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ACTIVITY REPORT

Project-Team MIMESIS

Computational Anatomy and Simulation for Medicine

IN COLLABORATION WITH: ICube

DOMAIN

Digital Health, Biology and Earth

THEME

Computational Neuroscience and Medicine

Contents

Project-Team MIMESIS

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Keywords

Computer sciences and digital sciences

A2.5. – Software engineering

A3.1.1. – Modeling, representation

A3.1.4. – Uncertain data

A3.2.2. – Knowledge extraction, cleaning

A5.1. – Human-Computer Interaction

A5.3.4. – Registration

A5.4.4. – 3D and spatio-temporal reconstruction

A5.4.5. – Object tracking and motion analysis

A5.6. – Virtual reality, augmented reality

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

A6.1.2. – Stochastic Modeling

A6.1.5. – Multiphysics modeling

A6.2.3. – Probabilistic methods

A6.2.4. – Statistical methods

A6.2.5. – Numerical Linear Algebra

A6.2.8. – Computational geometry and meshes

A6.3.1. – Inverse problems

A6.3.2. – Data assimilation

A6.3.3. – Data processing

A6.3.4. – Model reduction

A9.2. – Machine learning

A9.10. – Hybrid approaches for AI

Other research topics and application domains

B1.2. – Neuroscience and cognitive science

B2.2.6. – Neurodegenerative diseases

B2.4. – Therapies

B2.4.3. – Surgery

B2.6. – Biological and medical imaging

B2.7. – Medical devices

B2.7.1. – Surgical devices

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2 Overall objectives

2.1 Team Overview

The MIMESIS team develops numerical methods for computer-based training, surgical planning and computer-assisted interventions. Our aim is to facilitate the development of digital twins and improve their predictive capabilities through novel numerical methods, data assimilation techniques and machine learning. To pursue these directions we have assembled a team with a multidisciplinary background, and have established close collaborations with academic and clinical partners. We contribute to the development of the SOFA framework as a means to disseminate our results to the community.

2.2 Challenges

In a first research axis, our research aims at developing more advanced simulations, with stronger mathematical and biomechanical foundations, and their adaptation to a specific patient. We want, in particular, to develop more stable numerical methods that would, at the same time, be suited for the automatic generation of digital twins of organs. We chose to investigate immersed boundary methods that do not require an exact discretization of the domain. It led to the development of Φ-FEM, a finite element method on domains defined by level-sets that provides better convergence while significantly simplifying the mesh generation process. To achieve real-time computation using complex models based on nonlinear PDEs, we investigate the use of deep learning techniques for accelerating physics-based simulations. Given that our main field of application is computer-guided surgery, we also study the numerical aspects of contact problems. Such problems are very hard to solve in real time, as they involve non-smooth dynamics. In addition, we investigate data assimilation methods to estimate patient-specific model parameters from sparse observations, as they typically occur during surgical interventions. Random processes play an important role in biological systems and need specific mathematical analysis. In neuroscience, stochastic fluctuations have been shown to control oscillatory brain states that may be induced by neurostimulation in clinical practice. To improve our understanding of nonlinear neural dynamics during neurostimulation and thus improve experimental neurostimulation protocols in single patients, we have extended the mathematical analysis of additive noise-induced system evolution.

Our second research axis is derived from our application context and essentially consists of developing optimization and control methods for computer-assisted interventions. At the core of our activity is the hypothesis that data-driven simulation has the potential to bridge the gap between medical data (most often images) and clinical routine by updating pre-operative knowledge with the information available at the time of the procedure. We have been pioneers in the use of biomechanical models and real-time finite element simulation to perform augmented reality on deformable organs. In the field of non-rigid registration, we have demonstrated the benefit of our physics-based approaches as they bring not only an implicit regularization of the solution but also a plausible explanation of the deformation. We have continued this work with an emphasis on robustness to uncertainty and outliers in the information extracted in real-time from image data, and in real-time parameter estimation. The work, initially done using Bayesian methods, has been recently extended through optimal control methods. Optimal control may be achieved in a closed feedback loop and we investigate its implementation in a neurostimulation setup. The objective of this loop is to control the spectral power density of a subject's brain activity. In a Kalman observer feedback model, brain observations are fed into a Kalman Filter which estimates instantaneous stimulation input to the brain in real-time. Another approach treats the brain as a linear time-invariant system and optimizes the brain stimulation input by direct feedback control based on observed brain signals. Finally, in the field of robotic control of flexible structures, we are developing methods for autonomous insertion of needles during percutaneous procedures and autonomous navigation of catheters and guidewires during endovascular interventions. This research combines our expertise in real-time simulation of deformable structures and our results in contact modeling, while the control is either performed via differentiable simulations or using reinforcement learning methods.

3 Research program

3.1 Interactive computational models

3.1.1 Immersed Boundary Methods

For several years, we have investigated finite element methods that fall under the class of unfitted (also known as immersed boundary) methods. Because such methods do not require a discretization that strictly conforms to the domain boundary, they are particularly suited for the development of digital twins, as they facilitate the automatic generation of patient-specific simulations on complex geometries. Our current results have focused on the development, the numerical analysis and mathematical foundations of a new method called Φ-FEM. The main advantage of our method is that it uses the classical Finite Element tools on unfitted meshes. We have also highlighted that the method significantly improves the convergence when compared to a similar, fitted, discretization of the domain. The benefit and applicability of the Φ-FEM method have already been demonstrated on different problems: heat transfer, crack, interface between two material, and fluid structure interaction. We are now working on extending the method to 3D (non-linear) elasticity with both Neumann and Dirichlet boundary conditions.

3.1.2 Scientific Machine Learning

Various dimensionality reduction techniques have been proposed to speed up the simulation of non-linear solids. These techniques remain essentially linear transformations that may, in some cases, be insufficient to capture correctly the nonlinearity that can be found in biological tissues. In 2018, we proposed to address these limitations by developing physics-based deep neural networks, a supervised version of the Physically Informed Neural Networks (PINNs) approach. As preliminary work, we developed a neural network that learns the relationship between an input force and the resulting displacement field via a U-Net architecture [4]. The choice of this U-net architecture is not random, as it matches the model reduction process through a neural network (with the latent space representing the reduced model). The predictions were about 100 times faster than our reference FEM computation while providing sufficient accuracy for our applications. This work was followed by several new ideas and publications. We proposed to solve elastic registration problems for augmented surgery using the same network architecture but trained to learn a mapping between a partial, noisy point cloud and the deformed state of an elastic body. We added a physics-based loss to a fully connected network to improve its prediction accuracy and to make it “physics-aware”. We also enforced the robustness of the solution by integrating the prediction of the network within a classical Newton Raphson algorithm. Our next steps concern the extension of our methods to the case of dynamic simulation, and also the development of neural network architectures that provide more genericity in the solution space (by being somewhat invariant to the meshing of the domain for instance).

3.1.3 Non-Smooth Mechanics

Many clinical interventions rely on mechanical interactions between a device and the anatomy. Surgery and interventional radiology are the two main areas where these interactions are essential and generally complex. During this evaluation period we have continued our activity on constraint modeling and simulation of contacts with friction. The complexity of the problem often leads to unstable numerical approaches, inaccuracy of the solution and slow computation times. Our latest works address the issue of computational performance through an asynchronous Cholesky decomposition and by exploiting matrix sparsity and time-consistency.

3.1.4 Order in random systems by stochastic perturbations

The brain is a complex system with several spatial and temporal scales. The microscopic scales are rather unstructured in space and activity observations show random fluctuations, whereas upper hierarchical levels at the mesoscopic and macroscopic scales exhibit more regular dynamics. Some years ago, we found in theoretical studies that additive random input on the microscopic scale to random networks tunes the systems stability and may induce stability change. Such so-called bifurcations induce ordered structures, being in space or time or in both. For instance, additive noise may induce coherence resonance in Erdős-Rényi neural networks which exhibit an oscillatory spatially coherent state with frequency of 40 Hz. Since this oscillatory state evolves in the gamma frequency range in which visual information is processed, this theoretical result indicates that the brain may tune internal random fluctuations to induce coherence resonance and hence process visual information.

3.2 Optimization and control for Computer-Aided-Interventions

3.2.1 Optimal control and differentiable simulation

We recently started to investigate optimal control as a solution to several challenges in the field of computer-aided intervention. The first problem we addressed was the elastic intraoperative registration of a preoperative liver model and, as an extension, force estimation during robotic surgery. Both are formulated as optimal control problems where the unknown is the surface force distribution applied onto the organ. The deformation is computed using an hyperelastic model, and the optimization problem is solved using an adjoint method. This approach provides greater control over the set of admissible forces and leads to physically-consistent displacement fields. As a byproduct, it permits the recovery of the forces that led to the deformation, and can provide visual haptic feedback in medical robotics. We also rely on optimal control in other problems addressed in the team, such as autonomous endovascular navigation, where we have a similar control challenge. In this case the deformable structure is the catheter or guidewire rather than an organ. Finally, to address the relatively slow computation times that are typical of such optimization methods, we have started the development of differentiable algorithms. They exploit both GPU acceleration and the automatic differentiation tools from frameworks such as PyTorch. This significantly speeds up the computation of the adjoint. This approach is combined with the use of deep neural networks to predict the solution of the forward elastic problem in just a few milliseconds.

3.2.2 Data Assimilation

An essential step in the development of digital twins is the parametrization of the underlying model. A possibility is to rely on Bayesian inference. Model parameters are estimated using a reduced-order unscented Kalman filter based on observations taken, for instance, from laparoscopic image streams. As an example, estimating boundary conditions rather than using generic data from the literature improves the accuracy of the simulation by 75% when compared to methods integrating a priori knowledge as boundary conditions. Our approach significantly improves the accuracy during registration problems involving sparse and noisy observations. We also demonstrated that our data assimilation method can be used for the reconstruction of the spatiotemporal profile of soft tissue temperature evolution during laser irradiation.

3.2.3 Closed loop control for neurostimulation

Today typical clinical neurostimulation, such as transcranial electric or magnetic stimulation, applies stimulation protocols with pre-defined parameters, such as stimulation intensity, duration and inter-stimulus interval. However, such patient-unspecific open-loop stimulation protocols may not be effective for all patients. We propose to develop a closed-loop neurostimulation protocol that estimates the optimal stimulation intensity in real-time adaptively from observed brain activity. The new stimulation protocol aims to tune the brain's spectral power distribution in a pre-defined way which has been determined in previous experimental open-loop neurostimulation studies. Two PhD projects address different approaches. In one project, observed brain activity is fed into a Kalman observer model (implemented as an Ensemble Kalman Filter (ETKF) which estimates the optimal stimulation and is applied to the brain instantaneously. The nonlinear Kalman observer model defines the target spectral power distribution. In a different project, the closed-loop technique assumes linear brain dynamics and applies conventional feedback control techniques taking into account feedback delay and model errors. In contrast to the first project, which is rather heuristic, this second project applies mathematical analysis techniques to develop the optimal stimulation.

3.2.4 Control in medical robotics

Standard robotic solutions address the deformation problem by extracting a set of features from live images (visual servoing) and adjusting the pose/motion of the robot locally to compensate for the deformations. Nevertheless, visual servoing raises several limitations, particularly for needle insertion applications: 1) intraoperative images usually offer poor visibility of anatomical structures and extracting meaningful information in real-time is challenging; 2) when large deformations occur, the control law of the robot can be significantly modified, which is extremely difficult to relate with image-based displacements; 3) traditional controllers do not exploit biomechanical models capable of predicting the deformation of organs in real-time, which is essential for some control. To address this problem, we proposed a numerical solution to solve inverse Finite Elements simulations (iFE) and derive robotic commands to steer a needle in soft tissues. The method combines a non-rigid registration process to keep the model aligned with the actual organ. Then, we derive robotic commands by computing, from the FE simulation, the Jacobian linking the displacement of the base of the needle (controlled by the robot) and the corresponding displacement of the needle tip inside the tissue. We showed that the Jacobian helps account for complex nonlinear and discontinuous interactions (such as friction and contacts) and allows adapting the robot's behavior faster than waiting for image-based corrections. We recently extended the method with a shared control strategy to increase the safety, stability, and accuracy and the developed solution's acceptance. The primary motivation is to leave potentially dangerous decisions and actions to the practitioner. Other controls of the needle, e.g. to compensate for breathing motion, are performed automatically.

4 Application domains

4.1 Patient-specific stent design through shape optimization

Cardiovascular disease is the world's leading cause of death. Many pathologies can be treated using image-guided catheter procedures such as balloon angioplasty and stenting. However, the risk of post-operative complications and follow-up surgery due to pathological tissue reactions, such as restenosis, is relatively high. This is what motivates computational methods as a tool for improving understanding of the underlying causes and for the computer-aided design of new endovascular devices to prevent postoperative complications in the future. Due in part to their complex geometry and the significant deformations they undergo during insertion, effective simulation of the structure of endoprostheses and their interaction with their environment is necessary and remains a challenge. In this project, we aim at optimizing the stent design to better adapt to the geometry and mechanical characteristics of the artery, and therefore reduce the risk of post-operative complications.

4.2 Computer-based surgical training

Virtual training helps medical students to get familiar with surgical procedures before manipulation of real patients. The development of simulation used for medical training usually requires important computational power, since realistic behaviors are key to deliver a high-fidelity experience to the trainee. Further, the quality of interaction with the simulator (usually via visual and haptic rendering) is also of paramount importance. All these constraints make the development of training systems time-consuming, thus limiting the deployment of virtual simulators in standard medical curriculum.

Our activity in this area is twofold: we continue the development of fast and accurate numerical solutions for computing the interactions between a medical device and anatomical structures, and we investigate means of assessing trainee's performance and ways of providing valuable feedback in the form of a virtual coach.

4.3 Pre-operative planning

Beyond training, clinicians ask for innovative tools that can assist them in the pre-operative planning of an intervention. Using the patient information acquired before the operation, physics-based simulations allow to simulate the effect of therapy with no risk to the patient. The clinicians can thus virtually assess different strategies and select the optimal procedure. Compared to a training simulation, a planning system requires a high accuracy to ensure reliability. Constrained by the time elapsed between the preoperative acquisition and the intervention, the computation must also be efficient.

4.4 Intra-operative guidance

Besides the surgery training and planning, another major need from clinicians is surgical guidance. While the clinician is performing the operation, a guidance system provides enriched visual feedback. This is especially useful with the emergence of minimally invasive surgery (MIS) where the visual information is often strongly limited. It can be used for example to avoid critical areas such as vessels or to highlight the position of a tumor during its resection. In the MIS technique, the clinician does not interact with organs directly as in the open surgery, but manipulates instruments inserted through trocars placed in small incisions in the wall of the abdominal cavity. The surgeon can observe these instruments on a display showing a video stream captured by an endoscopic camera inserted through the navel. The main advantage of the method resides in reducing pain and time recovery, in addition to reducing bleeding and risks of infection. However, from a surgical standpoint, the procedure is quite complex since the field of view is considerably reduced and the direct manipulation of organs is not possible.

4.5 Feedback control of neural activity

In the medical treatment of mental disorders, pharmacological medication plays an important role. However, it is well-known that patients develop resistencies against the medication after some time and hence alternative treatment is mandatory. Besides psycho-cognitive treatment, neurostimulation plays a more and more important role. Today typical clinical neurostimulation, such as transcranial electric or magnetic stimulation, applies stimulation protocols with pre-defined parameters, such as stimulation intensity, duration and inter-stimulus interval. However, such patient-unspecific open-loop stimulation protocols may not be effective for all patients. Our research aims to develop a closed-loop neurostimulation protocol that estimates the optimal stimulation intensity in real-time adaptively based on observed brain activity. In this context, we work together with the laboratory INSERM 1114 and the ICube team IMIS.

4.6 Open source software

For many years, members of the team have considered essential to disseminate our research results (and the algorithms to produce them) in an open manner. The objective was to also develop a framework that could be used internally as a means to integrate our various contributions and facilitate validation and technology transfer. Many of our research results have since been released to the community as open source code, either through improvements of SOFA or as plugins of the framework.

SOFA is an efficient and accurate simulation framework written in C++, developed by our team and researchers from a couple of other Inria teams. It is one of the few open source frameworks for the simulation of heterogeneous mechanical systems. It is particularly aimed at real-time applications involving contacts. It is also often aimed at medical applications. Thanks to its high level of modularity, SOFA allows users to rapidly create complex simulations based on the large set of algorithms ranging from collision detection methods to volume rendering to finite element methods. It is structured around an open source core and many plugins, often open source as well. More than 30 researchers, students or engineers have contributed at various degrees to SOFA, for a total of about 1,500,000 lines of code. Today, the project has gone far beyond French borders.

5 Highlights of the year

Living systems are part of complex environments, which may perturb the systems functions. Nevertheless, most living systems, such as humans, exhibit resilience towards such environmental perturbations. Biophysical diversity enriches neural systems' dynamical repertoire while it remains challenging to reconcile with the robustness and persistence of brain function over time (resilience). We analyzed both analytically and numerically a complex biology-inspired neural network model and show that homogeneous networks demonstrate enhanced instability in response to a slowly-varying modulatory fluctuation [14]. Conversely, excitability heterogeneity was found to implement a homeostatic control mechanism enhancing network resilience. This points out the importance of heterogeneity in neural systems to retain the system's resilience.

Two startups have been created this year:

- EVE – EVolving Education: the objective of this startup is to develop a disruptive model of education and training in surgery, with a low-cost, portable, easy and fun-to-use simulator, mixing physics-based simulation and gaming. More here.
- Twinical: the goal of this startup is to develop a new paradigm for surgical planning and navigation in deformable anatomies. Our technology combines artificial intelligence, physics-based simulation, computer vision and augmented reality for digitally-enhanced visual guidance during a surgery. More here.

6 New software, platforms, open data

6.1 New software

6.1.1 DeepPhysX

Name: DeepPhysX: interfacing AI with multi-physics simulation

Keywords: Numerical simulations, Deep learning, Neural networks, Python

Functional Description: The purpose of DeepPhysX framework is to provide an interface between deep learning algorithms and numerical simulations. It is a full Python project with two main pipelines, allowing both to train artificial neural networks with simulated data and to use trained neural networks as components of numerical simulations. DeepPhysX manages not only the production of synthetic data with multiple numerical simulations in multiprocessing but also the storage of the produced dataset. Additional tools are provided to visualize numerical simulations and to follow the evolution of training sessions.

URL: `https://gitlab.inria.fr/mimesis/DeepPhysX`

Authors: Robin Enjalbert, Alban Odot, Stephane Cotin

Contact: Robin Enjalbert

6.1.2 SSD

Name: SimulationSimpleDatabase

Keywords: Numerical simulations, SQL database, 3D rendering, Python

Scientific Description: The SSD project provides Python3 tools allowing users to easily develop data storage and visualization strategies for their numerical simulations with a minimal lines of code.

This project has two main objectives: * Easy storage management system for any data from a numerical simulation, * Easy storage & rendering management systems for visual data from a numerical simulation.

The SSD project is mainly using the Peewee Python3 library and was mostly designed to fit the DeepPhysX and SOFA frameworks.

Functional Description: The open source project DeepPhysX, an interface between deep learning and numerical simulations, has many features that could be useful for the numerical simulation community that does not use deep learning. Some of these features are implemented for the whole numerical simulation community in this external project - which is now a dependency of DeepPhysX.

A compatibility package is also implemented to take full advantage of this project for the SOFA framework.

Release Contributions: The last version of the SSD project includes changes made to SOFA's Python bindings API. Read and write acces has been optimized on databases with several tables: parallelization has been implemented to speed up interactions with the database, which was previously sequential. This was particularly useful for managing visual data. Finally, a new rendering library is available as an option: it is now possible to visualize with either Vedo or Open3D.

URL: `https://github.com/RobinEnjalbert/SimulationSimpleDatabase.`

Contact: Robin Enjalbert

7 New results

7.1 Digital twins of organs

Participants: Michel Duprez, Vanessa Lleras, Vincent Italiano, Frederique Lecourtier, Stéphane Cotin.

For several years, we have investigated finite element methods that falls under the class of unfitted (also known as immersed boundary) methods. Because such methods do not require a discretization that strictly conforms to the domain boundary, they are particularly suited for the development of digital twins, as they facilitate the automatic generation of patient-specific simulations on complex geometries.

We use a patient-specific bio-mechanical model to reproduce real-time deformations of an organ by combining finite-element simulations and deep neural networks in order to satisfy the rapidity and accuracy requirements of medical applications [7]. We worked in particular on hyperparameter tuning, implementation improvements, and validation of the method.

Moreover, our current results have focused on the development, the numerical analysis and mathematical foundations of a new method called Φ-FEM. The main advantage of our method is that it uses the classical Finite Element tools on unfitted meshes. We have also highlighted that the method significantly improves the convergence when compared to a similar, fitted, discretization of the domain. The benefit and applicability of the Φ-FEM method have already been demonstrated on different problems: heat transfer, crack, interface between two materials, and fluid structure interaction [10, 11]. Our current activity on Φ-FEM consists in an Open Source implementation in a SOFA plugin. This is done in relationship with another development activity that integrates automatic differentiation tools from the project FEniCS (www.fenicsproject.org) to quickly and efficiently add new constitutive models in our code base, through simple Python scripting. We are convinced of the impact of this work for both our research activity and the field in general. It also ties nicely with our work on deep learning for physics, as it offers an elegant alternative to graph networks to perform convolutions on unstructured meshes.

7.2 Accurate and real-time digital twin of the liver

Participants: Sidaty El Hadramy, Stéphane Cotin.

Due to the highly deformable nature of the liver, hepatic surgery presents unique challenges in retrieving the location of relevant landmarks and securing tumor resection while avoiding undesired damage to vascular structures. Recent developments in real-time registration methods have made it possible to bring Augmented Reality (AR) into the operating room [6]. In this work, we propose to use untracked IntraVascular Ultrasound (IVUS) as an intraoperative modality for an accurate and real-time digital twin of the organ. To this end, we introduce a novel method for trackerless ultrasound volume reconstruction, particularly in the realm of minimally invasive surgery. The proposed approach employs a Siamese architecture, featuring a recurrent neural network that utilizes ultrasound image features and optical flow to estimate the relative position of frames. The method operates without the need for additional sensors and was evaluated using ex vivo porcine data [20]. The vascular tree is segmented from the IVUS volume where the centerlines are computed and used to update a biomechanical model [17] built with the preoperative Computer Tomography (CT)data of the patient. In addition, we have proposed an alternative approach where we aim to augment intra-operative Non-contrasted CT (NCCT) images as a means to improve needle CT-guided techniques while reducing the need for contrast agent injection during tumor ablation procedures. This is done by using a neural network that learns local vessel tree image features in an NCCT by leveraging the known vessel tree geometry and topology extracted from a matching Contrasted CT. The augmented CT is generated by fusing the predicted vessel tree with the NCCT [21].

7.3 Physics-informed neural networks for organ shape prediction from fluoroscopic images

Participants: Francois Lecomte, Stéphane Cotin.

In minimally invasive image-guided surgery, several sources of visual information are used. In our context, pre-operative CT-Scan enables the practitioner to segment anatomical structures, while intra-operative fluoroscopic imaging is used for intra-operative navigation. During surgery, deformation of the anatomy leads to a significant mismatch between the fluoroscopic image and the preoperative CT scan. The aim of this work is to develop a non-rigid registration method to correct the mismatch between 3D preoperative imaging and 2D intra-operative imaging. The 2D nature of intra-operative imaging implies a loss of information, making it difficult to reconstruct 3D anatomy from a 2D fluoroscopic image. Moreover, there are no 3D/2D image pairs in sufficient quantities to directly train a neural network to solve this problem. Consequently, a synthetic data generation method has been developed to generate training data for learning the 2D/3D registration task. A neural network architecture has also been introduced to address this ill-posed problem. Our first results [22] were presented during the Hamlyn Symposium (London, June 2023) and received a lot of attention.

7.4 Physically inspired regularization for deformable image registration

Participants: Pablo Alvarez, Stéphane Cotin.

Numerous regularization methods for deformable image registration aim at enforcing smooth transformations, but are difficult to tune-in *a priori* and lack a clear physical basis. To cope with this problem, physically motivated regularization has been introduced. These methods consider the organs in medical images as hyperelastic bodies, and exploit the theory of continuum mechanics for the design of regularization strategies. In addition to their strong physical basis, they also inherently strengthen desirable properties such as transformation smoothness and invertibility. However, to date, they still require complex domain discretization and resolution schemes. In our work, we have extended on these ideas to propose a physically-derived regularization strategy that can be computed at arbitrary points in the domain, therefore not requiring any discretization. Consequently, our strategy is compatible with existing deformable image registration frameworks and optimizers, while maintaining the desirable properties of physically motivated regularization. We have implemented our regularization scheme using deep neural networks [25], and have obtained promising results in a 4DCT lung database widely used in the literature for evaluation of deformable image registration methods.

We plan on using this regularization approach in more challenging deformable registration context such as 2D-3D registration, as well as in the regularization of deep learning methods for digital twins, where observations are scarce.

7.5 Patient-specific stent design through shape optimization

Participants: Michel Duprez, Stéphane Cotin.

Cardiovascular disease, which disrupts blood flow to the heart, brain, arms and legs, is the world's leading cause of death. This high number of deaths motivates the design of minimally invasive procedures and explains the success of image-guided catheter treatment procedures such as balloon angioplasty and stent insertion. However, the risk of post-operative complications and follow-up surgery due to pathological tissue reactions, such as restenosis, is relatively high. This is what motivates computational methods as a tool for improving understanding of the underlying causes and for the computer-aided design of new endovascular devices to prevent postoperative complications in the future. Due in part to their complex geometry and the significant deformations they undergo during insertion, effective simulation of the structure of endoprostheses and their interaction with their environment is still necessary and remains a challenge. Atherosclerosis is characterized by the deposition of an essentially lipid-based plaque (known as atheroma) on artery walls. This plaque is not deposited uniformly throughout the artery. Stent design that takes into account this non-uniformity, as well as the geometry of the artery, can help reduce the risk of complications following stent placement. This is the aim of this project.

7.6 Recovering surgically induced deformations of the liver

Participants: Francois Lecomte, Juan Verde, Stéphane Cotin.

We have performed an extensive validation on recovering surgically induced deformations of the liver from synthetic X-Ray images [29, 22] The next steps are, other than methodological improvements, to validate the accuracy of the method on real X-Ray images implying experiments in collaboration with IHU Strasbourg.

7.7 Non-smooth mechanics

Participants: Ziqui Zeng, Hadrien Courtecuisse, Stéphane Cotin.

Non-smooth mechanics: many clinical interventions rely on mechanical interactions between a device and the anatomy. Surgery and interventional radiology are the two main areas where these interactions are essential and generally complex. During this evaluation period we have continued our activity on constraint modeling and simulation of contacts with friction. The complexity of the problem often leads to unstable numerical approaches, inaccuracy of the solution and slow computation times. Our latest work relies on the idea of solving the constrained problem as a Linear Complementarity Problem (LCP) through an iterative solver (Gauss Seidel in our case) and addresses the issue of computational performance. We use a preconditioner-based contact method relying on an asynchronous Cholesky decomposition. By exploiting the sparsity in assembled matrices, we propose a reduced and parallel computation scheme to address the expensive computation of the Schur complement. An additional numerical scheme that exploits the time consistency of contacts across multiple time steps makes it possible to obtain real-time simulations in the presence of hundreds of contacts. Our results have direct applications in CAI problems such as robotic control of needle insertion or endovascular navigation, but also in surgical training. They are also very relevant in Computer Graphics.

7.8 Order in random systems

Participants: Axel Hutt.

The brain is a complex system with several spatial and temporal scales. The microscopic scales are rather unstructured in space and activity observations show random fluctuations, whereas upper hierarchical levels at the mesoscopic and macroscopic scales exhibit more regular dynamics. In previous studies, we found that additive random input on the microscopic scale to random networks tunes the systems stability and may induce stability changes. Such so-called bifurcations induce ordered structures, being in space or time or in both. This additive noise-induced system evolution (ANISE) has been shown to describe successfully synchronization and desynchronization observed in electroencephalographic data [16].

Moreover, if neural networks exhibit heterogeneity in the nodes properties, then the systems response to external input is changed characteristically dependent on the degree of diversity. This has been shown in spiking networks [18] and rate-coding networks [14, 15].

7.9 Dynamics in systems under neurostimulation

Participants: Thomas Wahl, Axel Hutt.

Brain stimulation is a modern therapy in clinical practice. The various types of stimulation affect the brain's internal structure and functioning, which results to learning processes and, in case of mental disorders, to improvement of the patient's health situation. To understand better how neurostimulation modulates the brain dynamics, a data analysis study of previously recorded cortical Local Field Potential in rats has been performed. It shows that neurostimulation in the brainstem affects strongly the network synchronisation in the gamma-frequency range (30Hz-50Hz) while retaining connectivity in the beta-frequency range (0.5Hz-3Hz) [13].
These experimentally induced cortical modulations in certain frequency bands can also be achieved by a closed-loop feedback control method [19]. We developed a new method which affects the spectral power in pre-specified frequency bands in real-time.

7.10 Binaural beats affect the attention in healthy and attention-deficit human subjects

Participants: Gabriel Alves Castro, Axel Hutt.

Brain stimulation is a modern therapy in clinical practice. Non-invasive stimulation has the advantage against invasive stimulation that it does not rely on surgery and general anesthesia and thus is less costly for the patient's health. Most non-invasive neurostimulation techniques apply an electromagnetic stimulation, e.g. electric currents or magnetic fields applied to the subject's scalp. This procedure requires a scientific institution or laboratory to apply the stimulation. Today, electric neurostimulation devices can be purchased on the free market but are costly for the individual and rarely reimbursed by health assurances. To provide an alternative to such devices, non-electromagnetic stimulation techniques, such as auditory stimulation, may be preferable. We have developed a psycho-physical experimental setup to test subject's visual attention subjected to auditory tones (noise, monaural beats and binaural beats) [26, 28]. Synchronous recording of EEG in healthy subjects and subjects showing attention deficits have revealed that monaural beats may improve visual attention compared to the impact of noise stimulation, while binaural beats do not have a beneficial effect.

7.11 Optimal control to limit epidemia

Participants: Michel Duprez.

There exists no efficient vaccin against arboviruses like Malaria, Dengue, Lymphatic Filariasis, Zika, Chikungunya, Yellow fever, and Japanese encephalitis. One way to limit the propagation of such diseases is to fight their vector which is the mosquito. The sterile insect technique (SIT) is a biological control technique that can be used either to eliminate or decay a wild mosquito population under a given threshold to reduce the nuisance or the epidemiological risk. We have studied the mathematical properties of the optimal release strategies in order to maximize the efficiency of this technique. In [24, 8], we have studied the impact of the migration on the control strategy. Some theoretical results of controllability have been obtained in [9].

7.12 Error control in biomechanics

Participants: Michel Duprez.

The Finite Element Method (FEM) is a well-established procedure for computing approximate solutions to deterministic engineering problems described by partial differential equations. FEM produces discrete approximations of the solution with a discretisation error that can be an be quantified with a posteriori error estimates. The practical relevance of error estimates for biomechanics problems, especially for soft tissue where the response is governed by large strains, is rarely addressed. In [27], we propose an implementation of a posteriori error estimates targeting a user-defined quantity of interest, using the Dual Weighted Residual (DWR) technique tailored to biomechanics. The proposed method considers a general setting that encompasses three-dimensional geometries and model non-linearities, which appear in hyperelastic soft tissues. We take advantage of the automatic differentiation capabilities embedded in modern finite element software, which allows the error estimates to be computed generically for a large class of models and constitutive laws. First we validate our methodology using experimental measurements from silicone samples, and then we illustrate its applicability for patient-specific computations of pressure ulcers on a human heel.

7.13 Optimal control of computer-aided interventions

Participants: Stéphane Cotin, Alban Odot.

We recently started to investigate optimal control as a solution to several challenges in the field of computer-aided intervention. The first problem we addressed was the elastic intraoperative registration of a preoperative liver model and, as an extension, force estimation during robotic surgery. Both are formulated as optimal control problems where the unknown is the surface force distribution applied onto the organ. The deformation is computed using an hyperelastic model, and the optimization problem is solved using an adjoint method. This approach provides greater control over the set of admissible forces and leads to physically-consistent displacement fields. As a byproduct, it permits the recovery of the forces that led to the deformation, and can provide visual haptic feedback in medical robotics. We also rely on optimal control in other problems addressed in the team, such as autonomous endovascular navigation, where we have a similar control challenge. In this case the deformable structure is the catheter or guidewire rather than an organ. Finally, to address the relatively slow computation times that are typical of such optimization methods, we have started the development of differentiable algorithms. They exploit both GPU acceleration and the automatic differentiation tools from frameworks such as PyTorch. This significantly speeds up the computation of the adjoint. This approach is combined with the use of deep neural networks to predict the solution of the forward elastic problem in just a few milliseconds.

8 Bilateral contracts and grants with industry

Participants: Stephane Cotin, Vincent Italiano, Sidaty El Hadramy, Michel Duprez, Robin Enjalbert.

8.1 Bilateral contracts with industry

In July 2023, team members have been involved in the foundation of the start-up *EVE: EVolving Education*. Moreover, team members are involved in the new start-up *Twinical* founded in November. In the context of their foundation, research code has been transferred to both start-ups.

9 Partnerships and cooperations

Participants: Michel Duprez, Axel Hutt, Stephane Cotin.

9.1 International research visitors

9.1.1 Visits of international scientists

Other international visits to the team

Christian Uhl

Status Prof. Dr. rer. nat.

Institution of origin: University of Applied Sciences Ansbach

Country: Germany

Dates: 04/10/2023 - 06/10/2023

Context of the visit: Kick-off meeting of a future collaboration

Mobility program/type of mobility: Visiting Grant from BayFrance / Germany

9.2 National initiatives

ADT - AI for Surgical Vision

Title: AI for Surgical Vision

Duration: 2021 - 2024

Coordinator: Stéphane Cotin

Partners:

- BOPA innovation chair
- Paul Brousse Hospital

Inria contact: stephane.cotin@inria.fr

Summary: The objective of the project is to develop and integrate computer vision algorithms capable of processing images from the operating room in real time into a clinically usable augmented reality prototype. This project reinforces the work carried out in partnership with the "Augmented Operating Room" (BOPA) innovation chair at Hospital Paul Brousse in Paris. The project is part of the Blok-Viz axis whose goal is to process video feeds of the operating field to extract relevant information on which AI algorithms dedicated to attention analysis, registration and augmented reality can be based.

ANR - SPECULAR

Title: Simulation of needle insertion with virtual reality and haptics.

Duration: 2021 - 2025

Coordinator: Stephane Cotin (MIMESIS)

Partners:

- Inria Antenna in Strasbourg, MIMESIS team (France)
- Inria Research Center at Université de Lille, DEFROST team (France)
- InfinityTech 3D (France)

Inria contact: stephane.cotin@inria.fr

Summary: The objective of this project is to develop a complete virtual reality training system for radiofrequency ablation. The research program includes the real-time simulation of the needle-organ interactions, realistic and immersive rendering of the operating room, medical image generation and haptic feedback [23]. The results of this project will accelerate the training of these procedures and could change the standard of care which remains a surgery in many cases.

ANR - VATSOP

Title: Images and models for computer guidance during Video Assisted Thoracic Surgery (VATS).

Duration: 2021 - 2025

Coordinator: Jean-Louis Dillenseger (LTIS Rennes)

Partners:

- TIMC-IMAG Laboratory, Grenoble (France)

- Inria Antenna in Strasbourg, MIMESIS team (France)
- LTSI Laboratoire Traitement du Signal et de l'Image (Rennes, France)

Inria contact: stephane.cotin@inria.fr

Summary: In minimally invasive image-guided surgery, several sources of visual information are used. In our context, pre-operative CT scans enable the practitioner to segment anatomical structures, while intra-operative fluoroscopic imaging is used for intra-operative navigation. The 2D nature of intra-operative imaging implies a loss of information, making it difficult to reconstruct 3D anatomy from a single 2D fluoroscopic image. However, the pre-operative 3D anatomy is known from the pre-operative CT scan. To augment intra-operative fluoroscopic imaging with accurate 3D anatomical information, it is necessary to recover surgery-related deformations, an operation known as non-rigid registration. Our work aims to develop a non-rigid registration method to correct the mismatch between 3D pre-operative imaging and 2D intra-operative imaging. Our approach uses a fully convolutional network architecture to solve the associated inverse problem. Because there exists no dataset of 3D/2D image pairs suited to train a neural network to solve this problem, a synthetic data generation method is developed to generate a training dataset. Supervised learning is performed on this synthetic training data, with Digitally Reconstructed Radiographs as input and displacement fields as output. Contrary to other 2D-3D registration methods, this novel data generation approach does not rely on a statistical motion model. This enables the network to accurately predict deformations beyond predetermined motion patterns. As an example of clinical application, we show that our model can accurately handle surgery-induced deformations in the liver.

ANR - TRECOS

Title: New Trends in Control and Stabilization: Constraints and a Non-local Terms.

Duration: 2020 - 2024

Coordinator: Sylvain Ervedoza (Institut de Mathématiques de Bordeaux, Laboratoire Traitement du Signal et de l'Image)

Partners:

- IMT Institut de Mathématiques de Toulouse (France)
- Inria Antenna in Strasbourg, MIMESIS team (France)
- IMB Institut de mathématiques de Bordeaux (France)
- LJLL Laboratoire Jacques-Louis Lions, Paris (France)

Inria contact: michel.duprez@inria.fr

Summary: The goal of this project is to develop new solutions in control theory for partial differential equations, motivated by models arising in ecology and biology. The project focuses on two aspects. The first one is related to the constraints required on the controls or on the controlled trajectories, for instance positivity constraints, which appears naturally when the state models a temperature. The second aspect concerns the questions of controllability and stabilization d of problems involving non-local operators, such as integral operators in space, in order to take into account phenomena depending on the total mass of the population for instance, or delay and memory terms, such as in visco-elastic fluids, often used to a model blood flows, or more generally models described by systems coupling hyperbolic and parabolic effects.

ANR - S-KELOID

Title: Understanding Keloid Disorders: A multi-scale in vitro/in vivo/in silico approach towards digital twins of skin organoids on the chip.

Duration: 2021 - 2025

Coordinator: Raluca EFTIMIE and Stéphane BORDAS (Univ. Luxembourg)

Partners:

- Laboratoire de Mathématiques de Besançon (France)
- CHU de Besançon (France)
- FEMTO-ST, Besançon (France)
- Institut Mathématiques de Bourgogne, Dijon (France)
- Université du Luxembourg (Luxembourg)
- Inria Antenna in Strasbourg, MIMESIS team (France)

Inria contact: michel.duprez@inria.fr

Summary: Mathematical and numerical modeling approaches allow us to integrate pathological processes that occur across different scales: single cell, cell assembly and tissue. The S-Keloid project aims to investigate the role of mechanical and inflammatory environmental factors on cells associated with keloid disorders, which is formation of a type of scar. From applying experimental tests at tissue-scale and using a multiscale approach, the mechanical stress fields will be integrated into the 3D mathematical model. Parameter identification, optimization and their use across multiple scales will ensure the realism of the models and the quantitative and qualitative predictions of the keloid disorder.

ANR - PhiFEM

Title: ϕ-FEM : development of a Finite Element Method for the design of real-time digital twins in surgery

Duration: 2022 - 2026

Coordinator: Michel Duprez (Inria)

Partners:

- MIMESIS team
- Laboratoire de Mathématiques de Besançon (France)
- Institut de Mathématiques Alexander Grothendieck, Montpellier (France)
- Institut de Recherche en Mathématiques Appliquées, Strasbourg (France)
- Univertsité du Luxembourg (Luxembourg)

Inria contact: michel.duprez@inria.fr

Summary: ϕ-FEM is a recently proposed finite element method for the efficient numerical solution of partial differential equations posed in domains of complex shapes, using simple regular meshes. The main goal of this project is to further develop ϕ-FEM turning it into a tool for efficient, patient-specific and real-time simulations of human organs. To reach this objective, we shall adapt ϕ-FEM to the equations appropriate to biomechanics, provide an efficient implementation for it allowing for the use of actual organ geometries, and finally combine it with convolution neural networks to make it real time after training. The ultimate, long-term, goal is thus to contribute to the construction of digital twins of organs able to guide the surgical act in real time using information acquired before the operation and to reduce the costs of a medical doctors' training by working on visual organs. The innovation of ϕ-FEM lies in its ability to combine the ease of implementation of classical immersed boundary methods with the accuracy of more recent CutFEM/XFEM approaches. It incorporates, by its very construction, the popular description of geometry by Level Set functions, which can represent the real geometry with whatever accuracy desired which makes this approach numerically less expensive than classical finite element methods. The ϕ-FEM paradigm will also be used to develop efficient registration algorithms. Our results will be integrated into the open-source SOFA platform developed in the MIMESIS team to facilitate dissemination.

National Exploratory Action - A/D Drugs

Title: A/D Drugs

Duration: 2020 - 2023

Coordinator: Axel Hutt

Partners: Didier Pinault (INSERM 1114)

Participants: Axel Hutt, Joséphine Riedinger, Didier Pinault

Summary: When it comes to treating mental disorders, the emergence of resistance to medication is a major problem. Replacing chemical medicine with digital medicine (neural stimulation) could be one way of getting around the problem. This is the concept behind "A/D Drugs" (PI : Axel Hutt) which will deploy a process of data assimilation and control in order to adapt stimulation to each patient. But this research is not without its risks – very little is known about the links between the effect of the chemical molecules and neurostimulation (www.inria.fr/en/ad-drugs-exploratory-action-aimed-optimising-neurostimulation).

9.3 Regional initiatives

ITI HEALTHTECH Strasbourg - Master

Title: Optimal auditory neurostimulation to alleviate visual attention deficits in Attention-Deficit/Hyperactivity Disorder (ADHD)

Duration: 2022 - 2023

Coordinator: Axel Hutt

Partners: Anne Bonnefond (INSERM 1114)

Participants: Gabriel ALVES CASTRO

Summary: Attention-deficit/hyperactivity disorder (ADHD) is a neuropsychiatric disorder and patients suffer from inattention, hyperactivity and impulsivity. Since pharmacological treatment may yield adverse cognitive side effects, non-pharmacological neurostimulation is suggested as an alternative. The project investigates the impact of auditory beat stimulation on visual attention in healthy subjects showing ADHD symptoms. The student will perform psychophysical experiments in the presence of binaural beats or isochronic tones and will identify stimulation parameters that improve best visual attention in subjects.

10 Dissemination

Participants: Michel Duprez, Stephane Cotin, Axel Hutt, Pablo Arturo Alvarez Corrales, Josephine Riedinger.

10.1 Promoting scientific activities

10.1.1 Scientific events: organisation

General chair, scientific chair

- Axel Hutt has organized the mini-symposium *Theoretical and computational approaches in neuroscience: Non-invasive neurostimulation* at the conference *NeuroFrance23*, Lyon, May 25, 2023

Member of the organizing committees

- Axel Hutt has been member of the organization committee of the Summer School *Advanced tools for data analysis in Neuroscience* on Aug 31 - Sept 9, 2023.

10.1.2 Scientific events: selection

Chair of conference program committees Axel Hutt has been Co-Chair of the Programme Committee of the *Computational Neuroscience Organization* (CNS), 2023-2024. The CNS organizes the yearly Computational Neuroscience Conference.

Reviewer Pablo Alvarez has been reviewer for the *26th International Conference on Medical Image Computing and Computer Assisted Intervention (MICCAI 2023), Vancouver, October 8-12, 2023*

10.1.3 Journal

Member of the editorial boards

- Axel Hutt is Chief Section Editor of the section *Dynamical Systems* in *Frontiers in Applied Mathematics and Statistics*
- Axel Hutt is Associate Editor for the *Journal of Clinical Medicine*

Reviewer - reviewing activities

- Axel Hutt has been reviewer for journals *European Physical Journal, Qeios, Sensors, Behavioral Sciences, Cells, PLoS One*
- Michel Duprez has been reviewer for *Optimal Control, Applications and Methods, Journal de Mathématiques Pures et Appliquées, Computational and Applied Mathematics* and *Applied Mathematics and Computation.*
- Pablo Alvarez has been reviewer for *IEEE Transactions of Biomedical Engineering.*

10.1.4 Invited talks

- Axel Hutt has been invited to
  - *Nonlinear Data Analysis and Modeling: Advances, Applications, Perspectives*, Potsdam, March 17
  - *Neural fields equations, from Wilson-Cowan to neural engineering*, Paris, June 20
  - *Canadian Computational Neuroscience Spotlight*, online, October 5
- Joséphine Riedinger has been invited to the mini-symposium *Theoretical and computational approaches in neuroscience: Non-invasive neurostimulation* at the conference *NeuroFrance23*, Lyon, May 25.
- Michel Duprez has been invited to
  - *SMAI 2023*, May
  - *CFC 2023*, May
  - the *LJK laboratory* (Grenoble), June 2023
  - the conference *ENUMATH 2023*, September
- Stéphane Cotin has been invited to
  - *Essilor-Luxottica* as part of their seminar series (Charenton-Le-Pont), April
  - the *17th U. S. National Congress of Computational Mechanics* (Albuquerque, USA), July
  - the *J.FIG conference 2023* (Montpellier), November

10.1.5 Scientific expertise

- Axel Hutt has been reviewer for the Research Agency *National Research and Development Agency (ANID) of the Ministry of Science, Technology, Knowledge and Innovation of Chile*
- Axel Hutt has been a grant reviewer for *The Fields Institute for Research in Mathematical Sciences Toronto / Canada*.

10.1.6 Research administration

- Axel Hutt has been member of the jury for the *Chaire Professeur Junior* on *Computational Neuroscience* in Strasbourg 2023
- Stéphane Cotin has been member of the committee in charge of selecting the head of the new AI department at IMT Atlantique (October 2023)

10.2 Teaching - Supervision - Juries

10.2.1 Teaching

- Lecture: Valentina Scarponi, *Mecanobiologie du vivant*, 4h, University of Strasbourg
- License:
  - Michel Duprez, *Numerical analysis techniques*, 15h, L3, University of Strasbourg.
  - Sidathy El Hadramy, *MPA Algebra and Analysis*, 20h, L1 and L2, University of Strasbourg
- Master:
  - Valentina Scarponi, *Introduction To Scientific Reporting*, M2, ITI HealthTech Master, University of Strasbourg
  - Valentina Scarponi, *Continuum Mechanics*, 8h, ITI HealthTech Master, University of Strasbourg
  - Michel Duprez, *Optimal control*, 28h, M2, University of Strasbourg.
  - Michel Duprez, *Incertitude quantification*, 14h, M2, University of Strasbourg.
  - Michel Duprez, *Calcul Scientifique*, 10h, M2, University of Strasbourg
  - Hadrien Courtecuisse, *Real-time simulation*, 80h, M2, University of Strasbourg
  - Axel Hutt, *Spectral Analysis*, 6h, M2, University of Strasbourg, February
- Stéphane Cotin, *Numerical simulation and machine learning*, ITI HealthTech Strasbourg, May
- Stéphane Cotin, *Medical imaging, simulation, and AI*, ITI IRMIA Strasbourg, November
- Axel Hutt, Tutorial on *Spectral Analysis* for participants of the *Computational Neuroscience Conference 2023*, Leipzig, July 15

10.2.2 Supervision

- Axel Hutt supervises Joséphine Riedinger (2020-2023). Title: *Closed-loop transcranial electric stimulation of neural networks in a rat psychosis model.*
- Axel Hutt supervises Thomas Wahl (2021-2024). Title: *Model-based closed-loop neurostimulation with application to schizophrenia.*
- Hadrien Courtecuisse has supervised Ziqiu Zeng (2019-2023). Title: *Real-Time FE Simulation for Large-Scale Problems Using Precondition-Based Contact Resolution and Isolated DOFs Constraints.*

- Michel Duprez supervises Killian Vuillemot (October 2022-September 2025) together with Vanessa Lleras and Mohammadi Bijan. Title: *Unfitted finite element method for the development of organ digital twins.*
- Michel Duprez supervises Valentina Scarponi (2021-2024) together with Florent Nageotte and Stéphane Cotin. Title: *Autonomous Catheter Navigation.*
- Michel Duprez supervises Frédérique Lecourtier (2023-2026) together with Emmanuel Franck and Vanessa Lleras. Title: *Finite element methods and neural network for the augmented surgery.*
- Stephane Cotin supervises Sidaty El Hadramy (2022-2025) together with Benoit Gallix (ICube). Title: *AI-enabled Intraoperative planning for liver surgery using ultrasound imaging.*
- Stephane Cotin has supervised Alban Odot (2020-2023). Title: *Data-driven computational biomechanics using deep neural networks.* The thesis was defended in November.
- Stephane Cotin supervises Nicola Zotto (2022-2025) together with Benoit Gallix (ICube). Title: *Combining AI and biomechanics for computer-assisted interventions.*
- Stephane Cotin supervises Francois Lecomte (2021-2024) together with Jean-Louis Dillenseger (Univ Rennes). Title: *Physics informed neural networks for organ shape prediction from interventional images. Application to Augmented Lung Surgery.*

10.2.3 Juries

- Stéphane Cotin has been member of the PhD committee (and reviewer) of PhD-thesis of Nora Hagmeyer, Universität der Bundeswehr München, June 2023
- Stéphane Cotin has been member of the PhD committee (and reviewer) of the thesis of Saurabh Deshpande, Luxembourg University, October
- Stéphane Cotin has been member of thePhD committee (and supervisor) of the thesis of Alban Odot, Strasbourg University, November

10.3 Popularization

10.3.1 Interventions

Joséphine Riedinger has made a two-hour presentation in front of terminal high school students at the high school *Le Gymnase* in Strasbourg.

11 Scientific production

11.1 Major publications

[1] N. Golse. 'Anatomical, Hemodynamic and Physiological Modeling in Liver Surgery'. Université Paris-Saclay, 20th Sept. 2021. URL: https://tel.archives-ouvertes.fr/tel-03355990.

[2] A. Hutt, S. Rich, T. Valiante and J. Lefebvre. 'Intrinsic neural diversity quenches the dynamic volatility of neural networks'. In: *Proceedings of the National Academy of Sciences of the United States of America* 120.28 (2023), e2218841120. DOI: 10.1073/pnas.2218841120. URL: https://inria.hal.science/hal-04177196.

[3] J. Lefebvre and A. Hutt. 'Induced synchronisation by endogenous noise modulation in finite-size random neural networks: a stochastic mean-field study'. In: *Chaos: An Interdisciplinary Journal of Nonlinear Science* (14th July 2023). DOI: 10.1063/5.0167771. URL: https://inria.hal.science/hal-04162581.

[4] A. Mendizabal, P. Márquez-Neila and S. Cotin. 'Simulation of hyperelastic materials in real-time using deep learning'. In: *Medical Image Analysis* 59 (2019), p. 101569. DOI: 10.1016/j.media.2019.101569. URL: https://hal.inria.fr/hal-02097119.

[5] Z. Zeng, S. Cotin and H. Courtecuisse. 'Real-Time FE Simulation for Large-Scale Problems Using Precondition-Based Contact Resolution and Isolated DOFs Constraints'. In: *Computer Graphics Forum* 41.6 (6th June 2022), pp. 418–434. DOI: 10.1111/cgf.14563. URL: https://hal.science/hal-03694167.

11.2 Publications of the year

International journals

[6] B. Acidi, M. Ghallab, S. Cotin, E. Vibert and N. Golse. 'Augmented reality in liver surgery'. In: *Journal of Visceral Surgery* 160.2 (Apr. 2023), pp. 118–126. DOI: 10.1016/j.jviscsurg.2023.01.008. URL: https://inria.hal.science/hal-04414274.

[7] S. Cotin, G. Mestdagh and Y. Privat. 'Organ registration from partial surface data in augmented surgery from an optimal control perspective'. In: *Proceedings of the Royal Society A: Mathematical, Physical and Engineering Sciences* 480 (22nd Mar. 2023), p. 20230197. DOI: 10.1098/rspa.2023.0197. URL: https://hal.science/hal-04043695.

[8] Y. Dumont and M. Duprez. 'Modeling the impact of rainfall and temperature on sterile insect control strategies in a Tropical environment'. In: *Journal of Biological Systems* (5th Jan. 2024). DOI: 10.1142/S0218339024500128. URL: https://hal.science/hal-03811327.

[9] M. Duprez, M. González-Burgos and D. Souza. 'Remarks on the controllability of parabolic systems with non-diagonalizable diffusion matrix'. In: *Discrete and Continuous Dynamical Systems - Series S* 16.6 (2023), pp. 1346–1382. DOI: 10.3934/dcdss.2023086. URL: https://hal.science/hal-03772372.

[10] M. Duprez, V. Lleras and A. Lozinski. 'ϕ-FEM: an optimally convergent and easily implementable immersed boundary method for particulate flows and Stokes equations'. In: *ESAIM: Mathematical Modelling and Numerical Analysis* 57 (May 2023), pp. 1111–1142. DOI: 10.1051/m2an/2023010. URL: https://hal.science/hal-03588715.

[11] M. Duprez, V. Lleras, A. Lozinski and K. Vuillemot. 'phi-FEM for the heat equation: optimal convergence on unfitted meshes in space'. In: *Comptes Rendus. Mathématique* 361.G11 (21st Dec. 2023), pp. 1699–1710. DOI: 10.5802/crmath.497. URL: https://hal.science/hal-03685445.

[12] A. Hutt. 'Editorial on Insights in Dynamical Systems 2022'. In: *Frontiers in Applied Mathematics and Statistics* 9 (2023). DOI: 10.3389/fams.2023.1254646. URL: https://inria.hal.science/hal-04387591.

[13] A. Hutt and A. G. Hudetz. 'Arousal system stimulation and anesthetic state alter visuoparietal connectivity'. In: *Frontiers in Systems Neuroscience* 17 (17th Apr. 2023). DOI: 10.3389/fnsys.2023.1157488. URL: https://inria.hal.science/hal-04071044.

[14] A. Hutt, S. Rich, T. Valiante and J. Lefebvre. 'Intrinsic neural diversity quenches the dynamic volatility of neural networks'. In: *Proceedings of the National Academy of Sciences of the United States of America* 120.28 (2023), e2218841120. DOI: 10.1073/pnas.2218841120. URL: https://inria.hal.science/hal-04177196.

[15] A. Hutt, D. Trotter, A. Pariz, T. A. Valiante and J. Lefebvre. 'Diversity-induced trivialization and resilience of neural dynamics'. In: *Chaos: An Interdisciplinary Journal of Nonlinear Science* (2024). URL: https://inria.hal.science/hal-04162586.

[16] J. Lefebvre and A. Hutt. 'Induced synchronisation by endogenous noise modulation in finite-size random neural networks: a stochastic mean-field study'. In: *Chaos: An Interdisciplinary Journal of Nonlinear Science* (14th July 2023). DOI: 10.1063/5.0167771. URL: https://inria.hal.science/hal-04162581.

[17] A. Mazier, S. El Hadramy, J.-N. Brunet, J. S. Hale, S. Cotin and S. P. A. Bordas. 'SOniCS: Develop intuition on biomechanical systems through interactive error controlled simulations'. In: *Engineering with Computers* (12th July 2023). URL: https://inria.hal.science/hal-04167398.

[18] A. Pariz, D. Trotter, A. Hutt and J. Lefebvre. 'Selective control of synaptic plasticity in heterogeneous networks through transcranial alternating current stimulation (tACS)'. In: *PLoS Computational Biology* (2023). DOI: 10.1371/journal.pcbi.1010736. URL: https://inria.hal.science/hal-04071053.

[19] T. Wahl, J. Riedinger, M. Duprez and A. Hutt. 'Delayed closed-loop neurostimulation for the treatment of pathological brain rhythms in mental disorders: a computational study'. In: *Frontiers in Neuroscience* (23rd Mar. 2023). DOI: 10.3389/fnins.2023.1183670. URL: https://hal.science/hal-04037276.

International peer-reviewed conferences

[20] S. El Hadramy, J. Verde, K.-P. Beaudet, N. Padoy and S. Cotin. 'Trackerless Volume Reconstruction from Intraoperative Ultrasound Images'. In: MICCAI 2023. Vancouver, Canada, 8th Oct. 2023. URL: https://inria.hal.science/hal-04108248.

[21] S. El Hadramy, J. Verde, N. Padoy and S. Cotin. 'Intraoperative CT augmentation for needle-based liver interventions'. In: MICCAI 2023. Vancouver, Canada, 8th Oct. 2023. URL: https://inria.hal.science/hal-04167447.

[22] F. Lecomte, V. Scarponi, P. A. Alvarez, J. M. Verde, J.-L. Dillenseger, E. Vibert and S. Cotin. 'Enhancing Fluoroscopy-Guided Interventions: a Neural Network to Predict Vessel Deformation without Contrast Agents'. In: *Hamlyn Symposium on Medical Robotics*. The Hamlyn Symposium on Medical Robotics. London, United Kingdom: The Hamlyn Centre, Imperial College London London, UK, 26th June 2023, pp. 75–76. DOI: 10.31256/HSMR2023.38. URL: https://hal.science/hal-04356336.

[23] C. Martin, Z. Zeng and H. Courtecuisse. 'Efficient Needle Insertion Simulation using Hybrid Constraint Solver and Isolated DOFs'. In: Eurographics 2023 - Short Papers. Saarbrücken, Germany: The Eurographics Association, 2023. DOI: 10.2312/egs.20231003. URL: https://hal.science/hal-04181906.

Conferences without proceedings

[24] Y. Dumont, M. Duprez and Y. Privat. 'About sterile insect control strategies in a two patches system'. In: BIOMATH 2023 - International Conference on Mathematical Methods and Models in Biosciences. Pomorie, Bulgaria, 18th June 2023. URL: https://hal.science/hal-04162767.

Reports & preprints

[25] P. Alvarez and S. Cotin. *Deformable Image Registration with Stochastically Regularized Biomechanical Equilibrium*. 21st Dec. 2023. URL: https://hal.science/hal-04356505.

[26] G. Alves Castro, A. Hutt and A. Bonnefond. *Optimal auditory neurostimulation to alleviate visual attention deficits in Attention-Deficit/Hyperactivity Disorder (ADHD)*. 2023. URL: https://inria.hal.science/hal-04225013.

[27] M. Duprez, F. Chouly, P.-Y. Rohan, S. P. A. Bordas, M. Bucki, H. P. Bui and A. Lejeune. *Automatic mesh refinement for soft tissue*. 15th Sept. 2023. URL: https://hal.science/hal-04208610.

[28] A. Hutt. *Conversion of power estimation in Audacity to real Sound Pressure Level in ear phones*. INRIA Nancy Grand Est, 4th Aug. 2023. URL: https://inria.hal.science/hal-04177151.

[29] F. Lecomte, J.-L. Dillenseger and S. Cotin. *CNN-based real-time 2D-3D deformable registration from a single X-ray projection*. 27th Mar. 2023. DOI: 10.48550/arXiv.2212.07692. URL: https://inria.hal.science/hal-04387845.

[30] A. Odot, R. Haferssas and S. Cotin. *DeepPhysics: a physics aware deep learning framework for real-time simulation*. 14th Mar. 2023. DOI: 10.1002/nme.6943. URL: https://hal.science/hal-03327818.

[31] Z. Zeng and H. Courtecuisse. *An efficient implicit constraint resolution scheme for interactive FE simulations*. 11th June 2023. URL: https://hal.science/hal-04125042.

[32] Z. Zeng and H. Courtecuisse. *Efficient parallelization strategy for real-time FE simulations*. 8th June 2023. URL: https://hal.science/hal-04122582.