RESEARCH CENTRE

Saclay - Île-de-France

IN PARTNERSHIP WITH:

Ecole Polytechnique

2021 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 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

B1.1.8. – 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]
- Dominique Chapelle [Inria, Senior Researcher, 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]

Post-Doctoral Fellow

- Colin Laville [CNRS, from Mar 2021]

PhD Students

- Mathieu Barré [Inria]
- Ezgi Berberoglu [Institut fédérale de technologie Zurich - Suisse, until May 2021]
- Andre Dalmora [CEA]
- Tiphaine Delaunay [Inria]
- 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]
- Giulia Merlini [École polytechnique, from Oct 2021]
- Alice Peyraut [CNRS, from Oct 2021]
- Nicole Tueni [École polytechnique]
- Vincenzo Zarra [École polytechnique]

Technical Staff

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

Interns and Apprentices

- Elie Attias [École polytechnique, from Jun 2021 until Jul 2021]
- Adrien Ceripa [École polytechnique, from Feb 2021 until Jul 2021]
- Louis Pierre Chaintron [École Normale Supérieure de Paris, from Apr 2021 until Aug 2021]
- Giulia Merlini [École polytechnique, until Jun 2021]
- Othmane Mouzhi [Inria, from May 2021 until Aug 2021]
- Eleonore Strauch-Hausser [Inria, from Jun 2021 until Aug 2021]

Administrative Assistant

- Bahar Carabetta [Inria]

Visiting Scientists

- Valentino Caputo [Assistance publique/Hôpitaux de Paris, from Feb 2021 until Jul 2021]
- Melanie Sambres [Université de Paris, from Feb 2021 until Jul 2021]
- Vincent Sounthakith [Assistance publique/Hôpitaux de Paris, until Jul 2021]

External Collaborators

- Matthieu Caruel [Univ Paris-Val de Marne]
- Radomir Chabiniok [Centre médical de l'Université du Texas Southwestern Dallas - USA]
- Louis Pierre Chaintron [École Normale Supérieure de Paris, from Sep 2021]
- Anna Gaubert [Assistance publique/Hôpitaux de Paris, from Jun 2021]
- Alexandre Imperiale [CEA, from Sep 2021]
- Didier Lucor [CNRS]
- Marc Teyssier [Self-employed, until Jul 2021]
- Fabrice Vallée [Assistance publique/Hôpitaux de Paris]
- Maya de Buhan [CNRS, from Aug 2021, HDR]

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 Social and environmental responsibility

5.1 Impact of research results

5.1.1 Arthur Le Gall

2021 has seen the first PhD defense of an active physician supervised in M3DISIM, Arthur Le Gall, a member of the critical care department of the Lariboisière Hospital (AP-HP) [38]. The aim of this PhD was to explore the use of mathematical modeling components of the cardiovascular system to enhance the monitoring of patients during anesthesia or in intensive care. More specifically, some specific modeling tools have been identified and further developed, and then extensively assessed based on actual clinical data. This has resulted into various successful proofs-of-concept that have also paved the way for the AnaestAssist innovation project (see next section).

5.1.2 AnaestAssist project and impact for anaesthesia

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 measured physiological signals. The model will be personalised for the patient, thus creating a digital twin of the patient's cardiovascular system. With this digital twin, 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 make it possible to determine (through predictive modeling) 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's condition through a reduction of the risk related to general anaesthesia and a wiser exposition to drugs, and to reduce the costs for the health care system due to a lower rate of complications and shorter hospital stays.

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

5.1.3 COVID research

In response to the ongoing COVID-19 pandemic caused by SARS-CoV-2, governments are taking a wide range of non-pharmaceutical interventions (NPI). These measures include interventions as stringent as strict lockdown but also school, bar and restaurant closures, curfews and barrier gestures, i.e. social distancing. Disentangling the effectiveness of each NPI is crucial to inform response to future outbreaks. To this end, we propose to develop a multi-level estimation of the French COVID-19 epidemic over a period of one year. This work performed with colleagues from project-teams Sistm and Monc among others is under review and is already available in medrxiv. This work was disseminated to public audience in newspapers Le Monde (28/07/2021) and Liberation (2/12/2021)

More specifically in this work, we rely on a global extended Susceptible-Infectious-Recovered (SIR) mechanistic model of the infection including a dynamical (over time) transmission rate containing a Wiener process accounting for modeling error. Random effects are integrated following an innovative population approach based on a Kalman-type filter where the log-likelihood functional couples data across French regions. We then fit the estimated time-varying transmission rate using a regression model depending on NPI, while accounting for vaccination coverage, apparition of variants of concern (VoC) and seasonal weather conditions. We show that all NPI considered have an independent significant effect on the transmission rate. We additionally demonstrate a strong effect from weather conditions which decrease transmission during the summer period, and also estimate increased transmissibility of VoCs.

6 Highlights of the year

- The ANR ElastoHeart and the ANR CorMecha were funded
- Francois Kimmig received the iPhDGrand Prix award
- New code HELEN developed with real time cardiac simulation for anesthesia application
- Launch of the Bernoulli Lab – joint AP-HP Inria laboratory – under the scientific guidance of Dominique Chapelle

6.1 Awards

Francois Kimmig received the iPhDGrand Prix distinction.

7 New software and platforms

This year the team has released the new software HELEN (Heart Estimator For Live Evaluation in aNesthesia) dedicated to real-time monitoring in anesthesia.

7.1 New software

7.1.1 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

Contact: Sebastien Gilles

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

7.1.2 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

7.1.3 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

Contact: Philippe Moireau

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

7.1.4 HELEN

Name: Heart Estimator For Live Evaluation in aNesthesia

Keywords: Low rank models, Dimensionality reduction, Cardiovascular and respiratory systems, Kalman filter, Dynamical system

Functional Description: Real-time fractional heartbeat simulation for on-board monitoring devices. Certified models and implementation with respect to numerical errors. Estimation of state and parameters by sequential filtering for model inversion.

Release Contributions: Launching simulations from option files in text format Choice of modeling components from the option file Simulation results exported in csv format and visualization module available. Modules for the direct problem and the inverse problem (Kalman filter type algorithm). Unit tests implemented and workflow implementation on Inria's continuous integration platform. Non-regression tests implemented (integration test) and implementation of the workflow on Inria's continuous integration platform

Contact: Philippe Moireau

Participants: Laurent Steff, Sebastien Gilles

7.1.5 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, Sebastien Gilles, Philippe Moireau

7.1.6 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/

Contact: Vivien Mallet

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

8 New results

8.1 Mathematical and Mechanical Modeling

8.1.1 Shell elements with transient High-Order spectral finite elements for guided waves in predeformed structures

Participants: Andre Dalmora *(correspondant)*, Alexandre Imperiale, Sébastien Imperiale, Philippe Moireau.

In leading edge industrial applications, assessing structure integrity is an important aspect of safety requirements. Structural Health Monitoring (SHM) proposes to use sensors and signal processing units in situ for such purpose. Ultrasonic SHM systems are already implemented in industry applications but their usage are limited due to environmental and operational conditions, such as internal stresses due to structural loading/deformation. We present a model, and corresponding numerical methods, for elastic wave propagation in a predeformed medium. We use a shell formulation for nonlinear mechanics to compute the effects of structure loading. The computed displacement is fed into a spectral element method (SFEM) kernel to solve the time-domain linearized elastodynamics problem representing the wave propagation.

8.1.2 Multiscale mechanical model based on patient-specific geometry: application to early keratoconus development

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

Keratoconus is a pathology of the cornea associated with a tissue thinning and a weakening of its mechanical properties. However, it remains elusive which aspect is the leading cause of the disease. To investigate this question, we combined a multiscale model with a patient-specific geometry in order to simulate the mechanical response of healthy and pathological corneas under intraocular pressure. The constitutive behavior of the cornea is described through an energy function which takes into account the isotropic matrix of the cornea, the geometric structure of collagen lamellae and the quasi-incompressibility of the tissue. A micro-sphere description is implemented to take into account the typical features of the collagen lamellae as obtained experimentally, namely their orientation, their stiffness and their dispersion, as well as their unfolding stretch, at which they start to provide a significant force. A set of reference parameters is obtained to fit experimental inflation data of the literature. We show that the most sensitive parameter is the unfolding stretch, as a small variation of this parameter induces a major change in the corneal apex displacement. The keratoconus case is then studied by separating the impact of the geometry and that of the mechanics. We computed the evolution of the SimK (a clinical indicator of cornea curvature) and elevation maps: we were able to reproduce the reported changes of SimK with pressure only by a mechanical weakening, and not by a change in geometry. More specifically, the weakening has to target the lamellae and not the matrix. The mechanical weakening leads to elevations close to early stage keratoconus, but our model lacks the remodeling component to couple the changes in mechanics with changes in geometry.

8.1.3 Micro to macro pulmonary poro-mechanical model

Participants: Madhi Manoochehrtayebi *(correspondant)*, Martin Genet, Aline Bel-Brunon *(INSA Lyon)*, Dominique Chapelle.

This work concerns the enhancing of the macroscopic pulmonary poro-mechanical models through integrating a micro-mechanical model. We developed various micro-structural models of the lungs at the alveolar scale, allowing to mimic micro-imaging data. We then performed linear periodic homogenization, allowing to derive a complete homogenized poro-elastic behavior from the micro-mechanical model, which we compared to the standard linearized poro-mechanical behavior law. Perspectives of this work include the extension to micro-mechanical model to (geometric and material) nonlinearity, as well as an upscaling strategy, in order to feed an actual nonlinear poromechanical behavior law.

8.1.4 Cellular transduction of mechanical oscillations in plants by the plasma-membrane mechanosensitive channel MSL10

Participants: Jean-Marc Allain.

Plants spend most of their life oscillating around 1 to 3 Hz due to the effect of the wind. Therefore, stems and foliage experience repetitive mechanical stresses through these passive movements. However, the mechanism of the cellular perception and transduction of such recurring mechanical signals remains an open question. Multimeric protein complexes forming mechanosensitive (MS) channels embedded in the membrane provide an efficient system to rapidly convert mechanical tension into an electrical signal. So far, studies have mostly focused on non-oscillatory stretching of these channels. In this work, we show that the plasma-membrane MS channel MscS-LIKE 10 (MSL10) from the model plant Arabidopsis thaliana responds to pulsed membrane stretching with rapid activation and relaxation kinetics in the range of 1 s. Under sinusoidal membrane stretching, MSL10 presents a greater activity than under static stimulation. In a previous work we observed this amplification mostly in the range of 0.3 to 3 Hz. Above these frequencies the channel activity is very close to that under static conditions. With a localization in aerial organs naturally submitted to wind-driven oscillations, our results suggest that the MS channel MSL10, and by extension MS channels sharing similar properties, represents a molecular component allowing the perception of oscillatory mechanical stimulations by plants.

8.1.5 Analysis of a linearized poromechanics model for incompressible and nearly incompressible materials

Participants: Mathieu Barré *(correspondant)*, Céline Grandmont *(Inria Paris, COMMEDIA)*, Philippe Moireau.

Biological tissues can be seen as porous media in which elastic fibers (such as the heart muscle, lung parenchyma, gray matter) and incompressible viscous fluids (blood, lymph, cerebrospinal fluid) are in interaction. Recently, a new model based on the mixture theory was proposed to simulate biological tissues perfusion. This is a fully dynamical model in which the fluid and solid equations are strongly coupled through the interstitial pressure. As such, it generalizes Darcy, Brinkman and Biot equations of poroelasticity. In previous works, the mathematical and numerical analysis of this model was performed for a compressible porous material.

In [40], we focus on the nearly-incompressible case with a semigroup approach that also enables to prove the existence of weak solutions. We show the existence and uniqueness of strong and weak solutions in the incompressible limit, which corresponds to the physiological regime and for which a non-standard divergence constraint arises. Due to the special form of the coupling, the underlying problem is not coercive. Nevertheless, by using the notion of T-coercivity, we obtain stability estimates and well-posedness results. Our study also provides guidelines to propose a stable and robust approximation of the problem with mixed finite elements. In particular, we recover an inf-sup condition independent of the phase field. Finally, we investigate numerically the elliptic regularity of the associated steady-state problem and illustrate the sensitivity of the solution with respect to the various model parameters.

8.1.6 Hierarchical modeling of length-dependent force generation in cardiac muscles and associated thermodynamically-consistent numerical schemes

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

In the context of cardiac muscle modeling, the availability of the myosin heads in the sarcomeres varies over the heart cycle contributing to the Frank-Starling mechanism at the organ level. In the work [25], we propose a new approach that allows to extend the Huxley'57 muscle contraction model equations to incorporate this variation. This extension is built in a thermodynamically consistent manner, and we also propose adapted numerical methods that satisfy thermodynamical balances at the discrete level. Moreover, this whole approach both for the model and the numerics is devised within a hierarchical strategy enabling the coupling of the microscopic sarcomere-level equations with the macroscopic tissue-level description. As an important illustration, coupling our model with a previously proposed simplified heart model, we demonstrate the ability of the modeling and numerical framework to capture the essential features of the Frank-Starling mechanism.

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

Participants: Jessica Manganotti *(correspondant)*, François Kimmig, Philippe Moireau, Sébastien Imperiale.

In the work [26] 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 stable numerically and informative physiologically. These latter two properties are verified by numerical experiments.

8.1.8 Upscaling of nonlinear multiscale structures

Participants: Patrick Le Tallec.

Predicting the long term evolution of the fuel assemblies inside a nuclear reactor is capital for operational and safety purposes. For some years, CEA has developed the study of the progressive deformations of fuel assemblies during a succession of irradiation cycles within a PWR (Pressurized Water Reactor) core.

A finite element model of the core is generally built with a simplified mechanical representation of each assembly, using beam elements and discrete elements. In order to gain in representativeness without increasing the size and time of these multi-body calculations including fluid-structure interaction, a new method of model order reduction has been developed. It is specially adapted to this context and borrows the concepts of NTFA non-linear homogenization. The theoretical foundations and the application to a slender structure have been developed. A first example allows to validate the method on a simple case, with spatially homogeneous characteristics. Finally, the case of the creep of a fuel assembly under realistic heterogeneous loads was treated. The integration of contact and friction is under progress.

8.1.9 Modeling of the fluid–structure interactions of a biocapsule with bending resistance

Participants: Patrick Le Tallec *(correspondant)*, , Marina Vidrascu *(Inria Paris, COMMEDIA)*.

We address the question of the modeling of the fluid-structure interactions for a microcapsule enclosed by a finite-thickness wall, and of the prediction of the buckling behavior when it is subjected to large displacements and deformations. Specifically, we model the strong coupling between the solid (the wall dynamics) and fluid (the flow inside and outside the capsule) mechanics, for a wall material that can be strain-hardening or softening, while accounting for the bending resistance due to thickness. The fluid flow is assumed to be inertia-less on the capsule scale, which allows the use of the boundary integral formulation for the fluid velocity. We discuss the different simplifications that are made when designing a fluid–shell interaction model for large deformations, and present an upgraded shell model that allows for a nonlinear wall stretching law. The performance of the model is illustrated on a simple example, where an initially ellipsoidal capsule is freely suspended in a plane hyperbolic flow and is subjected to such stringent deformation, that its short axis becomes the long one. We show that a simple membrane model, where bending resistance is neglected, predicts reasonably well the overall shape of the capsule, but cannot capture the detailed post buckling behavior, for which a robust shell model is necessary. The proposed shell model by contrast complies with dominant membrane effects, remains stable even under large deformation and avoids numerical locking. It allows predicting post-buckling behaviour, which depends on the material constitutive law.

8.1.10 A quasistatic poromechanical model of the lungs

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

The lung vital function of providing oxygen to the body heavily relies on its mechanical behavior, and the interaction with its complex environment. In particular, the large compliance and the porosity of the pulmonary tissue are critical for lung inflation and air inhalation, and the diaphragm, the pleura, the rib cage and intercostal muscles all play a role in delivering and controlling the breathing driving forces. In this paper, we introduce a novel poromechanical model of the lungs. The constitutive law is derived within a general poromechanics theory via the formulation of lung-specific assumptions, leading to a hyperelastic potential reproducing the volume response of the pulmonary mixture to a change of pressure. Moreover, physiological boundary conditions are formulated to account for the interaction of the lungs with their surroundings, including a following pressure and bilateral frictionless contact. A strategy is established (presented in [36]) to estimate the unloaded configuration from a given loaded state, with a particular focus on ensuring a positive porosity. Finally, we illustrate through several realistic examples the relevance of our model and its potential clinical applications.

8.1.11 Pressure-driven micro-poro-mechanics: A variational framework for modeling the response of porous materials

Participants: Martin Genet.

Porous materials are highly relevant in engineering and medical applications due to their enhanced properties and lightweight nature. Current micromechanical models of porous materials can accurately predict the response under the assumptions of small deformations and drained conditions, typically driven by imposed deformations. However, the theoretical framework for the micromechanical modeling of porous material driven by pore pressure in the large-deformation range has been understudied. In this work, we develop a finite-deformation variational framework for pressure-driven foams, i.e., materials where the pore pressure in the cavities produces the deformation. We further consider different kinematical constraints in the formulation of boundary conditions: kinematic uniform displacements, periodic displacements and uniform traction. We apply the proposed model in the numerical simulation of lung porous tissue using a spherical alveolar geometry and an image-based geometry obtained from micro-computed-tomography images of rat lung. Our results show that the stress distributions in the spherical alveolar model are highly dependent on the kinematical constraints. In contrast, the stress distribution in the image-based alveolar model is not affected by the choice of boundary conditions. Further, when comparing the response of pressure-driven versus deformation-driven models, we conclude that hydrostatic stresses experience a marked shift in their distribution, whereas the deviatoric stresses remain unaffected. Our findings of how stresses are affected by the choice of boundary conditions and geometry take particular relevance in the simulation of the lungs, where the pressure-driven and deformation-driven cases are related to mechanical ventilation and spontaneous breathing.

8.1.12 Asymptotic analysis of abstract two-scale wave propagation problems

Participants: Sébastien Imperiale.

The work [43] addresses the mathematical analysis, by means of asymptotic analysis, of linear wave propagation problems involving two scales, represented by a single small parameter, and written in an abstract setting. This abstract setting is defined using linear operators in Hilbert spaces and also enters the framework of semi-group theory. In this setting, we show, under some assumptions on the structure of the wave propagation problems, weak and strong convergence of solutions with respect to the small parameter towards the solution of a well-defined limit problem.

8.2 Numerical Methods

8.2.1 Construction and convergence analysis of conservative second order local time discretisation for linear wave equations

Participants: Juliette Chabassier *(Inria Bordeaux, Magique 3D)*, Sébastien Imperiale.

In this work we present and analyse a time discretisation strategy for linear wave equations that aims at using locally in space the most adapted time discretisation among a family of implicit or explicit centered second-order schemes. The proposed family of schemes is adapted to domain decomposition methods such as the mortar element method. They correspond in that case to local implicit schemes and to local time stepping. We show that, if some regularity properties of the solution are satisfied and if the time step verifies a stability condition, then the family of proposed time discretisations provides, in a strong norm, second order space-time convergence. Finally, we provide 1D and 2D numerical illustrations that confirm the obtained theoretical results and we compare our approach on 1D test cases to other existing local time stepping strategies for wave equations (see [17]).

8.2.2 Pseudo-compressibility, dispersive model and acoustic waves in shallow water flows

Participants: Anne-Sophie Bonnet-BenDhia *(Inria Saclay, Poems)*, Jacques Sainte-Marie *(Inria Paris, Ange)*, Sébastien Imperiale *(correspondant)*.

In this paper we study a dispersive shallow water type model derived from the free surface compressible Navier-Stokes system. The compressible effects allow to capture the acoustic-like wave propagation and can be seen as a relaxation of an underlying incompressible model. The first interest of such a model is thus to capture both acoustic and water waves. The second interest lies in its numerical approximation. Indeed, at the discrete level, the pseudo-compressibility terms circumvent the resolution of an elliptic equation to capture the non-hydrostatic part of the pressure. This drastically reduces the cost of the numerical resolution of dispersive models especially in 2d and 3d (see [14]).

8.3 Inverse Problems

8.3.1 Solving inverse source wave problem: from observability to observer design

Participants: Tiphaine Delaunay *(correspondant)*, Muriel Boulakia *(Inria Paris, Commedia)*, Sébastien Imperiale, Philippe Moireau.

This work is divided into two parts. First, we are interested in the estimation of a function $\theta(x)$ in a source term $\lambda(t)\theta(x)$ with interior measurements (field or velocity measurements) on a subdomain ω. Identifiability is proven by combining a classical initial condition observability (by multiplier technique or by SGCC) and by a Voltera equation. The identifiability is shown in a $H^{-1}(\Omega)$ norm for measurements in L^2 norm. The problem is ill-posed of order 1 for velocity measurements and of order 2 for velocity measurements. We then perform a Tikhonov regularization with a cost-functional to minimize. We also perform a convergence analysis with respect to the square root of the noise level. We use a parameter observer equivalent to the minimization of the cost function. We then show that the observer enables us to reconstruct the parameter by equivalence to the minimization of the cost functional.

Second, we are interested in the estimation a function $\theta(x)$ in a source term $\lambda(x,t)\theta(x)$ from interior measurements on a subdomain ω. We use Carleman estimates to obtain an L^2-norm identifiability of the parameter for $\partial_t u$ velocity measurements on ω in H^1-norm or u field measurements in H^2-norm. The problem is then ill-posed of order 1 for the velocity measurements and of order 2 for the field measurements. This time, we regularize by lifting the measurements. We again perform an analysis according to the noise by introducing a well-chosen cost function. Finally, we define the observer equivalent to the minimization of the cost function.

8.3.2 Stabilization of the high-order discretized wave equation for data assimilation problems

Participants: Tiphaine Delaunay *(correspondant)*, Sébastien Imperiale, Philippe Moireau.

The objective of this work is to propose and analyze numerical schemes to solve data assimilation problems by observers for wave-like hyperbolic systems. The efficiency of these observers relies on the proof of the exponentially stable character of the underlying system when we add the dissipative term linked to the observations. This exponential stability depends on observability inequalities where the energy of the system is proven to be controlled by the observations. To demonstrate these inequalities, the multiplier approach is very natural and provides near-optimal results for 1D problems. Unfortunately, the multiplier method is incompatible with the discretization needs because the exponential stability is not preserved at the discrete level due to the presence of spurious waves. Our goal is therefore to propose correctors in the discretization that enable us to prove exponential stability at the discrete level when using high-order finite element approximation. The main idea is to add a stabilizing term which damps the oscillating functions (such as spurious waves). This term is built from a discrete multiplier analysis. This gives us the exponential stability of the semi-discrete problem at any order without affecting the order of convergence.

8.3.3 Estimation for dynamical systems using a population-based Kalman filter – Applications in computational biology

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

Estimating dynamical systems — in particular identifying theirs parameters — involved in computational biology – for instance in pharmacology, in virology or in epidemiology – is fundamental to put in accordance the model trajectory with the measurements at hand. Unfortunately, when the sampling of data is very scarce or the data are corrupted by noise, parameters mean and variance priors must be chosen very adequately to balance our measurement distrust. Otherwise the identification procedure fails. A circumvention consists in using repeated measurements collected in configurations that share common priors – for instance with multiple population subjects in a clinical study or clusters in an epidemiology investigation. This common information is of benefit and is typically modeled in statistics by nonlinear mixed-effect models. In this paper, we introduce a data assimilation methodology compatible with such mixed-effect strategy without being strangled by the potential resulting curse of dimensionality. In [41] we define population-based estimators through maximum likelihood estimation. Then, from filtering theory, we set up an equivalent robust large population sequential estimator that integrates the data as they are collected. Finally, we limit the computational complexity by defining a reduced-order version of this population Kalman filter clustering subpopulations of common observation background. The resulting algorithm performances are evaluated on classical pharmacokinetics benchmark. The versatility of the proposed method is finally fully challenged in a real-data epidemiology study of COVID spread in regions and departments of France.

8.3.4 Combining Data Assimilation and Machine Learning to build data-driven models for unknown long time dynamics – Applications in cardiovascular modeling

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

We propose in [31] 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 separation 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.

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

Participants: Alexandre Imperiale, 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 work [24] 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.

8.4 Experimental Assessments

8.4.1 Characterization of the mechanical response of the human cornea

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

Background: The objective of the work is to characterize the mechanical response of the human cornea under a wide range of pressures with a view to building a reference deformation profile for identification processes.

Methods: Twenty human corneas were tested under three different mechanical loadings: (i) Creep tests at physiological pressure to mimic transplant, (ii) inflation tests to characterize the mechanical response of the cornea under a wide range of pressures, (iii) creep tests at high pressure to capture the time dependent behavior of the cornea. Throughout the tests, 2- and 3-Dimensional Optical Coherence Tomography (OCT) images were taken and analyzed using Digital Image/Volume correlation (DIC/DVC).

Results: At physiological pressure, although the cornea inflates (the vertical deformation is positive in the whole tissue), three distinct zones appear with different ranges of deformation: an anterior layer, a middle layer - which has the largest deformation - and a posterior layer. In addition, when looking at the vertical deformation profile near the apex, an S-shaped pattern is observed. During the inflation test, the three zones and the S-shaped pattern are obtained as well, but the deformation is not only positive anymore, the cornea is in compression (vertical deformation are negative) in the middle and anterior layers. Our measurements of apex displacement with pressure during this test are comparable to the ones found by Elsheikh's group. In order to better understand the mechanical response of the cornea under pressure, a simplified analytical model was built in which the tissue is represented as an elastic material with varying Young's modulus subjected to osmotic pressure. The model captures well the response pattern and allows both compression and dilatation of the tissue, thanks to the osmotic pressure term. A purely elastic response of the cornea would allow only compression. Finally, creep tests at high pressure point out the time-dependency of the mechanical behavior of the cornea, which compress more and more with time. This can be due to the pumping out of the endothelium, which would become active with time at high pressure. The model cannot capture those effects as time has not been introduced. Combining these experiments, reference deformation maps for the response of the cornea under pressure were created. They have to be manipulated with caution during identification processes, however, as the cornea is a very complex tissue, with varying mechanical properties through the thickness and also a time-dependency response varying with pressure.

8.5 Clinical Applications

8.5.1 AnaestAssist project

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

The AnaestAssist team coordinated the response to several calls for proposals at the national and European level in order to find some funding for the project's next phase of development. We built a EIT Health BP2022 project leading a international consortium composed of AP-HP, Philips (Netherlands), Université des Patients (Sorbonne Université) and Karolinska University Hospital (Sweden). The proposal obtained the score 79.4/100 after the remote evaluation, the threshold for an invitation to the hearings being 80/100. The AnaestAssist team co-coordinated with M3DISIM's partners at APHP-Lariboisière Hospital the Virtuose RHU project (Recherche Hospitalo-Universitaire) putting together a consortium made up of industrial partners: Philips France, Bioserenity and Intelligence Anesthesia; a medical risk insurance company, Relyens; academic partners, Inria, Université des Patients (Sorbonne Université) and Université de Paris and a clinical partner, AP-HP. The Virtuose project was not selected for the hearings. The AnaestAssist project has also been presented to the AMI Santé Numérique organised by Bpifrance. After the remote evaluation, we have been invited to the hearings and the project was declared eligible for the next steps of the AMI to participate in dedicated calls for proposals.

With the services of an external provider, we built a new high performance code for the simulation of reduced biophysical model of the cardiovascular system called HELEN. This code constitutes a step towards the realisation of the proof of concept of the AnaestAssist solution functioning in real time.

8.5.2 A 3D personalized cardiac myocyte aggregate orientation model using MRI data-driven low-rank basis functions

Participants: Martin Genet.

Cardiac myocyte aggregate orientation has a strong impact on cardiac electrophysiology and mechanics. Studying the link between structural characteristics, strain, and stresses over the cardiac cycle and cardiac function requires a full volumetric representation of the microstructure. In this work, we exploit the structural similarity across hearts to extract a low-rank representation of predominant myocyte orientation in the left ventricle from high-resolution magnetic resonance ex-vivo cardiac diffusion tensor imaging (cDTI) in porcine hearts. We compared two reduction methods, Proper Generalized Decomposition combined with Singular Value Decomposition and Proper Orthogonal Decomposition. We demonstrate the existence of a general set of basis functions of aggregated myocyte orientation which defines a data-driven, personalizable, parametric model featuring higher flexibility than existing atlas and rule-based approaches. A more detailed representation of microstructure matching the available patient data can improve the accuracy of personalized computational models. Additionally, we approximate the myocyte orientation of one ex-vivo human heart and demonstrate the feasibility of transferring the basis functions to humans.

8.5.3 Left Ventricular Torsion Obtained Using Equilibrated Warping in Patients with Repaired Tetralogy of Fallot

Participants: Martin Genet.

Patients after surgical repair of Tetralogy of Fallot (rTOF) may suffer a decrease in left ventricular (LV) function. The aim of our study is to evaluate a novel method of assessing LV torsion in patients with rTOF, as an early indicator of systolic LV dysfunction. Motion tracking based on image registration regularized by the equilibrium gap principle, known as equilibrated warping, was employed to assess LV torsion. Seventy-six cases of rTOF and ten normal controls were included. The group of controls was assessed for reproducibility using both equilibrated warping and standard clinical tissue tracking software (CVI42, version 5.10.1, Calgary, Canada). Patients were dichotomized into two groups: normal vs. loss of torsion. Torsion by equilibrated warping was successfully obtained in 68 of 76 (89%) patients and 9 of 10 (90%) controls. For equilibrated warping, the intra- and interobserver coefficients of variation were 0.095 and 0.117, respectively, compared to 0.260 and 0.831 for tissue tracking by standard clinical software. The intra- and inter-observer intraclass correlation coefficients for equilibrated warping were 0.862 and 0.831, respectively, compared to 0.992 and 0.648 for tissue tracking. Loss of torsion was noted in 32 of the 68 (47%) patients with rTOF. There was no difference in LV or RV volumes or ejection fraction between these groups. The assessment of LV torsion by equilibrated warping is feasible and shows good reliability. Loss of torsion is common in patients with rTOF and its robust assessment might contribute into uncovering heart failure in an earlier stage.

8.5.4 In-silico study of accuracy and precision of left-ventricular strain quantification from 3D tagged MRI

Participants: Martin Genet, Philippe Moireau.

Cardiac Magnetic Resonance Imaging (MRI) allows quantifying myocardial tissue deformation and strain based on the tagging principle. In this work, we investigate accuracy and precision of strain quantification from synthetic 3D tagged MRI using equilibrated warping. To this end, synthetic biomechanical left-ventricular tagged MRI data with varying tag distance, spatial resolution and signal-to-noise ratio (SNR) were generated and processed to quantify errors in radial, circumferential and longitudinal strains relative to ground truth. Results reveal that radial strain is more sensitive to image resolution and noise than the other strain components. The study also shows robustness of quantifying circumferential and longitudinal strain in the presence of geometrical inconsistencies of 3D tagged data. In conclusion, our study points to the need for higher-resolution 3D tagged MRI than currently available in practice in order to achieve sufficient accuracy of radial strain quantification.

8.5.5 Biomechanical Modeling to Inform Pulmonary Valve Replacement in Tetralogy of Fallot Patients after Complete Repair

Participants: Maria Gusseva, Dominique Chapelle, Philippe Moireau, Martin Genet, Radomir Chabiniok *(correspondant)*.

Background: A biomechanical model of the heart can be used to incorporate multiple data sources (electrocardiography, imaging, invasive hemodynamics). The purpose of the study presented in [22] was to use this approach in a cohort of patients with tetralogy of Fallot after complete repair (rTOF) to assess comparative influences of residual right ventricular outflow tract obstruction (RVOTO) and pulmonary regurgitation on ventricular health.

Methods: Twenty patients with rTOF who underwent percutaneous pulmonary valve replacement (PVR) and cardiovascular magnetic resonance imaging were included in this retrospective study. Biomechanical models specific to individual patient and physiology (before and after PVR) were created and used to estimate the RV myocardial contractility. The ability of models to capture post-PVR changes of right ventricular (RV) end-diastolic volume (EDV) and effective flow in the pulmonary artery (Q_{eff}) was also compared with expected values.

Results: RV contractility before PVR (mean 66 ± 16 kPa, mean ± standard deviation) was increased in patients with rTOF compared with normal RV (38-48 kPa) ($P < 0.05$). The contractility decreased significantly in all patients after PVR ($P < 0.05$). Patients with predominantly RVOTO demonstrated greater reduction in contractility (median decrease 35%) after PVR than those with predominant pulmonary regurgitation (median decrease 11%). The model simulated post-PVR decreased EDV for the majority and suggested an increase of Q_{eff} both in line with published data.

Conclusions: This study used a biomechanical model to synthesize multiple clinical inputs and 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.

8.5.6 Prediction of Ventricular Mechanics After Pulmonary Valve Replacement in Tetralogy of Fallot by Biomechanical Modeling: A Step Towards Precision Healthcare

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

Clinical indicators of heart function are often limited in their ability to accurately evaluate the current mechanical state of the myocardium. Biomechanical modeling has been shown to be a promising tool in addition to clinical indicators. By providing a patient-specific measure of myocardial active stress (contractility), biomechanical modeling can enhance the precision of the description of patient's pathophysiology at any given point in time. In [23] we aim to explore the ability of biomechanical modeling to predict the response of ventricular mechanics to the progressively decreasing afterload in repaired tetralogy of Fallot (rTOF) patients undergoing pulmonary valve replacement (PVR) for significant residual right ventricular outflow tract obstruction (RVOTO). We used 19 patient-specific models of patients with rTOF prior to pulmonary valve replacement (PVR), denoted as PSM_{pre}, and patient-specific models of the same patients created post-PVR (PSM_{post}) – both created in our previous published work. Using the PSMpre and assuming cessation of the pulmonary regurgitation and a progressive decrease of RVOT resistance, we built relationships between the contractility and RVOT resistance post-PVR. The predictive value of such *in silico* obtained relationships were tested against the PSM_{post}, i.e. the models created from the actual post-PVR datasets. Our results show a linear 1-dimensional relationship between the *in silico* predicted contractility post-PVR and the RVOT resistance. The predicted contractility was close to the contractility in the PSM_{post} model with a mean (± SD) difference of 6.5 (± 3.0)%. The relationships between the contractility predicted by *in silico* PVR vs. RVOT resistance have a potential to inform clinicians about hypothetical mechanical response of the ventricle based on the degree of pre-operative RVOTO.

8.5.7 Model-assisted time-synchronization of cardiac MR image and catheter pressure data

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

When combining cardiovascular magnetic resonance imaging (CMR) with pressure catheter measurements, the acquired image and pressure data need to be synchronized in time. The time offset between the image and pressure data depends on a number of factors, such as the type and settings of the MR sequence, duration and shape of QRS complex or the type of catheter, and cannot be typically estimated beforehand. In the present work [34] we propose using a biophysical heart model to synchronize the left ventricular (LV) pressure and volume (P-V) data. Ten patients, who underwent CMR and LV catheterization, were included. A biophysical model of reduced geometrical complexity with physiologically substantiated timing of each phase of the cardiac cycle was first adjusted to individual patients using basic morphological and functional indicators. The pressure and volume waveforms simulated by the patient-specific models were then used as templates to detect the time offset between the acquired ventricular pressure and volume waveforms. Time-varying ventricular elastance was derived from clinical data both as originally acquired as well as when time-synchronized, and normalized with respect to end-systolic time and maximum elastance value ($E^N_{\text{orig}}(t)$, $E^N_{\text{t-syn}}(t)$, respectively). $E^N_{\text{t-syn}}(t)$ was significantly closer to the experimentally obtained $E^N_{\text{exp}}(t)$ published in the literature ($p<0.05$, L^2 norm). The work concludes that the model-driven time-synchronization of P-V data obtained by catheter measurement and CMR allows to generate high quality P-V loops, which can then be used for clinical interpretation.

8.5.8 Translational Cardiovascular Modeling: Tetralogy of Fallot and Modeling of Diseases

Participants: Radomir Chabiniok *(correspondant)*, Maria Gusseva.

Translational cardiovascular modeling (TCM) combines clinical data with physiologically and biophysically based models of the heart, vessels or circulation, while aiming to contribute to diagnosis or optimal clinical management. Models of heart mechanics and electromechanical models are applicable when assessing ventricular function, contributing to planning of optimal intervention. During a perioperative period or acute exacerbation of heart failure, close to real time running models can be coupled with signals monitoring cardiovascular physiology. Blood flow assessed by combining phase contrast magnetic resonance imaging with flow models can contribute to the decision about a possible intervention e.g. on heart valves or large vessels. Furthermore, advanced imaging and image processing constrained by biophysical models allows for the study of distinct patterns, which could contribute to early detection or mapping a disease progress. In this work [37] we demonstrate applicability of some TCM methods on tetralogy of Fallot (TOF) – the most common cyanotic congenital heart disease. A number of already existing modeling techniques can be applied on the cohort of TOF. Likewise, some novel techniques developed specifically for the group of TOF patients could serve in some other pathologies. This whole approach leads to an acronym TOFMOD, standing for Tetralogy of Fallot and Modeling of Diseases.

9 Bilateral contracts and grants with industry

9.1 Bilateral contracts with industry

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

  Participants: Sébastien Imperiale.

10 Partnerships and cooperations

10.1 International initiatives

10.1.1 Inria associate team not involved in an IIL or an international program

ToFMod

Title: Cardiac Biomechanical Modeling of Chronic Right Ventricular Loading

Duration: 2018 - 2022

Coordinator: Radomir Chabiniok

Partners:

- 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 objective, indeed.

10.1.2 Inria international partners

- Inria-UTSW Medical Center Dallas Associated Team on modeling for Tetralogy of Fallot patients TOFMOD (3rd year of TOFMOD received: 11kEUR by Inria France; US 43k$ by UTSW)

10.2 National initiatives

10.2.1 Sachems

Participants: Sébastien Imperiale, Philippe Moireau, Andre Dalmora.

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 funded in 2019 under the SESAME system of the Ile-de-France region, aims to create a federative platform for research and innovation for the SHM, 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.

10.2.2 ANR

- **ANR JCJC LungManyScale (383 k€)**

  Participants: Martin Genet, Philippe Moireau, Dominique Chapelle, Madhi Manoochehrtayebi.

  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, (154 k€)**

Participants: Philippe Moireau, Sébastien Imperiale, Tiphaine Delaunay.

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 estimation algorithms for infinite-dimensional systems arising from hyperbolic PDE systems.

- **ANR SIMR (97 k€)**

Participants: Philippe Moireau, Dominique Chapelle, Jérôme Diaz, Martin Genet.

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 (55k€)**

Participants: Martin Genet, Collin Laville.

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.

- **ANR Elastoheart (212k€)**

Participants: Philippe Moireau, Sébastien Imperiale, Dominique Chapelle.

The objective of this project is to develop a comprehensive mathematical and numerical modeling (direct and inverse) of 3D Shear-Wave (SW) propagation in cardiac realistic physiological models, and to demonstrate in vivo that shear velocity can assess important cardiac function and characteristics in experimental pathological models and in patients.

- **ANR CorMecha (191k€)**,

Participants: Jean-Marc Allain.

This project aims at: (i) setting up an atlas of cornea 3D structure from the sub-micrometer scale (intra-lamellar organization of collagen fibrils) to the millimeter-centimeter scale, (ii) accurately measuring the biomechanical properties linked to this structure in physiological conditions and in various pathological conditions, and (iii) building a model of corneal biomechanics based on these microstructural and macroscopic data in order to provide insight into the role of specific stromal structures. It relies on the highly original combination of well-controlled inflation device and state-of-the-art imaging setups, mainly polarization-resolved second harmonic generation microscope. Specific bioimage informatics tools and pipelines will be developed to process the very large data sets (Gb to Tb) generated by this new device and quantify clinically-relevant parameters of interest. Advanced statistical analysis of the series of clinical, structural and mechanical data obtained on the same cornea will then be performed for normal, keratoconic and photo-ablated corneas. The ultimate goals are twofold: (i) to translate the structural features observed with advanced research microscopes into easily-detectable features using commonly used techniques in clinical ophthalmology, in order to enable the diagnosis of structural defects related to defective mechanical properties; (ii) to develop a patient-specific simplified model to serve as a predictive tool by clinicians, mainly to improve refractive surgery procedures.

10.2.3 Other funding

- AMIES Project WithCardiacModels, in parthnership with Withings company (98k€)

Participants: Philippe Moireau, Jérôme Diaz, François Kimmig, Dominique Chapelle.

Connected objects are now emerging as an effective tool for non-invasive monitoring of the general state of health day and night. In order to process the generated data streams, many signal processing and learning algorithms are required to reconstruct actionable outputs about the user's health. Many objects providing interesting cardiovascular information for the general public already exist on the market, such as the Withings Scanwatch, which measures an ECG and detects atrial fibrillation.

In this project, we propose to process the measurements collected by data assimilation approaches based on the modeling of the underlying biophysical processes. These models of the cardiovascular system and the real-time estimation methods developed by the M3DISIM team are ideally suited to the distal data on cardiovascular functioning collected by Withings. New algorithms for estimating the physiology of subjects respecting the constraints of optimal regularization of signals, detection of defects by searching for causality, privacy on shared data will make it possible tomorrow to detect deterioration in the cardiovascular health of heart failure patients, for example.

11 Dissemination

Member of the conference program committees

- P. Moireau, member of the conference program committees of World Congress of Biomechanics B2022

Reviewer

- M. Genet, reviewer for the 46th Congress of the Biomechanics Francophone Society

11.0.1 Journal

- D. Chapelle, member of the editorial boards of Computers & Structures, and ESAIM:M2AN
- P. Moireau, Guest Editor for the journal Maths-in-Action

Reviewer - reviewing activities

- J.-M. Allain, reviewer for Acta Biomateriala, Journal of the Mechanics and Physics of Solids.
- M. Genet, reviewer for “Biomechanics and Modeling in Mechanobiology”, “Journal of Computational Physics” and “Frontiers in Bioengineering and Biotechnology”
- S. Imperiale, reviewer for “applicable analysis” and “SIAM SINUM”
- P. Moireau, reviewer for “IJNMBE” and “Environmental Modeling & Assessment”

11.0.2 Invited talks

- J.-M. Allain, invited seminars at LiPhy, U. Grenoble-Alpes (15 June)
- D. Chapelle, invited seminar at Académie des Sciences (section mécanique et informatique, 30 Nov.)
- F. Kimmig, invited seminars at Jean Mandel Seminar (24.06.2021) and at FIMH2021 MIS-C special session (24.06.2021) and Journée rencontre Onde - asymptotique - problèmes inverses (03.12.2021)
- M. Genet, invited seminars at the 2nd Biomedical Engineering (BME) Symposium, Institut Polytechnique de Paris, Palaiseau (June) and at the Multiscale Modeling and Simulation Laboratory (MSME, CNRS/UPEC/UPEM), Créteil (June)
- P. Moireau, invited seminar at SantExpo (9.03.2021) and at CEMRACS 2021, CIRM Marseille, (27.07.2021), and Journées Poems-Defi-M3disim (3.12.2021)

11.0.3 Scientific expertise

- J.-M. Allain, Reviewer for ANR
- S. Imperiale, Reviewer for ANR
- P. Moireau, Member of the Jury ANR CE46 2020-2021
- P. Moireau, Member of the expert group PEPR Santé Numérique (multiscale models)

11.0.4 Research administration

- J.-M. Allain, Scientific Advisory Board, chair BioMecAM
- J.-M. Allain, in charge of the axis « mécanique et matériaux pour le bio » at the Fédération Francilienne de Mécanique
- D. Chapelle, Scientific head of the joint APHP-Inria laboratory "Daniel Bernoulli"
- P. Le Tallec, Dean of the bachelor programme at Ecole Polytechnique
- P. Moireau, Member of the steering committee of Department of Mathematics, Institut Polytechnique de Paris
- P. Moireau, Member of the LMS board
- P. Moireau, Member of the Commission scientifique and technique, Corps des Mines

11.1 Teaching - Supervision - Juries

11.1.1 Teaching

- All-level: J.-M. Allain, referent for disability at Ecole polytechnique, France
- Bachelor: J. Manganotti, “Mechanics and Heat”, 32h, L1, École Polytechnique, France
- Bachelor: J. Manganotti, ‘Maths in Practise Calculus”, L1, École Polytechnique, France
- Bachelor: C. Giraudet, “PHY101 - Physics I: Mechanics and Heat”, 32h, L1, Ecole Polytechnique, France
- Bachelor: J.-M. Allain, Academic advisor for mechanics at the Bachelor program 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
- Master: M. Barré and T. Delaunay, “ANN201 – La méthode des éléments finis“, 14h, M1, ENSTA Paris, France
- Master: J.-M. Allain, “Statistical mechanics: application to cell motility”, 20h, M2, Ecole Polytechnique, France
- Master: J.-M. Allain, “Introduction à la mécanique des milieux continus”, 30h, M2, Ecole Polytechnique, France
- Master: J.-M. Allain, “Biosolids”, 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 discrétisation 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

11.1.2 Supervision

- M1: O. Mouzhi, “Modélisation numérique et asymptotique d’un problème d’élastodynamique sur une sphere mince”, supervisor: S. Imperiale, Ensta, Defended September 2021
- M1: É. Strauch-Hausser, “Validation of a biophysical cardiovascular system model calibration algorithm and sensitivity analysis”, supervisors: F. Kimmig, École polytechnique, Defended May 2021
- M2: G. Merlini, “Patient specific models with incomplete and mixed data: the example of the human cornea”, supervisors: C. Giraudet and P. Le Tallec, Politecnico di Milano, defended July 2021

- M2: L.-P. Chaintron “Stochastic modelling for striated muscle and asymptotic filtering”, supervisor: P. Moireau, Defended Sept 2021
- PhD A. Le Gall, defended on 12 Sept, “Coupling data measured in operating theatre with patient-specific biomechanical model of heart and vessels to augment haemodynamic monitoring of patients undergoing general anaesthesia”, supervisors: D. Chapelle, R. Chabiniok and E. Gayat (APHP-Lariboisière)
- PhD: N. Tueni, “Multiscale modeling and experiment of the myocardium”, defended in 06/2021, supervisors: M. Genet and J.-M. Allain
- PhD in progress: E. Berberoglu, “Magnetic Resonance Imaging of Myocardial Strain and Image-Guided Computational Mechanics of the Heart”, started 02/2017, supervisors: M. Genet and S. Kozerke (ETH Zurich)
- PhD in progress: M. Gusseva, “Patient-specific cardiovascular biomechanical modeling to augment interpretation of clinical data and assist planning interventions for patients with congenital heart disease”, started in December 2017, supervisors: R. Chabiniok, D. Chapelle, T. Hussain (UTSW)
- PhD in progress: M. Manoochertayebi, “Manyscale modeling of lung poromechanics”, started 11/2020, supervisors: M. Genet, A. Bel-Brunon (INSA-Lyon) and D. Chapelle
- PhD in progress: A. Peyraut, “Modeling and estimation of lung poromechanics”, started 10/2021, supervisors: M. Genet
- PhD in progress: C. Giraudet, “Cornea biomechanics”, started 10/2018; supervisors: J.-M. Allain and P. Le Tallec
- PhD in progress: Bertrand Leturcq " Réductions de modèles thermomécaniques non-linéaires pour l’évaluation des déformations du cœur de réacteur", started in November 2017 in collaboration with CEA DEN.
- PhD: H. Methenni, “Mathematical modelling and numerical method for the simulation of ultrasound structural health monitoring of composite plates”, started 2017 defended early 2021, supervised by S. Imperiale, S. Fliss from Inria Saclay - POems and A. Imperiale from CEA-List.
- PhD in progress: J. Manganotti, “Mathematical modeling and numerical simulation of left heart hemodynamics”, started 2019, supervised by S. Imperiale and P. Moireau.
- PhD in progress: A. Beni Hamad, “Modeling and numerical simulation of electromagnetic waves in coaxial cables”, started 2019, supervised by S. Imperiale and P. Joly from Inria Saclay - POems.
- PhD in progress: T. Delaunay, “Adaptative observers for propagative systems and associated discretization: formulation and analysis”, started 2020, supervised by S. Imperiale and P. Moireau.
- PhD in progress: A. Dalmora, “ Modeling and estimation by data-assimilation of pre-stresses in non destructive testing experiments”, started 2020, supervised by A. Imperiale, S. Imperiale and P. Moireau.
- PhD in progress: J. Dubois, “Water waves and acoustic waves in the oceans: from modelisation to early warning systems”, started 2020, supervised by S. Imperiale and J. Sainte-Marie from Inria Paris - Ange
- PhD in progress: G. Merlini, “Mechanical and numerical modelling of elastographic measurements in the cornea”, started 2021, supervised by J.-M. Allain and S. Imperiale.
- PhD in progress: M. Barré, “Mathematical framework for biological tissue perfusion modeling and simulation”,started 2020, supervised by C. Grandmont from Inria-Paris - Commedia and P. Moireau.

11.1.3 Juries

- J.-M. Allain, Habilitation Jury of J. Etienne, Université Grenoble-Alpes, President: Irina Mihalcescu, June
- J.-M. Allain, PhD Jury of Q. Qu, PSL Université de Paris, PhD Advisor: Martine Ben Amar, July
- J.-M. Allain, PhD Jury of A. Hemmati, Université Paris-Saclay, PhD Advisor: E. Vennat and N. Schmidt, December
- D. Chapelle, PhD Jury of N. Golse (Université Paris-Saclay, 20 Sept.)

11.2 Popularization

- J. Manganotti, supervision of a research activity for the RJMI (Rendez-vous des Jeunes Mathématiciennes et Informaticiennes) organized by Inria. February 25th and 26th.
- J. Manganotti, speaker at the round table "Parcours et carrière" for the WiDS (Women in Data Science Paris Saclay 2021). June 3rd.
- "Fête de la Science" at IP Paris, Organization of the event (logistic) and realization of a promoting video of the edition (script writing, participants interviews and realization of the voice-over). October 8-9th.
- IP Paris Science Forum, Organization of the poster session by the PhD students of the IP Paris doctoral school, October 21st.
- M. Barré, Organization committee member of the *Rendez-vous des Jeunes Mathématiciennes et Informaticiennes* at Inria Saclay (online). February 25th and 26th
- M. Barré, Storyboard of a comic strip entitled "Les maths font battre mon coeur" as part of the project *La recherche sort de sa bulle* led by La Diagonale Paris-Saclay
- M. Barré and T. Delaunay, Screenwriting of a video entitled "Modélisation mathématique et simulation numérique" that was presented at the *Village des sciences* of Paris-Saclay (online), October
- M. Barré and T. Delaunay, Leading of a scientific activity at the *Fête des Sciences* organized by IP Paris, October 8th and 9th
- T. Delaunay, conference speaker at Créteil Academy to secondary school and high school students. October 16th.
- P. Moireau, F. Kimmig, F. Vallée, D. Chapelle, video promoting the team research activites at SantExpo 2021
- Work of P. Moireau on COVID estimation was discussed in newspapers Le Monde (28/07/2021) and Liberation (2/12/2021)

11.2.1 Internal or external Inria responsibilities

- S. Imperiale, co-head of “commission d’aide au development technologique”.

12 Scientific production

12.1 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.

12.2 Publications of the year

International journals

[12] 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.

[13] F. Álvarez-Barrientos, D. E. Hurtado and M. Genet. 'Pressure-driven micro-poro-mechanics: A variational framework for modeling the response of porous materials'. In: *International Journal of Engineering Science* 169 (2021), p. 103586. DOI: 10.1016/j.ijengsci.2021.103586. URL: https://hal.archives-ouvertes.fr/hal-03364755.

[14] 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'. In: *SEMA SIMAI Springer Series* (21st May 2021), pp. 209–250. URL: https://hal.inria.fr/hal-02493518.

[15] J. Cartailler, C. Touchard, P. Parutto, E. Gayat, C. Paquet and F. Vallée. 'Brain fragility among middle-aged and elderly patients from electroencephalogram during induction of anaesthesia'. In: *European Journal of Anaesthesiology* 38.12 (2021), pp. 1304–1306. DOI: 10.1097/EJA.0000000000001524. URL: https://hal.inria.fr/hal-03487108.

[16] D. A. Castellanos, K. Škardová, A. Bhattaru, E. Berberoglu, G. Greil, A. Tandon, J. Dillenbeck, B. Burkhardt, T. Hussain, M. Genet and R. Chabiniok. 'Left ventricular torsion obtained using equilibrated warping in patients with repaired Tetralogy of Fallot'. In: *Pediatric Cardiology* 42.6 (2021), pp. 1275–1283. DOI: 10.1007/s00246-021-02608-y. URL: https://hal.archives-ouvertes.fr/hal-03204943.

[17] J. Chabassier and S. Imperiale. 'Construction and convergence analysis of conservative second order local time discretisation for linear wave equations'. In: *ESAIM: Mathematical Modelling and Numerical Analysis* 55.4 (July 2021), pp. 1507–1543. DOI: 10.1051/m2an/2021030. URL: https://hal.archives-ouvertes.fr/hal-03309010.

[18] R. Chabiniok, J. Hron, A. Jarolímová, J. Málek, K. R. Rajagopal, K. Rajagopal, H. Švihlová and K. Tůma. 'A benchmark problem to evaluate implementational issues for three-dimensional flows of incompressible fluids subject to slip boundary conditions'. In: *Applications in Engineering Science* 6 (11th Feb. 2021). DOI: 10.1016/j.apples.2021.100038. URL: https://hal.archives-ouvertes.fr/hal-03178710.

[19] F. Clément, F. Robin and R. Yvinec. 'Stochastic nonlinear model for somatic cell population dynamics during ovarian follicle activation'. In: *Journal of Mathematical Biology* 82.3 (2021), pp. 1–52. DOI: 10.1007/s00285-021-01561-. URL: https://hal.inria.fr/hal-02057983.

[20] M. COUTROT, E. Dudoignon, J. J. Md, E. Gayat, F. Vallee and F. Depret. 'Perfusion Index: Physical Principles, Physiological Meanings and Clinical Implications in Anaesthesia and Critical Care'. In: *Anaesthesia Critical Care & Pain Medicine* (2021). URL: https://hal.inria.fr/hal-03475091.

[21] C. Dupont, M. Vidrascu, P. Le Tallec, D. Barthès-Biesel and A.-V. Salsac. 'Modelling the fluid-structure interactions of a capsule using a nonlinear thin shell model: effect of wall thickness'. In: *Journal of Fluids and Structures* (2021). URL: https://hal.utc.fr/hal-03409766.

[22] M. Gusseva, T. Hussain, C. H. Friesen, P. Moireau, A. Tandon, C. Patte, M. Genet, K. Hasbani, G. Greil, D. Chapelle and R. Chabiniok. 'Biomechanical Modeling to Inform Pulmonary Valve Replacement in Tetralogy of Fallot Patients after Complete Repair'. In: *Canadian Journal of Cardiology* 37 (1st Nov. 2021), pp. 1798–1807. DOI: 10.1016/j.cjca.2021.06.018. URL: https://hal.inria.fr/hal-03313844.

[23] M. Gusseva, T. Hussain, C. Hancock Friesen, G. Greil, D. Chapelle and R. Chabiniok. 'Prediction of Ventricular Mechanics After Pulmonary Valve Replacement in Tetralogy of Fallot by Biomechanical Modeling: A Step Towards Precision Healthcare'. In: *Annals of Biomedical Engineering* 49.12 (1st Dec. 2021), pp. 3339–3348. DOI: 10.1007/s10439-021-02895-9. URL: https://hal.archives-ouvertes.fr/hal-03462902.

[24] 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.

[25] F. Kimmig, P. Moireau and D. Chapelle. 'Hierarchical modeling of length-dependent force generation in cardiac muscles and associated thermodynamically-consistent numerical schemes'. In: *Computational Mechanics* 68 (13th July 2021), pp. 885–920. DOI: 10.1007/s00466-021-02051-z. URL: https://hal.archives-ouvertes.fr/hal-03260494.

[26] J. Manganotti, F. Caforio, F. Kimmig, P. Moireau and S. Imperiale. 'Coupling reduced-order blood flow and cardiac models through energy-consistent strategies: modeling and discretization'. In: *Advanced Modeling and Simulation in Engineering Sciences* 8 (28th Sept. 2021). DOI: 10.1186/s40323-021-00206-4. URL: https://hal.archives-ouvertes.fr/hal-03382705.

[27] D. Marlevi, J. Mariscal-Harana, N. Burris, J. Sotelo, B. Ruijsink, M. Hadjicharalambous, L. Asner, E. Sammut, R. Chabiniok, S. Uribe, R. Winter, P. Lamata, J. Alastruey and D. Nordsletten. 'Altered Aortic Hemodynamics and Relative Pressure in Patients with Dilated Cardiomyopathy'. In: *Journal of Cardiovascular Translational Research* (9th Dec. 2021). DOI: 10.1007/s12265-021-10181-1. URL: https://hal.archives-ouvertes.fr/hal-03482480.

[28] C. A. Mauger, S. Govil, R. Chabiniok, K. Gilbert, S. Hegde, T. Hussain, A. D. Mcculloch, C. J. Occleshaw, J. Omens, J. C. Perry, K. Pushparajah, A. Suinesiaputra, L. Zhong and A. A. Young. 'Right-left ventricular shape variations in tetralogy of Fallot: associations with pulmonary regurgitation'. In: *Journal of Cardiovascular Magnetic Resonance* 23.1 (7th Oct. 2021). DOI: 10.1186/s12968-021-00780-x. URL: https://hal.archives-ouvertes.fr/hal-03369697.

[29] 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* 40.4 (2021), pp. 1240–1252. URL: https://hal.inria.fr/hal-03112239.

[30] C. Patte, M. Genet and D. Chapelle. 'A quasi-static poromechanical model of the lungs'. In: *Biomechanics and Modeling in Mechanobiology* (2022). DOI: 10.1007/s10237-021-01547-0. URL: https://hal.inria.fr/hal-03474200.

[31] F. Regazzoni, D. Chapelle and P. Moireau. 'Combining Data Assimilation and Machine Learning to build data-driven models for unknown long time dynamics - Applications in cardiovascular modeling'. In: *International Journal for Numerical Methods in Biomedical Engineering* 37.7 (July 2021). DOI: 10.1002/cnm.3471. URL: https://hal.inria.fr/hal-03207037.

[32] 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.

[33] J. Stimm, S. Buoso, E. Berberoğlu, S. Kozerke, M. Genet and C. Stoeck. 'A 3D personalized cardiac myocyte aggregate orientation model using MRI data-driven low-rank basis functions'. In: *Medical Image Analysis* 71 (July 2021), p. 102064. DOI: 10.1016/j.media.2021.102064. URL: https://hal.archives-ouvertes.fr/hal-03364742.

International peer-reviewed conferences

[34] M. Gusseva, J. S. Greer, D. A. Castellanos, M. Abdelghafar Hussein, G. Greil, S. R. Veeram Reddy, T. Hussain, D. Chapelle and R. Chabiniok. 'Model-Assisted Time-Synchronization of Cardiac MR Image and Catheter Pressure Data'. In: *Proceedings of Functional Imaging and Modeling of Heart (FIMH 2021)*. FIMH 2021 - Functional Imaging and Modeling of Heart (FIMH 2021). Stanford, CA, United States, 18th June 2021, pp. 362–372. DOI: 10.1007/978-3-030-78710-3_35. URL: https://hal.inria.fr/hal-03313857.

Conferences without proceedings

[35] E. Berberoglu, C. Stoeck, S. Kozerke and M. Genet. 'Quantification of Left Ventricular Strain by Joint Analysis of 3D Tagging and Cine MR Images'. In: 2021 ISMRM & SMRT Annual Meeting & Exhibition. Online, United States, 2021. URL: https://hal.archives-ouvertes.fr/hal-03364768.

[36] M. Genet, C. Patte, C. Fetita, P.-Y. Brillet and D. Chapelle. 'Personalized Pulmonary Poromechanics in Health and Idiopathic Pulmonary Fibrosis'. In: 17th International Symposium on Computer Methods in Biomechanics and Biomedical Engineering (CMBBE 2021). Bonn, Germany, 2021. URL: https://hal.archives-ouvertes.fr/hal-03364765.

Scientific book chapters

[37] R. Chabiniok, K. Škardová, R. Galabov, P. Eichler, M. Gusseva, J. Janoušek, R. Fučík, J. Tintěra, T. Oberhuber and T. Hussain. 'Translational Cardiovascular Modeling: Tetralogy of Fallot and Modeling of Diseases'. In: *Modeling Biomaterials*. 2021. URL: https://hal.archives-ouvertes.fr/hal-03363107.

Doctoral dissertations and habilitation theses

[38] A. Le Gall. 'Coupling data measured in operating theatre with patient-specific biomechanical model of heart and vessels to augment haemodynamic monitoring of patients undergoing general anaesthesia.' Institut polytechnique de Paris, 12th Oct. 2021. URL: https://hal.archives-ouvertes.fr/tel-03501138.

[39] N. Tueni. 'Multiscale experimental and theoretical investigation of the structure-property relationships in the myocardium'. Institut Polytechnique de Paris, 1st July 2021. URL: https://tel.archives-ouvertes.fr/tel-03330458.

Reports & preprints

[40] M. Barré, C. Grandmont and P. Moireau. *Analysis of a linearized poromechanics model for incompressible and nearly incompressible materials*. 23rd Dec. 2021. URL: https://hal.inria.fr/hal-03501526.

[41] A. Collin, M. Prague and P. Moireau. *Estimation for dynamical systems using a population-based Kalman filter – Applications in computational biology*. 10th Nov. 2021. URL: https://hal.inria.fr/hal-02869347.

[42] C. Giraudet, J. Diaz, P. Le Tallec and J.-M. Allain. *Multiscale mechanical model based on patient-specific geometry: application to early keratoconus development*. 3rd Dec. 2021. URL: https://hal.archives-ouvertes.fr/hal-03437194.

[43] S. Imperiale. *Asymptotic analysis of abstract two-scale wave propagation problems*. 29th July 2021. URL: https://hal.inria.fr/hal-03306856.