IN PARTNERSHIP WITH:
Ecole Polytechnique

Activity Report 2019

Project-Team M3DISIM

Mathematical and Mechanical Modeling with Data Interaction in Simulations for Medicine

IN COLLABORATION WITH: Laboratoire de Mécanique des Solides

RESEARCH CENTER
Saclay - Île-de-France

THEME
Modeling and Control for Life Sciences

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

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1. Team, Visitors, External Collaborators

Research Scientists

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Sébastien Imperiale [Inria, Researcher]

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Martin Genet [Ecole polytechnique, Associate Professor]
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Romain Yvinec [INRA]
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Florent Wijanto [PhD Student, from Jul 2019 until Sep 2019]

2. Overall Objectives

2.1. Overall Objectives

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

3. Research Program

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

Over the past decade, we have laid out the foundations of a multi-scale 3D model of the cardiac mechanical contraction responding to electrical activation. Several collaborations have been crucial in this enterprise, see below references. By integrating this formulation with adapted numerical methods, we are now able to represent the whole organ behavior in interaction with the blood during complete heart beats. This subject was our first achievement to combine a deep understanding of the underlying physics and physiology and our constant concern of proposing well-posed mathematical formulations and adequate numerical discretizations. In fact, we have shown that our model satisfies the essential thermo-mechanical laws, and in particular the energy balance, and proposed compatible numerical schemes that – in consequence – can be rigorously analyzed, see [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. Highlights of the Year

4.1. Highlights of the Year

The team obtained 3 ANR fundings this year: LungManyScale, ODISSE and SIMR.

5. New Software and Platforms

5.1. 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.

- Participants: Radomir Chabiniok, Gautier Bureau, Martin Genet, Federica Caforio, Ustim Khristenko, Dominique Chapelle and Philippe Moireau
- Contact: Philippe Moireau
- URL: https://raweb.inria.fr/rapportsactivite/RA2013/m3disim/uid14.html

5.2. Verdandi

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

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

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

5.3. 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

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

5.4. MoReFEM

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)

- Participants: Philippe Moireau, Patrick Le Tallec, Antoine Olivier, Dominique Chapelle, Ustim Khristenko, François Kimmig, Gautier Bureau and Sébastien Gilles
- Contact: Sébastien Gilles
- URL: https://gitlab.inria.fr/MoReFEM

6. New Results

6.1. Mathematical and Mechanical Modeling

6.1.1. Stochastic modeling of chemical-mechanical coupling in striated muscles

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

In [18] we propose a chemical–mechanical model of myosin heads in sarcomeres, within the classical description of rigid sliding filaments. In our case, myosin heads have two mechanical degrees-of-freedom (dofs)—one of which associated with the so-called power stroke—and two possible chemical states, i.e., bound to an actin site or not. Our major motivations are twofold: (1) to derive a multiscale coupled chemical–mechanical model and (2) to thus account—at the macroscopic scale—for mechanical phenomena that are out of reach for classical muscle models. This model is first written in the form of Langevin stochastic equations, and we are then able to obtain the corresponding Fokker–Planck partial differential equations governing the probability density functions associated with the mechanical dofs and chemical states. This second form is important, as it allows to monitor muscle energetics and also to compare our model with classical ones, such as the Huxley'57 model to which our equations are shown to reduce under two different types of simplifying assumptions. This provides insight and gives a Langevin form for Huxley'57. We then show how we can calibrate our model based on experimental data—taken here for skeletal muscles—and numerical simulations demonstrate the adequacy of the model to represent complex physiological phenomena, in particular the fast isometric transients in which the power stroke is known to have a crucial role, thus circumventing a limitation of many classical models.

6.1.2. Upscaling of elastic network models

Participant: Patrick Le Tallec.

This work is done in collaboration with Julie Diani from École Polytechnique. The purpose of the approach is to develop general upscaling strategy for deriving macroscopic constitutive laws for rubberlike materials from the knowledge of the network distribution and a mechanical description of the individual chains and of their free energy. It is based on a variational approach in which the microscopic configuration is described by the position of the crosslinks and is obtained not by an affine assumption but by minimizing the corresponding free energy on stochastic large Representative Volume Elements with adequate boundary conditions. This general framework is then approximated by using a microsphere (directional) description of the network and by performing a local minimisation of the network free energy on this simplified configuration space under a maximal advance path kinematic constraint. This approximation framework takes into account anisotropic damage and is extended to handle situations with tube like constraints and stress induced cristallisation. For more detail see [23].

6.1.3. Stochastic construction of surrogate multiphase materials

Participant: Patrick Le Tallec.

Random microstructures of heterogeneous materials play a crucial role in the material macroscopic behavior and in predictions of its effective properties. A common approach to modeling random multiphase materials is to develop so-called surrogate models approximating statistical features of the material. However, the surrogate models used in fatigue analysis usually employ simple microstructure, consisting of ideal geometries such as ellipsoidal inclusions, which generally does not capture complex geometries. In our work , we introduce a simple but flexible surrogate microstructure model for two-phase materials through a level-cut of a Gaussian random field with covariance of Matern class. In addition to the traditional morphology descriptors such as porosity, size and aspect ratio of inclusions, our approach provides control of the regularity of the inclusions interface and sphericity. These parameters are estimated from a small number of real material images using Bayesian inversion. An efficient process of evaluating the samples, based on the Fast Fourier Transform, makes possible the use of Monte-Carlo methods to estimate statistical properties for the quantities of interest in a given material class. This work in progress is done in collaboration with Andrei Constantinescu (École Polytechnique), Ustim Khristenko and Barbara Wohlmuth (Technical University Munich) and Tinsley Oden (University of Texas at Austin). This work has been submitted for publication in an international journal.

6.1.4. Apprehending the effects of mechanical deformations in cardiac electrophysiology – A homogenization approach

Participants: Annabelle Collin [MONC], Sébastien Imperiale, Philippe Moireau, Jean-Frédéric Gerbeau [Inria Siège], Dominique Chapelle [correspondant].

In this work [22], we follow a formal homogenization approach to investigate the effects of mechanical deformations in electrophysiology models relying on a bidomain description of ionic motion at the microscopic level. To that purpose, we extend these microscopic equations to take into account the mechanical deformations, and proceed by recasting the problem in the frame- work of classical two-scale homogenization in periodic media, and identifying the equations satisfied by the first coefficients in the formal expansions. The homogenized equations reveal some interesting effects related to the microstructure – and associated with a specific cell problem to be solved to obtain the macroscopic conductivity tensors – in which mechanical deformations play a non-trivial role, i.e. do not simply lead to a standard bidomain problem posed in the deformed configuration. We then present detailed numerical illustrations of the homogenized model with coupled cardiac electrical-mechanical simulations – all the way to ECG simulations – albeit without taking into account the abundantly-investigated effect of mechanical deformations in ionic models, in order to focus here on other effects. And in fact our numerical results indicate that these other effects are numerically of a comparable order, and therefore cannot be disregarded.

6.1.5. Patient-specific pulmonary mechanics - Modelling and estimation. Application to pulmonary fibrosis.

Participants: Cecile Patte [correspondant], Martin Genet, Dominique Chapelle.

Interstitial pulmonary diseases, like Idiopathic Pulmonary Fibrosis (IPF), affect the alveolar structure of lung tissue, which impacts lung mechanical properties and pulmonary functions. In this work [43], we aim to better understand the pulmonary mechanics in order to improve IPF diagnosis. We developped a poromechanical model for the lung at the organ scale and at the breathing scale. This model is then used to estimate regional mechanical parameters based on clinical data. In the future, this process can be used as an augmented diagnosis tool for clinicians. This work has been presented at the CSMA conference.

6.1.6. Energy preserving cardiac circulation models: formulation, reduction, coupling, inversion, and discretization

Participants: Jessica Manganotti, Philippe Moireau, Sébastien Imperiale [correspondant], Miguel Fernandez [Inria Paris, COMMEDIA].

The modeling of the heart cannot be satisfying if not coupled to the body circulation, and at least to the arterial circulation, which is its direct output "boundary condition". But more importantly in the clinical context, it is still difficult – ant very invasive – to access the ventricular pressure, which is absolutely necessary for specifying the heart activity. By comparison, more and more devices allow to register non-invasively a distal pressure, for instance at the wrist or the finger, which could be used to estimate the ventricular pressure by inversion of a well adapted arterial circulation model. Such relation is of major interest for clinicians, for example anesthetists, since it could allow real-time monitoring and prediction of the effects of injected drugs during a clinical intervention. Models of the arterial circulation is a well-known subject where dimension reduction has been widely studied for more than half a century. However, the question remains of formulating energy-consistent formulations that can be consistently maintained during the reduction, when coupled to a heart model, and also when discretized. Yet the question is crucial for a better understanding of the physical phenomena of blood flow ejection from the heart as well as the propagation in the arterial network. Moreover, as these models are non-linear, energy-preserving approaches are one of the few tools at our disposal to mathematically justify modeling, discretization or inversion approaches. Finally, inverting this unsteady model for estimation purposes of medical data also benefits from energy-preserving formulation as the inverse approach should also satisfy some stability properties. The subject here is twofold and part of the thesis of J. Manganotti. First we plan to develop accurate models, coupling strategies and robust numerical methods of the arterial network propagation coupled to the heart. Second, we want to develop observer-based strategies that will allow to easily feed these models with measurements in order to perform state estimation of hidden variables or identify key biophysical parameters.

6.1.7. Hierarchical modeling of force generation in cardiac muscle

Participants: Matthieu Caruel, François Kimmig [correspondant].

Performing physiologically relevant simulations of the beating heart in clinical context requires to develop detailed models of the microscale force generation process. These models however may be difficult to implement in practice due to their high computational costs and complex calibration. We propose a hierarchy of three interconnected cardiac muscle contraction models – from the more refined to the more simplified – that are rigorously and systematically related with each other, offering a way to select, for a specific application, the model that yields the best trade-off between physiological fidelity, computational cost and calibration complexity. Our starting model takes into account the stochastic dynamics of the molecular motors force producing conformational changes– and in particular the power stroke – and captures all the timescales of appearing in classical experimental isotonic responses of a heart papillary muscle submitted to rapid load changes. Adiabatic elimination of fast relaxing variables of the stochastic model yields a formulation based on partial differential equations (PDEs) that falls into the family of the Huxley'57 model, while embedding some properties of the process occurring at the fastest timescales. The third family of models is deduced from the PDE model by making minimal assumptions on the parameters, which leads to a computationally light formulation based on ordinary differential equations only. The three models families are compared to the same set of experimental data to systematically assess what physiological indicators can be reproduced or not and how these indicators constrain the model parameters. Finally, we discuss the applicability of these models for heart simulation. This work has been submitted for publication in an international journal.

6.1.8. A relaxed growth modeling framework for controlling growth-induced residual stresses

Participant: Martin Genet.

Background Constitutive models of the mechanical response of soft tissues have been established and are widely accepted, but models of soft tissues remodeling are more controversial. Specifically for growth, one important question arises pertaining to residual stresses: existing growth models inevitably introduce residual stresses, but it is not entirely clear if this is physiological or merely an artifact of the modeling framework. As a consequence, in simulating growth, some authors have chosen to keep growth-induced residual stresses, and others have chosen to remove them. **Methods** In this work, we introduce a novel "relaxed growth" framework allowing for a fine control of the amount of residual stresses generated during tissue growth. It is a direct extension of the classical framework of the multiplicative decomposition of the

transformation gradient, to which an additional sub-transformation is introduced in order to let the original unloaded configuration evolve, hence relieving some residual stresses. We provide multiple illustrations of the framework mechanical response, on time-driven constrained growth as well as the strain-driven growth problem of the artery under internal pressure, including the opening angle experiment. **Findings** The novel relaxed growth modeling framework introduced in this paper allows for a better control of growth-induced residual stresses compared to standard growth models based on the multiplicative decomposition of the transformation gradient. **Interpretation** Growth-induced residual stresses should be better handled in soft tissues biomechanical models, especially in patient-specific models of diseased organs that are aimed at augmented diagnosis and treatment optimization. See [27] for more detail.

6.1.9. Multiscale population dynamics in reproductive biology: singular perturbation reduction in deterministic and stochastic models

Participants: Frédérique Clément [correspondant], Romain Yvinec.

During the supervision of a CEMRACS2018 project performed by Céline Bonnet (CMAP) and Keltoum Chahour (LERMA and JLAD), we have described (with Marie Postel, Sorbonne Université and Romain Yvinec, INRA) different modeling approaches for ovarian follicle population dynamics, based on either ordinary (ODE), partial (PDE) or stochastic (SDE) differential equations, and accounting for interactions between follicles [50]. We have put a special focus on representing the population-level feedback exerted by growing ovarian follicles onto the activation of quiescent follicles. We have taken advantage of the timescale difference existing between the growth and activation processes to apply model reduction techniques in the framework of singular perturbations. We have first studied the linear versions of the models to derive theoretical results on the convergence to the limit models. In the nonlinear cases, we have provided detailed numerical evidence of convergence to the limit behavior. We have reproduced the main semi-quantitative features characterizing the ovarian follicle pool, namely a bimodal distribution of the whole population, and a slope break in the decay of the quiescent pool with aging.

6.1.10. Stochastic nonlinear model for somatic cell population dynamics during ovarian follicle activation

Participants: Frédérique Clément [correspondant], Frédérique Robin, Romain Yvinec.

In mammals, female germ cells are sheltered within somatic structures called ovarian follicles, which remain in a quiescent state until they get activated, all along reproductive life. We have investigated the sequence of somatic cell events occurring just after follicle activation [54]. We have introduced a nonlinear stochastic model accounting for the joint dynamics of two cell types, either precursor or proliferative cells. The initial precursor cell population transitions progressively to a proliferative cell population, by both spontaneous and self-amplified processes. In the meantime, the proliferative cell population may start either a linear or exponential growing phase. A key issue is to determine whether cell proliferation is concomitant or posterior to cell transition, and to assess both the time needed for all precursor cells to complete transition and the corresponding increase in the cell number with respect to the initial cell number. Using the probabilistic theory of first passage times, we have designed a numerical scheme based on a rigorous Finite State Projection and coupling techniques to assess the mean extinction time and the cell number at extinction time. We have also obtained analytical formulas for an approximating branching process. We have calibrated the model parameters using an exact likelihood approach using both experimental and in-silico datasets. We have carried out a comprehensive comparison between the initial model and a series of submodels, which help to select the critical cell events taking place during activation. We have finally interpreted these results from a biological viewpoint.

6.1.11. A multiscale mathematical model of cell dynamics during neurogenesis in the mouse cerebral cortex

Participant: Frédérique Clément.

This work is a collaboration with Marie Postel and Sylvie Schneider-Maunoury (Sorbonne Université), Alice Karam (Sorbonne Universités), Guillaume Pézeron (MNHN).

Neurogenesis in the murine cerebral cortex involves the coordinated divisions of two main types of progenitor cells, whose numbers, division modes and cell cycle durations set up the final neuronal output. In this work [33] we aim at understanding the respective roles of these factors in the neurogenesis process, we have combined experimental in vivo studies with mathematical modeling and numerical simulations of the dynamics of neural progenitor cells. A special focus is put on the population of intermediate progenitors (IPs), a transit amplifying progenitor type critically involved in the size of the final neuron pool. A multiscale formalism describing IP dynamics allows one to track the progression of cells along the subsequent phases of the cell cycle, as well as the temporal evolution of the different cell numbers. Our model takes into account the dividing apical progenitors (AP) engaged into neurogenesis, both neurogenic and proliferative IPs, and the newborn neurons. The transfer rates from one population to another are subject to the mode of division (symmetric, asymmetric, neurogenic) and may be time-varying. The model outputs have been successfully fitted to experimental cell numbers from mouse embryos at different stages of cortical development, taking into account IPs and neurons, in order to adjust the numerical parameters. Applying the model to a mouse mutant for Ftm/Rpgrip1l, a gene involved in human ciliopathies with severe brain abnormalities, reveals a shortening of the neurogenic period associated with an increased influx of newborn IPs from apical progenitors at mid-neurogenesis. Additional information is provided on cell kinetics, such as the mitotic and S phase indexes, and neurogenic fraction. Our model can be used to study other mouse mutants with cortical neurogenesis defects and can be adapted to study the importance of progenitor dynamics in cortical evolution and human diseases.

6.2. Numerical Methods

6.2.1. Numerical analysis for an energy-stable total discretization of a poromechanics model with inf-sup stability

Participants: Dominique Chapelle [correspondant], Philippe Moireau.

In this joint work with Bruno Burtschell [16], we consider a previously proposed general nonlinear poromechanical formulation, and we derive a linearized version of this model. For this linearized model, we obtain an existence result and we propose a complete discretization strategy–in time and space–with a special concern for issues associated with incompressible or nearly-incompressible behavior. We provide a detailed mathematical analysis of this strategy, the main result being an error estimate uniform with respect to the compressibility parameter. We then illustrate our approach with detailed simulation results and we numerically investigate the importance of the assumptions made in the analysis, including the fulfillment of specific inf-sup conditions.

6.2.2. Conservative and entropy controlled remap for multi-material ALE simulations

Participant: Patrick Le Tallec.

For many multi-material problems such as fluid-structure interaction, impact or implosion problems, materials are in very large strains due to their nature or to the applied forces. In our situations of interest, we also have a strong coupling between energy and momentum conservation laws, due to intense transfers between internal and kinetic energies and to strong advection effects. Such situations are classically governed by the Euler's equations, written in Lagrangian form, and using a multi-material, single velocity framework, but their numerical solution demands a strict control of energy conservation and entropy production, which is hard to achieve in situations where dynamic remeshing is mandatory. In this framework, our approach deals with the analysis of the impact of a second-order staggered remap using an intersection-based approach on conservation properties and on the entropy control. We show that an accurate remap with exact mesh intersections and exact integrations affects both the momentum and the kinetic energy because of node mass re-localizations and node velocity remap. We propose therefore a staggered remapping strategy in order to take into account these discrepancies at a low computational cost. While preserving the strict conservation of total energy, our strategy allows to recover a proper entropy control at the expense of strict momentum conservation and monotonicity losses. This work [32] is done in collaboration with Alexandra Claisse (CEA DAM) and Alexis Marboeuf (École Polytechnique and CEA DAM).

6.2.3. Multipatch isogeometric analysis for complex structures

Participant: Patrick Le Tallec.

This work – done in collaboration with Nicolas Adam (École Polytechnique and PSA) and Malek Zarroug (PSA) – introduces, analyzes and validates isogeometric mortar methods for the solution of thick shells problems which are set on a multipatch geometry. It concerns industrial parts of complex geometries for which the effects of transverse shear cannot be neglected. For this purpose, Reissner-Mindlin model was retained and rotational degrees of freedom (DOF) of the normal are taken into account. A particular attention is devoted to the introduction of a proper formulation of the coupling conditions at patches interfaces, with a particular interest on augmented lagrangian formulations, to the choice and validation of mortar spaces, and to the derivation of adequate integration rules. The relevance of the proposed approach is assessed numerically on various significative examples of industrial relevance. This work has been submitted for publication in an international journal.

6.2.4. Mathematical and numerical study of transient wave scattering by obstacles with the Arlequin Method

Participant: Sébastien Imperiale.

In this work [14] we extend the Arlequin method to overlapping domain decomposition technique for transient wave equation scattering by obstacles. The main contribution of this work is to construct and analyze from the continuous level up to the fully discrete level some variants of the Arlequin method. The constructed discretizations allow to solve wave propagation problems while using non-conforming and overlapping meshes for the background propagating medium and the surrounding of the obstacle respectively. Hence we obtain a flexible and stable method in terms of the space discretization – an inf-sup condition is proven – while the stability of the time discretization is ensured by energy identities.

6.2.5. Construction and analysis of fourth-order, energy consistent, family of explicit time discretizations for dissipative linear wave equations

Participants: Juliette Chabassier [MAGIQUE-3D], Julien Diaz [MAGIQUE-3D], Sébastien Imperiale [correspondant].

This work and the corresponding article [19], deal with the construction of a family of fourth order, energy consistent, explicit time discretizations for dissipative linear wave equations. The schemes are obtained by replacing the inversion of a matrix, that comes naturally after using the technique of the Modified Equation on the second order Leap Frog scheme applied to dissipative linear wave equations, by explicit approximations of its inverse. The stability of the schemes are studied using an energy analysis and a convergence analysis is carried out. Numerical results in 1D illustrate the space/time convergence properties of the schemes and their efficiency is compared to more classical time discretizations.

6.2.6. Energy decay and stability of a perfectly matched layer For the wave equation

Participants: Sébastien Imperiale [correspondant], Maryna Kachanovska [POEMS].

We follow a previous work where PML formulations was proposed for the wave equation in its standard second-order form. In the present work [15], energy decay and L^2 stability bounds in two and three space dimensions are rigorously proved both for continuous and discrete formulations with constant damping coefficients. Numerical results validate the theory.

6.2.7. A high-order spectral element fast Fourier transform for the poisson equation

Participants: Federica Caforio, Sébastien Imperiale [correspondant].

The aim of this work [17] is to propose a novel, fast solver for the Poisson problem discretised with High-Order Spectral Element Methods (HO-SEM) in canonical geometries (rectangle in 2D, rectangular parallelepiped in 3D). This method is based on the use of the Discrete Fourier Transform to reduce the problem to the inversion of the symbol of the operator in the frequency space. The proposed solver is endowed with several properties. First, it preserves the efficiency of the standard FFT algorithm; then, the matrix storage is drastically reduced (in particular, it is independent of the space dimension); a pseudo-explicit Singular Value Decomposition (SVD) is used for the inversion of the symbols; finally, it can be extended to non-periodic boundary conditions. Furthermore, due to the underlying HO-SEM discretisation, the multi-dimensional symbol of the operator can be efficiently computed from the one-dimensional symbol by tensorisation.

6.2.8. Thermodynamic properties of muscle contraction models and associated discrete-time principles

Participants: François Kimmig, Dominique Chapelle [correspondant], Philippe Moireau.

Considering a large class of muscle contraction models accounting for actin-myosin interaction, we present a mathematical setting in which solution properties can be established, including fundamental thermodynamic balances. Moreover, we propose a complete discretization strategy for which we are also able to obtain discrete versions of the thermodynamic balances and other properties. Our major objective is to show how the thermodynamics of such models can be tracked after discretization, including when they are coupled to a macroscopic muscle formulation in the realm of continuum mechanics. Our approach allows to carefully identify the sources of energy and entropy in the system, and to follow them up to the numerical applications. See [30] for more detail.

6.2.9. Mechanical and imaging models-based image registration

Participants: Radomir Chabiniok, Martin Genet [correspondant].

Image registration plays an increasingly important role in many fields such as biomedical or mechanical engineering. Generally speaking, it consists in deforming a (moving) source image to match a (fixed) template image. Many approaches have been proposed over the years; if new model-free machine learning-based approaches are now beginning to provide robust and accurate results, extracting motion from images is still most commonly based on combining some statistical analysis of the images intensity and some model of the underlying deformation as initial guess or regularizer. These approaches may be efficient even for complex type of motion; however, any artifact in the source image (e.g., partial voluming, local decrease of signal-to-noise ratio or even local signal void), drastically deteriorates the registration. This work introduces a novel approach of extracting motion from biomedical image series, based on a model of the imaging modality. It is, to a large extent, independent of the type of model and image data – the pre-requisite is to incorporate biomechanical constraints into the motion of the object (organ) of interest and being able to generate data corresponding to the real image, i.e., having an imaging model at hand. We will illustrate the method with examples of synthetically generated 2D tagged magnetic resonance images. This work was presented at the VipIMAGE 2019 conference. It also represents a part of the objectives supported by the Inria-UTSW Associated Team TOFMOD. See [44] for more detail. This work was done in collaboration with Katerina Skardova (Czech Technical University in Prague) and Matthias Rambausek (École Polytechnique).

6.2.10. Validation of finite element image registration-based cardiac strain estimation from magnetic resonance images

Participants: Martin Genet [correspondant], Philippe Moireau.

Accurate assessment of regional and global function of the heart is an important readout for the diagnosis and routine evaluation of cardiac patients. Indeed, recent clinical and experimental studies suggest that compared to global metrics, regional measures of function could allow for more accurate diagnosis and early intervention for many cardiac diseases. Although global strain measures derived from tagged magnetic resonance (MR) imaging have been shown to be reproducible for the majority of image registration techniques, the measurement of regional heterogeneity of strain is less robust. Moreover, radial strain is underestimated

with the current techniques even globally. Finite element (FE)-based techniques offer a mechanistic approach for the regularization of the ill-posed registration problem. This work presents the validation of a recently proposed FE-based image registration method with mechanical regularization named equilibrated warping. For this purpose, synthetic 3D-tagged MR images are generated from a reference biomechanical model of the left ventricle (LV). The performance of the registration algorithm is consequently tested on the images with different signal-to-noise ratios (SNRs), revealing the robustness of the method. See [35] for more detail.

6.3. Inverse Problems

6.3.1. Analysis of an observer strategy for initial state reconstruction of wave-like systems in unbounded domains

Participants: Sébastien Imperiale, Philippe Moireau [correspondant].

In [29] we are interested in reconstructing the initial condition of a wave equation in an unbounded domain configuration from measurements available in time on a subdomain. To solve this problem, we adopt an iterative strategy of reconstruction based on observers and time reversal adjoint formulations. We prove the convergence of our reconstruction algorithm with perfect measurements and its robustness to noise. Moreover, we develop a complete strategy to practically solve this problem on a bounded domain using artificial transparent boundary conditions to account for the exterior domain. Our work then demonstrates that the consistency error introduced by the use of approximate transparent boundary conditions is compensated by the stabilisation properties obtained from the use of the available measurements, hence allowing to still be able to reconstruct the unknown initial condition.

6.3.2. Analysis and numerical simulation of an inverse problem for a structured cell population dynamics model

Participants: Frédérique Clément, Frédérique Robin [correspondant].

We have studied (with Béatrice Laroche, INRA) a multiscale inverse problem associated with a multi-type model for age structured cell populations [20] (see also [21] for another application). In the single type case, the model is a McKendrick-VonFoerster like equation with a mitosis-dependent death rate and potential migration at birth. In the multi-type case, the migration term results in a unidirectional motion from one type to the next, so that the boundary condition at age 0 contains an additional extrinsic contribution from the previous type. We consider the inverse problem of retrieving microscopic information (the division rates and migration proportions) from the knowledge of macroscopic information (total number of cells per layer), given the initial condition. We have first shown the well-posedness of the inverse problem in the single type case using a Fredholm integral equation derived from the characteristic curves, and we have used a constructive approach to obtain the lattice division rate, considering either a synchronized or non-synchronized initial condition. We have taken advantage of the unidirectional motion to decompose the whole model into nested submodels corresponding to self-renewal equations with an additional extrinsic contribution. We have again derived a Fredholm integral equation for each submodel and deduced the well-posedness of the multi-type inverse problem. In each situation, we illustrate numerically our theoretical results.

6.3.3. Inverse problem based on data assimilation approaches for protein aggregation

Participants: Philippe Moireau [correspondant], Cécile Della Valle [MAMBA], Marie Doumic [MAMBA].

Estimating reaction rates and size distributions of protein polymers is an important step for understanding the mechanisms of protein misfolding and aggregation. In a depolarization configuration, we here extend some previous results obtained during the PhD Thesis of A. Armiento. Now, the depolarization rate is time-dependent or in the presence of an additional vanishing viscosity term. We continue to develop our framework mixing inverse problems methodologies and optimal control approaches typically encountered in data assimilation, allowing to justify mathematically the methods but also to adopt efficient numerical strategies. Publications of this work will be soon submitted.

6.3.4. Front shape similarity measure for data-driven simulations of wildland fire spread based on state estimation: Application to the RxCADRE field-scale experiment

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

Data-driven wildfire spread modeling is emerging as a cornerstone for forecasting real-time fire behavior using thermal-infrared imaging data. One key challenge in data assimilation lies in the design of an adequate measure to represent the discrepancies between observed and simulated firelines (or "fronts"). A first approach consists in adopting a Lagrangian description of the flame front and in computing a Euclidean distance between simulated and observed fronts by pairing each observed marker with its closest neighbor along the simulated front. However, this front marker registration approach is difficult to generalize to complex front topology that can occur when fire propagation conditions are highly heterogeneous due to topography, biomass fuel and micrometeorology. To overcome this issue, we investigate in this paper an object-oriented approach derived from the Chan–Vese contour fitting functional used in image processing. The burning area is treated as a moving object that can undergo shape deformations and topological changes. We combine this non-Euclidean measure with a state estimation approach (a Luenberger observer) to perform simulations of the time-evolving fire front location driven by discrete observations of the fireline. We apply this object-oriented data assimilation method to the three-hectare RxCADRE S5 field-scale experiment. This collaboration with CERFACS (M. Rochoux) and University of Maryland (C. Zhang and A. Trouvé) led to a publication [34] in the Proceedings of the Combustion Institute.

6.3.5. Model assessment through data assimilation of realistic data in cardiac electrophysiology

Participants: Antoine Gerard [CARMEN], Annabelle Collin [MONC], Gautier Bureau, Philippe Moireau [correspondant], Yves Coudière [CARMEN].

We consider a model-based estimation procedure – namely a data assimilation algorithm – of the atrial depolarization state of a sub- ject using data corresponding to electro-anatomical maps. Our objective is to evaluate the sensitivity of such a model-based reconstruction with respect to model choices. The followed data assimilation approach is capable of using electrical activation times to adapt a monodomain model simulation, thanks to an ingenious model-data fitting term inspired from image processing. The resulting simulation smoothes and completes the activation maps when they are spatially incomplete. Moreover, conductivity parameters can also be inferred. The model sensitivity assessment is performed based on synthetic data generated with a validated realistic atria model and then inverted using simpler modeling ingredients. In particular, the impact of the muscle fibers definition and corresponding anisotropic conductivity parameters is studied. Finally, an application of the method to real data is presented, showing promising results. This collaborative work has been published, see [37].

6.4. Experimental Assessments

6.4.1. Combination of traction assays and multiphoton imaging to quantify skin biomechanics

Participant: Jean-Marc Allain.

An important issue in tissue biomechanics is to decipher the relationship between the mechanical behavior at macroscopic scale and the organization of the collagen fiber network at microscopic scale. We have formalized a definitive protocol [46] to combine traction assays with multiphoton microscopy in ex vivo murine skin. This multiscale approach provides simultaneously the stress/stretch response of a skin biopsy and the collagen reorganization in the dermis by use of second harmonic generation (SHG) signals and appropriate image processing.

6.4.2. Monitoring dynamic collagen reorganization during skin stretching with fast polarization-resolved second harmonic generation imaging

Participant: Jean-Marc Allain.

The mechanical properties of biological tissues are strongly correlated to the specific distribution of their collagen fibers. Monitoring the dynamic reorganization of the collagen network during mechanical stretching is however a technical challenge, because it requires mapping orientation of collagen fibers in a thick and deforming sample. In this work [24], a fast polarization-resolved second harmonic generation microscope is implemented to map collagen orientation during mechanical assays. This system is based on line-to-line switching of polarization using an electro-optical modulator and works in epi-detection geometry. After proper calibration, it successfully highlights the collagen dynamic alignment along the traction direction in ex vivo murine skin dermis. This microstructure reorganization is quantified by the entropy of the collagen orientation distribution as a function of the stretch ratio. It exhibits a linear behavior, whose slope is measured with a good accuracy. This approach can be generalized to probe a variety of dynamic processes in thick tissues.

6.4.3. Multiscale characterisation of skin mechanics through in-situ imaging

Participant: Jean-Marc Allain.

The complex mechanical properties of skin have been studied intensively over the past decades. They are intrinsically linked to the structure of the skin at several length scales, from the macroscopic layers (epidermis, dermis and hypodermis) down to the microstructural organization at the molecular level. Understanding the link between this microscopic organization and the mechanical properties is of significant interest in the cosmetic and medical fields. Nevertheless, it only recently became possible to directly visualize the skin's microstructure during mechanical assays, carried out on the whole tissue or on isolated layers. These recent observations have provided novel information on the role of structural components of the skin in its mechanical properties, mainly the collagen fibers in the dermis, while the contribution of others, such as elastin fibers, remains elusive. We performed in [45] a systematic review of the current methods used to observe skin's microstructure during a mechanical assay, along with their strengths and limitations, as well as a review of the unique information they provide on the link between structure and function of the skin.

6.4.4. Root Hair Sizer: an algorithm for high throughput recovery of different root hair and root developmental parameters

Participant: Jean-Marc Allain.

The root is an important organ for water and nutrient uptake, and soil anchorage. It is equipped with root hairs (RHs) which are elongated structures increasing the exchange surface with the soil. RHs are also studied as a model for plant cellular development, as they represent a single cell with specific and highly regulated polarized elongation. For these reasons, it is useful to be able to accurately quantify RH length employing standardized procedures. Methods commonly employed rely on manual steps and are therefore time consuming and prone to errors, restricting analysis to a short segment of the root tip. Few partially automated methods have been reported to increase measurement efficiency. However, none of the reported methods allow an accurate and standardized definition of the position along the root for RH length measurement, making data comparison difficult. In this work [28] we are developing an image analysis algorithm that semi-automatically detects RHs and measures their length along the whole differentiation zone of roots. This method, implemented as a simple automated script in ImageJ/Fiji software that we termed Root Hair Sizer, slides a rectangular window along a binarized and straightened image of root tips to estimate the maximal RH length in a given measuring interval. This measure is not affected by heavily bent RHs and any bald spots. RH length data along the root are then modelled with a sigmoidal curve, generating several biologically significant parameters such as RH length, positioning of the root differentiation zone and, under certain conditions, RH growth rate. Image analysis with Root Hair Sizer and subsequent sigmoidal modelling of RH length data provide a simple and efficient way to characterize RH growth in different conditions, equally suitable to small and large scale phenotyping experiments.

6.4.5. Calcium and plasma membrane force-gated ion channels behind development

Participant: Jean-Marc Allain.

During development, tissues are submitted to high variation of compression and tension forces. The roles of the cell wall, the cytoskeleton, the turgor pressure and the cell geometry during this process have received due attention. In contrast, apart from its role in the establishment of turgor pressure, the involvement of the plasma membrane as a transducer of mechanical forces during development has been under studied. Force-gated (FG) or Mechanosensitive (MS) ion channels embedded in the bilayer represent 'per se' archetypal mechanosensor able to directly and instantaneously transduce membrane forces into electrical and calcium signals. We reviewed in [26] how their fine-tuning, combined with their ability to detect micro-curvature and local membrane tension, allows FG channels to transduce mechanical cues into developmental signals.

6.5. Clinical Applications

6.5.1. Cardiac displacement tracking with data assimilation combining a biomechanical model and an automatic contour detection

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

Data assimilation in computational models represents an essential step in building patient-specific simulations. This work aims at circumventing one major bottleneck in the practical use of data assimilation strategies in cardiac applications, namely, the difficulty of formulating and effectively computing adequate data-fitting term for cardiac imaging such as cine MRI. We here provide a proof-of-concept study of data assimilation based on automatic contour detection. The tissue motion simulated by the data assimilation framework is then assessed with displacements extracted from tagged MRI in six subjects, and the results illustrate the performance of the proposed method, including for circumferential displacements, which are not well extracted from cine MRI alone. This work was presented at the Functional Imaging and Modeling of Heart Conference (FIMH2019, Bordeaux, France) and published in [36].

6.5.2. Minimally-invasive estimation of patient-specific end-systolic elastance using a biomechanical heart model

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

The end-systolic elastance (E_{es}) – the slope of the end-systolic pressure-volume relationship (ESPVR) at the end of ejection phase – has become a reliable indicator of myocardial functional state. The estimation of E_{es} by the original multiple-beat method is invasive, which limits its routine usage. By contrast, non-invasive single-beat estimation methods, based on the assumption of the linearity of ESPVR and the uniqueness of the normalised time-varying elastance curve $E^N(t)$ across subjects and physiology states, have been applied in a number of clinical studies. It is however known that these two assumptions have a limited validity, as ESPVR can be approximated by a linear function only locally, and $E^N(t)$ obtained from a multi-subject experiment includes a confidence interval around the mean function. Using datasets of 3 patients undergoing general anaesthesia (each containing aortic flow and pressure measurements at baseline and after introducing a vasopressor noradrenaline), we first study the sensitivity of two single-beat methods — by Sensaki et al. and by Chen et al. — to the uncertainty of $E^N(t)$. Then, we propose a minimally-invasive method based on a patient-specific biophysical modelling to estimate the whole time-varying elastance curve $E^{model}(t)$. We compare E_{es}^{model} with the two single-beat estimation methods, and the normalised varying elastance curve $E^{N,model}(t)$ with $E^N(t)$ from published physiological experiments. This work was presented at the Functional Imaging and Modeling of Heart conference (FIMH2019, Bordeaux, France) and published in [38].

6.5.3. Model-based indices of early-stage cardiovascular failure and its therapeutic management in Fontan patients

Participant: Radomir Chabiniok.

Investigating the causes of failure of Fontan circulation in individual patients remains challenging despite detailed combined invasive cardiac catheterisation and magnetic resonance (XMR) exams at rest and during stress. In this work, we use a biomechanical model of the heart and Fontan circulation with the components of systemic and pulmonary beds to augment the diagnostic assessment of the patients undergoing the XMR stress exam. We apply our model in 3 Fontan patients and one biventricular “control" case. In all subjects, we obtained important biophysical factors of cardiovascular physiology – contractility, contractile reserve and changes in systemic and pulmonary vascular resistance – which contribute to explaining the mechanism of failure in individual patients. Finally, we used the patient-specific model of one Fontan patient to investigate the impact of changes in pulmonary vascular resistance, aiming at in silico testing of pulmonary vasodilation treatments. This work (in collaboration with Bram Ruijsink and Kuberan Pushparajah from St Thomas Hospital, King’s College London) was presented at the Functional Imaging and Modeling of Heart conference (FIMH2019, Bordeaux, France) and published in [40]. It also represents a part of the objectives supported by the Inria-UTSW Associated Team TOFMOD.

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

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

Understanding (patho)physiological phenomena and mechanisms of failure in patients with Fontan circulation — a surgically established circulation for patients born with a functionally single ventricle — remains challenging due to the complex hemodynamics and high inter-patient variations in anatomy and function. In this work, we present a biomechanical model of the heart and circulation to augment the diagnostic evaluation of Fontan patients with early-stage heart failure. The proposed framework employs a reduced-order model of heart coupled with a simplified circulation including venous return, creating a closed-loop system. We deploy this framework to augment the information from data obtained during combined cardiac catheterization and magnetic resonance exams (XMR), performed at rest and during dobutamine stress in 9 children with Fontan circulation and 2 biventricular controls. We demonstrate that our modeling framework enables patient-specific investigation of myocardial stiffness, contractility at rest, contractile reserve during stress and changes in vascular resistance. Hereby, the model allows to identify key factors underlying the pathophysiological response to stress in these patients. In addition, the rapid personalization of the model to patient data and fast simulation of cardiac cycles makes our framework directly applicable in a clinical workflow. We conclude that the proposed modeling framework is a valuable addition to the current clinical diagnostic XMR exam that helps to explain patient-specific stress hemodynamics and can identify potential mechanisms of failure in patients with Fontan circulation. This work has been submitted for publication in an international journal. This work (in collaboration with Bram Ruijsink and Kuberan Pushparajah from St Thomas Hospital, King’s College London and Tarique Hussain, UT Southwestern Medical Center Dallas) also represents a part of the objectives supported by the Inria-UTSW Associated Team TOFMOD.

6.5.5. Signed-distance function based non-rigid registration of image sequences with varying image intensity

Participant: Radomir Chabiniok.

In this work we deal with non-rigid registration of the image series acquired by the Modified Look-Locker Inversion Recovery (MOLLI) magnetic resonance imaging sequence, which is used for a pixel-wise estimation of T_1 relaxation time. The spatial registration of the images within the series is necessary to compensate the patient’s imperfect breath-holding. The evolution of intensities and a large variation of the image contrast within the MOLLI image series, together with the myocardium of left ventricle (the object of interest) typically not being the most distinct object in the scene, makes the registration challenging. We propose a method for locally adjusted optical flow-based registration of multimodal images, which uses the segmentation of the object of interest and its representation by the signed-distance function. We describe all the components of the proposed OF^{dist} method and their implementation. The OF^{dist} method is then compared to the performance of a standard mutual information maximization-based registration method, applied either to the original image (MIM) or to the signed-distance function (MIM^{dist}). Several experiments with synthetic and real MOLLI

images are carried out. On synthetic image with a single object, MIM performed the best, while OF^{dist} and MIM^{dist} provided better results on synthetic images with more than one object and on real images. When applied to signed-distance function of two objects of interest, MIM^{dist} provided a larger registration error (but more homogeneously distributed) compared to OF^{dist}. For the real MOLLI image sequence with left ventricle pre-segmented using level-set method, the proposed OF^{dist} registration performed the best, as is demonstrated visually and by measuring the increase of mutual information in the object of interest and its neighborhood. This collaborative work (Katerina Skardova, Czech Technical University, Institute of Clinical and Experimental Medicine in Prague) has been submitted for publication in an international journal. It also represents a part of the objectives supported by the Inria-UTSW Associated Team TOFMOD.

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

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

Background During general anaesthesia, direct analysis of the arterial pressure or aortic flow waveforms may be confusing in complex haemodynamic situations. Patient-specific biomechanical modelling allows to simulate Pressure-Volume (PV) loops and obtain functional indicators of the cardiovascular (CV) system, such as ventricular-arterial coupling (Vva), cardiac efficiency (CE) or myocardial contractility. It therefore augments the information obtained by monitoring and could help in medical decision-making. **Methods** Patients undergoing GA for neuroradiological procedure were included in this prospective observational study. A biomechanical model of heart and vasculature specific to each patient was built using transthoracic echocardiography and aortic pressure and flow signals. If intraoperative hypotension (IOH) appeared, diluted noradrenaline (NOR) was administered and the model readjusted. **Results** The model was calibrated for 29 (64%) normotensive and for 16 (36%) hypotensive patients before and after NOR administration. The simulated mean aortic pressure (MAP) and stroke volume (SV) were equivalent to the measurements (Percentage Error: 6% for MAP and 18% for SV) in all 45 datasets at baseline. After NOR administration, the percentage of concordance with 10% exclusion zone between measurement and simulation was > 95% for both MAP and SV. The modelling results showed a decreased Vva (0.64 ± 0.37 vs 0.88 ± 0.43; p=0.039), and an increased CE (0.8 ± 0.1 vs 0.73 ± 0.11; p=0.042) in hypotensive as compared with normotensive patients. After NOR administration, Vva increased by $92\pm101\%$, CE decreased by $13\pm11\%$ (p<0.001 for both) and contractility increased by $14\pm11\%$ (p=0.002). **Conclusions** The numerical models built for individual patients were applied to estimate patients' PV loops and functional indicators of CV system during haemodynamic alterations and during restoration by NOR. This study demonstrates the feasibility of patient-specific cardiovascular modelling using clinical data readily available during GA and paves the way for model-augmented haemodynamic monitoring at operating theatres and intensive care units. This work is about to be submitted for publication in an international journal. It also represents a part of the objectives supported by the Inria-UTSW Associated Team TOFMOD.

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

Participant: Radomir Chabiniok.

Work in collaboration with Radek Fucik, Department of Mathematics, Faculty of Nuclear Sciences and Physical Engineering, Czech Technical University in Prague.

Objective The accuracy of phase-contrast magnetic resonance imaging (PC-MRI) measurement is investigated using a computational fluid dynamics (CFD) model with the objective to determine the magnitude of the flow underestimation due to turbulence behind a narrowed valve in a phantom experiment. **Materials and Methods** An acrylic stationary flow phantom is used with three insertable plates mimicking aortic valvular stenoses of varying degrees. Positive and negative horizontal fluxes are measured at equidistant slices using standard PC-MRI sequences by 1.5T and 3T systems. The CFD model is based on the 3D lattice Boltzmann method (LBM). The experimental and simulated data are compared using the Bland-Altman-derived limits of agreement. Based on the LBM results, the turbulence is quantified and confronted with the level of flow underestimation. **Results** Matching results of PC-MRI flow were obtained for valves up to moderate stenosis

on both field strengths. The flow magnitude through a severely stenotic valve was underestimated due to signal void in the regions of turbulent flow behind the valve, consistently with the level of quantified turbulence intensity. **Discussion** Flow measured by PC-MRI is affected by noise and turbulence. LBM can simulate turbulent flow efficiently and accurately, it has therefore the potential to improve clinical interpretation of PC-MRI. This collaborative work (Czech Technical University, Institute of Clinical and Experimental Medicine in Prague and Inria) has been submitted for publication in an international journal. It also represents a part of the objectives supported by the Inria-UTSW Associated Team TOFMOD.

6.5.8. Left ventricular torsion obtained using equilibrated warping in patients with repaired Tetralogy of Fallot

Participants: Martin Genet, Radomir Chabiniok [correspondant].

Work in collaboration with Katerina Skardova, Department of Mathematics, Department of Mathematics, Faculty of Nuclear Sciences and Physical Engineering, Czech Technical University in Prague and Tarique Hussain UT Southwestern Medical Center Dallas.
Background Patients after surgical repair of Tetralogy of Fallot (rTOF) have right ventricular (RV) dysfunction and may subsequently suffer a decrease in left ventricular (LV) function. Previous studies evaluating the assessment of LV torsion have shown poor reproducibility using cardiovascular magnetic resonance imaging (CMR). The aim of our study is to evaluate a novel finite element method of image registration to assess LV torsion in patients with rTOF and explore the relationship between LV torsion and cardiac parameters routinely obtained with CMR. **Methods** The assessment of torsion is based on the finite element method for image registration, and the equilibrium gap principle for problem regularization, known as equilibrated warping developed by M. Genet (Inria Saclay). It has been shown to be able to predict global torsion in regular cine images as well in 3D tagged images, despite low contrast. Seventy-six cases of rTOF and ten controls were included. The group of control patients were assessed for reproducibility using equilibrated warping and standard tissue tracking software (cvi42, version 5.10.1, Calgary, Canada). RV end-systolic volume (RVESV), RV end-diastolic volume (RVEDV), RV ejection fraction (RVEF), LVESV, LVEDV, LVEF, LV peak systolic torsion and peak systolic torsion gradient (normalized by mesh length) were obtained for each patient with rTOF. Patients were dichotomized into two groups: those with normal torsion (systolic basal clockwise rotation and apical counterclockwise rotation, representative example is shown in Image 1) and those with loss of torsion, defined as a reversal of normal systolic basal clockwise rotation (representative example is shown in Image 2). **Results** Torsion by equilibrated warping was successfully obtained in 68 of 76 (89%) patients with rTOF and 9 of 10 (90%) normal controls. For equilibrated warping, the intra- and inter-observer coefficients of variation were 0.095 and 0.117, respectively; compared to 0.668 and 0.418 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 0.250 and 0.621 for tissue tracking. Loss of torsion was noted in 32 of the 68 (47%) patients with rTOF and there was a significant difference in peak systolic torsion gradient between patients with normal torsion and loss of torsion. There was no difference in LV or RV volumes or function between these groups. **Conclusion** The equilibrated warping method of image registration to assess LV torsion is feasible in patients with rTOF and shows good reliability. Loss of torsion is common in patients with rTOF. In our study, there was no significant association between loss of torsion and other ventricular parameters indicative of a worsening cardiac condition. Future studies committed to the long- term follow-up of this population are needed to assess the role of torsion in predicting ventricular dysfunction and death. This work was accepted for presentation at SCMR conference 2020 (Society for Cardiovascular Magnetic Resonance). It also represents a part of the objectives supported by the Inria-UTSW Associated Team TOFMOD.

6.5.9. Volume administration protocol to assess ventricular mechanics during interventional cardiac magnetic resonance procedures

Participant: Radomir Chabiniok.

Work in collaboration with Joshua Greer and Tarique Hussain UT Southwestern Medical Center Dallas.

Background Failure in Fontan circulation occurs with supposed normal ventricular systolic and diastolic function, including normal ventricular end-diastolic pressures and ventricular ejection fraction. This highlights the difficulty in assessing systolic and diastolic ventricular function in patients with single ventricle physiology. Interventional cardiac magnetic resonance (CMR) provides an opportunity for simultaneous acquisition of pressure and volume measurements that may lend itself well to analysis of ventricular mechanics in this population. We aim to develop a protocol of volume administration to assess ventricular pressure and volume during the cardiac cycle to construct pressure-volume loops under different loading conditions and perform their biomechanical interpretation. **Methods** This is a single center prospective study conducted on single ventricle patients with Glenn or Fontan circulation referred for interventional CMR procedures. With a catheter advanced into the ventricle, a pressure tracing and a cine sequence accelerated by kt-BLAST is obtained. Two 2.5 mL/kg fluid boluses are then rapidly administered into the catheter sheath with repeated acquisition of the pressure tracing and cine imaging immediately following each. Cine images are post-processed after the procedure to obtain ventricular volumes. The data are combined to construct pressure-volume loops and plot the end-diastolic pressure-volume relationship (EDPVR). **Results** The protocol has been performed in six patients. Ventricular end-diastolic pressure readings increased by a median of 2.5 mmHg (range of 1-3 mmHg) after the first volume administration and a median of 1.5 mmHg (range of 1-8 mmHg) after the second volume administration. Ventricular end-diastolic volumes increased by a median of 4.1 mL (range of 1.7-19.3 mL) after the first volume administration and a median of 1.5 mL (range of 0.4-24.2 mL) after the second volume administration. The data obtained during simultaneous volume and pressure measurements allowed for the construction of ventricular pressure-volume loops. Ventricular stroke work increased by a median of 0.0825 Joules (range of 0.010-0.167 Joules) after the first volume administration then decreased by a median of -0.062 Joules (range of -0.083 to 0.005 Joules) after the second volume administration. EDPVR curves were derived from the pressure-volume loops and differentiated patients with similar starting end-diastolic pressures. **Conclusions** We present a novel method for the acquisition of data to construct pressure-volume loops. Our protocol focuses on rapid volume administration and fast data acquisition with the goal of increasing preload but recording data prior to compensatory changes in afterload. In each patient, administration of 2.5 mL/kg fluid boluses achieved measurable increases in ventricular end-diastolic pressure and ventricular end-diastolic volume. The construction of pressure-volume loops with varying loading may facilitate in-depth assessment of ventricular mechanics in patients with single ventricle heart disease. The variation of preload may allow for the assessment of EDPVR, therefore ventricular stiffness, and to some extent also the contractile response in such a physiology-modifying situation. This work was submitted to the CHOP 2020 conference. It also represents a part of the objectives supported by the Inria-UTSW Associated Team TOFMOD.

6.5.10. Computational quantification of patient specific changes in ventricular dynamics associated with pulmonary hypertension

Participant: Martin Genet.

Pulmonary arterial hypertension (PAH) causes an increase in the mechanical loading imposed on the right ventricle (RV) that results in progressive changes to its mechanics and function. Here, we quantify the mechanical changes associated with PAH by assimilating clinical data consisting of reconstructed three-dimensional geometry, pressure, and volume waveforms, as well as regional strains measured in patients with PAH ($n = 12$) and controls ($n = 6$) within a computational modeling framework of the ventricles. Modeling parameters reflecting regional passive stiffness and load-independent contractility as indexed by the tissue active tension were optimized so that simulation results matched the measurements. The optimized parameters were compared with clinical metrics to find usable indicators associated with the underlying mechanical changes. Peak contractility of the RV free wall (RVFW) $\gamma_{RVFW,max}$ was found to be strongly correlated and had an inverse relationship with the RV and left ventricle (LV) end-diastolic volume ratio (i.e., RVEDV/LVEDV) (RVEDV/LVEDV)+0.44, $R^2 = 0.77$). Correlation with RV ejection fraction ($R^2 = 0.50$) and end-diastolic volume index ($R^2 = 0.40$) were comparatively weaker. Patients with $RVEDV/LVEDV > 1.5$ had 25% lower $\gamma_{RVFW,max}$ ($P < 0.05$) than that of the control. On average, RVFW passive stiffness progressively increased with the degree of remodeling as indexed by RVEDV/LVEDV.

These results suggest a mechanical basis of using RVEDV/LVEDV as a clinical index for delineating disease severity and estimating RVFW contractility in patients with PAH. See [25] for more detail.

6.5.11. Validation of equilibrated warping-image registration with mechanical regularization-on 3D ultrasound images

Participant: Martin Genet.

Image registration plays a very important role in quantifying cardiac motion from medical images, which has significant implications in the diagnosis of cardiac diseases and the development of personalized cardiac computational models. Many approaches have been proposed to solve the image registration problem; however, due to the intrinsic ill-posedness of the image registration problem, all these registration techniques, regardless of their variabilities, require some sort of regularization. An efficient regularization approach was recently proposed based on the equilibrium gap principle, named equilibrated warping. Compared to previous work, it has been formulated at the continuous level within the finite strain hyperelasticity framework and solved using the finite element method. Regularizing the image registration problem using this principle is advantageous as it produces a realistic solution that is close to that of an hyperelastic body in equilibrium with arbitrary boundary tractions, but no body load.The equilibrated warping method has already been extensively validated on both tagged and untagged magnetic resonance images. In this paper, we provide full validation of the method on 3D ultrasound images, based on the 2011 MICCAI Motion Tracking Challenge data. See [39] for more detail.

7. Bilateral Contracts and Grants with Industry

7.1. Bilateral Contracts with Industry

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

8. Partnerships and Cooperations

8.1. National Initiatives

8.1.1. ANR

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

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

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

8.1.2. Other funding

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

8.2. European Initiatives

8.2.1. Collaborations with Major European Organizations

Partner 1: Division of Biomedical Engineering & Imaging Sciences (BMEIS), St Thomas' Hospital, King's College London, UK

Clinical-modeling topics mostly encompassing congenital heart diseases (BMEIS) acts as "Other participant" in the Inria Associate team ToFMOD, and R. Chabiniok additionally performs clinical MRI exams at St Thomas' hospital 0.5 days / week.

Partner 2: Department of Mathematics, Faculty of Nuclear Sciences and Physical Engineering, Czech Technical University in Prague, Czech Republic

Model-constrained image registrations, trans-valvular flow in pathological valves.

Partner 3: Institute for Clinical and Experimental Medicine in Prague

Cardiovascular MRI.

8.3. International Initiatives

8.3.1. Inria Associate Teams Not Involved in an Inria International Labs

8.3.1.1. ToFMod

Title: Cardiac Biomechanical Modeling of Chronic Right Ventricular Loading

International Partner (Institution - Laboratory - Researcher):

UT Southwestern Medical Center, Dallas,Texas (United States), Mohammad Tarique Hussain

Start year: 2018

See also: https://m3disim.saclay.inria.fr/associated-team/

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 M3DISIM 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 M3DISIM researchers. It is only by combining such invaluable longitudinal data with biomechanical modeling expertise that progress can be achieved in the above objective, indeed.

8.4. International Research Visitors

8.4.1. Invited researchers

- T. Hussain, A. Tandon (Senior researchers at UTSW Medical Center Dallas): joint work in the scope of the Inria Associate team ToFMOD
- F. Regazzoni (3rd year PhD student from MOX, Milan, Italy): From January until March 2019 and from December 2019, joint work on model learning and data assimilation coupling.

9. Dissemination

9.1. Promoting Scientific Activities

9.1.1. Scientific events organisation

9.1.1.1. General chair, scientific chair

F. Clément, Session *Biomathématiques, Bioinformatique et Biophysique pour la reproduction*, ReproSciences 2019 Toulouse (France), April 24-26

D. Chapelle, M. Genet: Session co-chairs at the 6th International Conference on Computational and Mathematical Biomedical Engineering (CMBE2019), Sendai City (Japan), June 10-12

9.1.1.2. Member of organizing committees

J.M. Allain, Member of the workshop Biomechanics from cells to tissues organising committee

D. Chapelle, Chair of the organizing committee of the VPH2020 conference (Paris, August 2020)

F. Clément, ReproSciences 2019, Toulouse (France), April 24-26

M. Genet, D. Chapelle, Co-organizers of the Paris-Saclay University Biomechanics Seminar Series (Until June 2019)

P. Moireau, Member of the organizing committee of the VPH2020 conference (Paris, August 2020)

9.1.2. Scientific events selection

9.1.2.1. Reviewer

J.M. Allain, Member of the European Society of Biomechanics conference scientific committee

R. Chabiniok, reviewer for FIMH2019

M. Genet, reviewer for the 10th international conference on Functional Imaging and Modeling of the Heart (FIMH, June 6-8, 2019, Bordeaux)

9.1.3. Journal

9.1.3.1. Member of editorial boards

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

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

F. Clément *Frontiers*, review editor (Systems Endocrinology)

P. Le Tallec, Member of the editorial board of journal *Computer Methods in Applied Mechanics and Engineering*

P. Le Tallec, Member of the editorial board of journal *Computer and Structures*

9.1.3.2. Reviewer - Reviewing activities

J.M. Allain, reviewer for "Acta Biomaterialia", "Journal of Anatomy", "Journal of Biomechanics" and "Journal of the Mechanical Behavior of Biomedical Materials"

R. Chabiniok, reviewer for "Philosophical Transactions of the Royal Society A"

F. Clément, reviewer for "Endocrinology", "PloS Comp. Biol.", "Appl. Math. Mod."

M. Genet, reviewer for "Acta Biomaterialia" and "Inverse Problems in Science & Engineering"

D. Chapelle, reviewer for "Biomechanics and Modeling in Mechanobiology", "Computers & Structures", "International Journal for Numerical Methods in Biomedical Engineering"

S. Imperiale, reviewer for "Numerische Mathematik" and "Proceeding of the royal society A"

P. Moireau, reviewer for "Journal of Computational Physics", "Biomechanics and Modeling in Mechanobiology"

9.1.4. Invited talks

F. Clément. Invited seminar at MaiAGE (France), invited mini-symposium talk to Equadiff, Leiden, The Netherlands

M. Genet, invited keynote at the 90th Annual Meeting of the International Association of Applied Mathematics and Mechanics (GAMM, February 18-22), Vienna, Austria

M. Genet, invited keynote at the francilian mechanics meeting (RFM, Mai 27-28), Fontainebleau

M. Genet, invited keynote at the "Biomechanics from cell to tissue" workshop (November 8), Gif-sur-Yvette

P. Le Tallec, invited speaker at at the 13th International Conference on Advanced Computational Engineering and Experimenting (ACEX, July 1-5), Athens, Greece

D. Chapelle, invited lecturer at iHeart workshop (22-24 July), Varese, Italy

P. Moireau, invited lecture at the GDR MAMOVI 2019 days, Tours, France

P. Moireau, invited lecture at BME symposium 2019, Ecole Polytechnique, France

P. Moireau, invited seminars at LMA Marseille France and CMAP Polytechnique, France

9.1.5. Leadership within the scientific community

D. Chapelle, Member of the board of directors of the VPH Institute

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

F. Clément, member of the direction and scientific board of GdR REPRO (Integrative and translational approaches of human and animal reproduction)

F. Clément, expert of the BCDE (Cell Biology, Development and Evolution) ITMO (Multi OrganizationThematic Institute) of the French National Alliance for Life and Health Sciences Aviesan.

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

9.1.6. Scientific expertise

J.M. Allain, Reviewer for the NSERC (Canadian ANR)

R. Chabiniok, Reviewer for Swiss National Science Foundation

F. Clément, member of the INRA DR2 admissibility and admission juries “Agronomie, biologie et amélioration des plantes, sciences du numérique, sciences économiques et sociales”

M. Genet, Reviewer for the Swedish Foundation for Strategic Research

S. Imperiale, Consultant for CEA

P. Moireau, Reviewer for ISCD (Data science Institute, Paris Sorbonne Université)

P. Moireau, Reviewer for ANR and Member of the evaluation committee 46 "Numercial models, simulations, applications"

P. Moireau, member of the MAP5 Paris Descartes, MCF (assistant professor) admission jury

9.1.7. Research administration

J.M. Allain, Scientific Advisory Board, chair BioMecAM

R. Chabiniok, in charge of the objectives of Inria Associate team ToFMOD (with UT Southwestern Medical center Dallas, USA)

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

P. Moireau, Member of the LMS board of direction

P. Le Tallec, Director of the Laboratory of Solid Mechanics at Ecole Polytechnique

9.2. Teaching - Supervision - Juries

9.2.1. Teaching

Bachelor: J.-M. Allain, Supervision of the introductory projects in physics, 15h, B1, Ecole Polytechnique, France

Bachelor: J.-M. Allain, “Classical mechanics”, 24h, B2, Ecole Polytechnique, France

Bachelor: J.-M. Allain, “Advanced labwork”, 12h, B3, Ecole Polytechnique, France

Bachelor: M. Genet, “Continuum Mechanics I”, B3, 40h, École Polytechnique, France

Bachelor: M. Genet, “Continuum Mechanics II”, B3, 40h, École Polytechnique, France

Bachelor: S. Imperiale, “MA102 – Analyse pour les EDP”, 24h, B3, ENSTA ParisTech, France

Bachelor: P. Le Tallec , “Mécanique des Milieux Continus 2. ”, 24h, L3, École Polytechnique, France

Bachelor: P. Le Tallec , “Mechanics of Continuous Media and Structure. ”, 24h, Y4, Shanghai Jiao Tong Elite Institute of Technology, China

Master: J.-M. Allain, “Statistical mechanics: application to cell motility”, 20h, M2, Ecole Polytechnique, France

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

Master: M. Genet, “Plasticity and Fracture”, 18h, M1, Ecole Polytechnique, France

Master: P. Le Tallec, “Solid and Continuum Mechanics”, 12h, M1, Master of Nuclear Energy, Université Paris-Saclay, France

Master: P. Moireau, “Biomechanical Modeling of Active Tissues”, 8h, M2, Université Paris-Saclay, France

Master: P. Moireau, “Méthodes et problèmes inverses en dynamique des populations”, 16h, M2, UPMC, 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

9.2.2. Supervision

PhD: F. Caforio, “Modélisation mathématique et numérique de la propagation d’ondes élastique dans le coeur”, supervisors: D. Chapelle and S. Imperiale, defended in January

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

PhD: F. Robin “Multiscale modeling of the morphodynamics in ovarian follicles”, supervisors: F. Clément & Romain Yvinec [INRA], defended in September

PhD: F. Wijanto, “Multiscale Mechanics of soft tissues”, supervisors: J.-M. Allain and M. Caruel, defended in December

PhD in progress: G. Ballif “Stochastic multiscale modeling in developmental and reproductive biology”, started October 2019, supervisors: F. Clément & R. Yvinec [INRA]

PhD in progress: J. Manganotti, “Energy preserving cardiac circulation models”, started october 2019, supervisors: S. Imperiale and P. Moireau,

PhD in progress: N. Tueni, “Multiscale properties of the passive cardiac muscle”, started 01/2018, supervisors: J.M. Allain and M. Genet

PhD in progress: C. Giraudet, “Cornea biomechanics”, started 10/2018; supervisors: J.M. Allain and P. Le Tallec

PhD in progress: E. Berberoglu (ETHZ, Switzerland), “Image Guided Computational Cardiac Mechanics”, started February 2017, supervisors: M. Genet and S. Kozerke (ETHZ, Switzerland)

PhD in progress: C. Della Valle, “Modélisation et estimation des dynamiques d’assemblage de proteines”, supervisors: M. Doumic and P. Moireau

PhD in progress: M. Gusseva, “Cardiac Biomechanical Modeling for Chronic Ventricular Loading”, supervisors: R. Chabiniok, D. Chapelle, T. Hussain, started in December 2017

PhD in progress: A. Le Gall, “Cardiac modelling for monitoring purposes during general anaesthesia and at Intensive Care Unit”, supervisors: R. Chabiniok, D. Chapelle, E. Gayat, started in November 2016

PhD in progress: C. Patte, “Lung multiscale poromechanical modeling: from breathing to pulmonary fibrosis-induced chronic remodeling”, supervisors: M. Genet and D. Chapelle, started November 2017

PhD in progress: J. Joachim “Développement d’une nouvelle méthode d’administration automatisée des médicaments utilisés chez les patients sous anesthésie générale basée sur un monitorage totalement non-invasif”, supervisor: E. Gayat, started September 2018

9.2.3. Juries

J.M. Allain, PhD Jury of T. Cochereau (referee), Grenoble University, PhD Advisor L. Bailly, March 18

J.M. Allain, PhD Jury of T. Rongsawat (referee), Montpellier University, PhD Advisor H. Sentenac, December 13

D. Chapelle, PhD Jury of M. Pfaller (referee), TUM, PhD Advisor W. Wall, April 26

D. Chapelle, PhD Jury of F. Vallée, PhD Advisor E. Gayat, Sorbonne Université, June 20

D. Chapelle, PhD Jury of T. Boucneau, PhD Advisor X. Maître, Université Paris-Saclay, July 3

F. Clément, PhD Jury of H. Martin, Sorbonne Université, July 15

F. Clément, PhD Jury of A. Perrillat-Mercerot, Université de Poitiers, October 22

P. Moireau, PhD Jury of Lorenzo Sala, PhD Advisor C. Prud'homme, Université de Strasbourg, September 27

P. Moireau, PhD Jury of Sebastian Reyes Riffo, PhD Advisor J. Salomon, Université Paris Dauphine, November 29

P. Moireau, PhD Jury of François Kimmig, PhD Advisor D. Chapelle, Institut Polytechnique de Paris, December 6

9.3. Popularization

C. Patte, J. Diaz and J. Manganotti, leading of a scientific activity for the Fête des Sciences day organized by Inria. October 11

C. Patte, creation of a scientific activity for middle and high school students as part of a popularization doctoral mission

C. Patte, supervision of a research activity for the RJMI (Rendez-vous des Jeunes Mathématiciennes et Informaticiennes) organized by Inria. October 21 & 22

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Major publications by the team in recent years

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Doctoral Dissertations and Habilitation Theses

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[13] F. KIMMIG. *Modélisation multi-échelles de la contraction musculaire : De la dynamique stochastique des moteurs moléculaires à la mécanique des milieux continus*, Université Paris-Saclay, December 2019, https://tel.archives-ouvertes.fr/tel-02439432

Articles in International Peer-Reviewed Journals

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