Programs in Biomedicine* 189 (2020). DOI: 10.1016/j.cmpb.2020.105345. URL: https://hal.archives-ouvertes.fr/hal-02456151.

International peer-reviewed conferences

[31] M. Genet, C. Patte, C. Fetita, P.-Y. Brillet and D. Chapelle. 'Personalized pulmonary poromechanics'. In: *Computer Methods in Biomechanics and Biomedical Engineering*. SB 2020 - 45ème Congrès de la Société de Biomécanique. Vol. 23. sup1. Metz, France, 2020, S119–S120. DOI: 10.1080/10255842.2020.1812842. URL: https://hal.archives-ouvertes.fr/hal-02950947.

Conferences without proceedings

[32] M. Genet, J. Diaz, D. Chapelle and P. Moireau. 'On a reduced cylindrical model of the left ventricular dynamics'. In: VPH 2020 - Virtual Physiological Human: when models, methods and experiments meet the clinics. Paris / Online, France, 2020. URL: https://hal.archives-ouvertes.fr/hal-02950940.

[33] M. Genet, C. Patte and D. Chapelle. 'Personalized Pulmonary Poromechanics'. In: WCCM-ECCOMAS 2020 - 14th World Congress on Computational Mechanics. Paris / Virtuel, France, 2020. URL: https://hal.archives-ouvertes.fr/hal-02513247.

[34] C. Patte, P.-Y. Brillet, C. Fetita, T. Gille, J.-F. Bernaudin, H. Nunes, D. Chapelle and M. Genet. 'Estimation of patient-specific mechanical parameters in pulmonary diseases'. In: VPH 2020 - Virtual Physiological Human: when models, methods and experiments meet the clinics. Paris / Online, France, 2020. URL: https://hal.archives-ouvertes.fr/hal-02942872.

Reports & preprints

[35] A.-S. Bonnet-Ben Dhia, M.-O. Bristeau, E. Godlewski, S. Imperiale, A. Mangeney and J. Sainte-Marie. *Pseudo-compressibility, dispersive model and acoustic waves in shallow water flows.* 29th May 2020. URL: https://hal.inria.fr/hal-02493518.

[36] J. Chabassier and S. Imperiale. *Construction and convergence analysis of conservative second order local time discretisation for linear wave equations.* 7th Oct. 2020. URL: https://hal.inria.fr/hal-01894357.

[37] A. Collin, M. Prague and P. Moireau. *Estimation for dynamical systems using a population-based Kalman filter - Applications to pharmacokinetics models.* 15th June 2020. URL: https://hal.inria.fr/hal-02869347.

[38] S. Fliss, S. Imperiale and A. Tonnoir. *Computation of the exact discrete transparent boundary condition for 1D linear equations.* 8th Nov. 2020. URL: https://hal.archives-ouvertes.fr/hal-02995046.

Other scientific publications

[39] M. Manoochehrtayebi. 'Combined Estimation of Material Law and Unloaded Configuration (Application to Pulmonary Poro-Mechanics)'. Ecole Polytechnique, 28th Sept. 2020. URL: https://hal.inria.fr/hal-03043448.