Activity Report 2017

Project-Team ASCLEPIOS

Analysis and Simulation of Biomedical Images

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Project-Team ASCLEPIOS

Creation of the Project-Team: 2005 November 01, end of the Project-Team: 2017 December 31

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Other Research Topics and Application Domains:

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1. Personnel

Research Scientists
    Nicholas Ayache [Team leader, Inria, Senior Researcher, HDR]
    Hervé Delingette [Inria, Senior Researcher, HDR]
    Hervé Lombaert [Inria, Starting Research Position, from Jun 2017 until Aug 2017]
    Marco Lorenzi [Inria, Researcher]
    Xavier Pennec [Inria, Senior Researcher, HDR]
    Maxime Sermesant [Inria, Researcher, HDR]

Post-Doctoral Fellows
    Nina Miolane [Inria, from Sep 2017]
    Fanny Orlhac [Inria, from Nov 2017]

PhD Students
    Thomas Demarcy [Oticon Medical, PhD Student, Thesis CIFRE, until July 2017]

Loïc Devilliers [Univ. Nice, PhD Student, ENS de Cachan, until Nov 2017]
Sophie Giffard Roisin [Inria, PhD Student, VP2HF, until Dec. 2017]
Shuman Jia [Inria, until 2020]
Julian Krebs [Inria, PhD Student, Siemens Heathcare, until 2019]
Pawel Mlynarski [Inria, PhD Student, Centre commun Inria-Microsoft, until 2018]
Pamela Moceri [Univ. Nice, PhD Student, until Jan. 2018]
Roch Philippe Molléro [Inria, PhD Student, MD-PAEDIGREE, until Jan 2018]
Marc Michel Rohe [Inria, PhD Student, MD-PAEDIGREE, until Sept. 2017]
Clement Abi Nader [Univ de Nice - Sophia Antipolis, from Jul 2017]
Luigi Antelmi [Univ de Nice - Sophia Antipolis, from May 2017]
Tania Marina Bacoyannis [Inria, from Oct 2017]
Jaume Banús Cobo [Univ de Nice - Sophia Antipolis, from Nov 2017]
Nicolas Cedilnik [Inria, from Sep 2017]
Raphaël Sivera [Univ. Nice, PhD Student, until 2018]
Wen Wei [Inria, PhD Student, grant CORDI-S, until 2019]
Qiao Zheng [Inria, PhD Student,ERC MedYMA, until 2019]

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Manon Muntaner [Univ de Nice - Sophia Antipolis, from Mar 2017 until Aug 2017]
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Thomas Tiennot [Inria, from Jul 2017]

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Isabelle Strobant [Inria]

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Alan Garny [Université Auckland, NZ]
Marco Milanesio [Univ de Nice - Sophia Antipolis, from Sep 2017]
Charles Bouveyron [Université Côte d'Azur, from Sep 2017]
Nicolas Duchateau [Lab. Creatis, Univ. Lyon]

2. Overall Objectives

2.1. Overall Objectives

There is an irreversible evolution of medical practice toward more quantitative and personalized decision processes for prevention, diagnosis and therapy.

This evolution is supported by a constantly increasing number of biomedical devices providing *in vivo* measurements of structures and processes inside the human body, at scales varying from the organ to the cellular and even molecular level. Among all these measurements, biomedical images of various forms play an even more central role everyday, along with the exploitation of the genetic information attached to each patient.

Facing the need for a more quantitative and personalized medicine based on larger and more complex sets of measurements, there is a crucial need for developing:

1. advanced image analysis tools capable of extracting the pertinent information from biomedical images and signals;

2. advanced models of the human body to correctly interpret this information; and

3. large distributed databases to calibrate and validate the models.

3. Research Program

3.1. Introduction

Tremendous progress has been made in the automated analysis of biomedical images during the past two decades [68]. Readers who are neophytes to the field of medical imaging will find an interesting presentation of acquisition techniques of the main medical imaging modalities in [60], [58]. Regarding target applications, a good review of the state of the art can be found in the book *Computer Integrated Surgery* [56], in N. Ayache's article [63] and in recent review articles [64], [68]. The scientific journals *Medical Image Analysis* [51], *Transactions on Medical Imaging* [57], and *Computer Assisted Surgery* [59] are also good reference material. One can have a good vision of the state of the art from the proceedings of the MICCAI'2010 (Medical Image Computing and Computer Assisted Intervention [54], [55]) and ISBI'2010 (Int. Symp. on Biomedical Imaging [53]) conferences.

For instance, for rigid parts of the body like the head, it is now possible to fuse in a completely automated manner images of the same patient taken from different imaging modalities (e.g. anatomical and functional), or to track the evolution of a pathology through the automated registration and comparison of a series of images taken at distant time instants [69], [79]. It is also possible to obtain from a Magnetic Resonance Image (MRI) of the head a reasonable segmentation of skull tissues, white matter, grey matter, and cerebro-spinal fluid [82], or to measure some functional properties of the heart from dynamic sequences of Magnetic Resonance [62], Ultrasound or Nuclear Medicine images [70].

Despite these advances and successes, statistical models of anatomy are still very crude, resulting in poor registration results in deformable regions of the body, or between different subjects. If some algorithms exploit the physical modeling of the image acquisition process, only a few actually model the physical or even the physiological properties of the human body itself. Coupling biomedical image analysis with anatomical and physiological models of the human body could not only provide a better understanding of observed images and signals, but also more efficient tools for detecting anomalies, predicting evolutions, simulating and assessing therapies.

3.2. Medical Image Analysis

The quality of biomedical images tends to improve constantly (better spatial and temporal resolution, better signal to noise ratio). Not only are the images multidimensional (3 spatial coordinates and possibly one temporal dimension), but medical protocols tend to include multisequence (or multiparametric) [1] and multimodal images [2] for each single patient.

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[1]Multisequence (or multiparametric) imaging consists in acquiring several images of a given patient with the same imaging modality (e.g. MRI, CT, US, SPECT, etc.) but with varying acquisition parameters. For instance, using MRI, patients followed for multiple sclerosis may undergo every six months a 3D multisequence MR acquisition protocol with different pulse sequences (called T1, T2, PD, Flair, etc.): by varying some parameters of the pulse sequences (e.g Echo Time and Repetition Time), images of the same regions are produced with quite different contrasts depending on the nature and function of the observed structures. In addition, one of the acquisitions (T1) can be combined with the injection of a contrast product (typically Gadolinium) to reveal vessels and some pathologies. Diffusion Tensor Images (DTI) can be acquired to measure the self diffusion of protons in every voxel, allowing the measurement for instance of the direction of white matter fibers in the brain (the same principle can be used to measure the direction of muscular fibers in the heart). Functional MRI of the brain can be acquired by exploiting the so-called Bold Effect (Blood Oxygen Level Dependency): slightly higher blood flow in active regions creates a subtle higher T2* signal which can be detected with sophisticated image processing techniques.

[2]Multimodal acquisition consists in acquiring from the same patient images of different modalities, in order to exploit their complementary nature. For instance, CT and MR may provide information on the anatomy (CT providing contrast between bones and soft tissues while MR within soft tissues of different nature) while SPECT and PET images may provide functional information by measuring a local level of metabolic activity.

Despite remarkable efforts and advances during the past twenty years, the central problems of segmentation and registration have not been solved in the general case. It is our objective in the short term to work on specific versions of these problems, taking into account as much *a priori* information as possible on the underlying anatomy and pathology at hand. It is also our objective to include more knowledge of the physics of image acquisition and observed tissues, as well as of the biological processes involved. Therefore the research activities mentioned in this section will incorporate the advances made in Computational Anatomy and Computational Physiology, as described in sections 3.3 and 3.4.

We plan to pursue our efforts on the following problems:

- multi-dimensional, multi-sequence and multi-modal image segmentation; and
- image Registration/Fusion.

3.3. Computational Anatomy

The aim of Computational Anatomy (CA) is to model and analyse the biological variability of the human anatomy. Typical applications cover the simulation of average anatomies and normal variations, the discovery of structural differences between healthy and diseased populations, and the detection and classification of pathologies from structural anomalies. [3]

Studying the variability of biological shapes is an old problem (cf. the book "On Shape and Growth" by D'Arcy Thompson [81]). Significant efforts have since been made to develop a theory for statistical shape analysis (one can refer to [67] for a good summary, and to the special issue of Neuroimage [80] for recent developments). Despite all these efforts, there are a number of challenging mathematical issues that remain largely unsolved. A particular issue is the computation of statistics on manifolds that can be of infinite dimension (e.g the group of diffeomorphisms).

There is a classical stratification of the problems into the following 3 levels [76]:

1. construction from medical images of anatomical manifolds of points, curves, surfaces and volumes;
2. assignment of a point to point correspondence between these manifolds using a specified class of transformations (e.g. rigid, affine, diffeomorphism);
3. generation of probability laws of anatomical variation from these correspondences.

We plan to focus our efforts on the following problems:

1. statistics on anatomical manifolds;
2. propagation of variability from anatomical manifolds;
3. linking anatomical variability to image analysis algorithms; and
4. grid-computing strategies to exploit large databases.

3.4. Computational Physiology

The objective of Computational Physiology (CP) is to provide models of the major functions of the human body and numerical methods to simulate them. The main applications are in medicine where CP can for instance be used to better understand the basic processes leading to the appearance of a pathology, to model its probable evolution and to plan, simulate, and monitor its therapy.

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[3]The NIH has launched in 2005 the Alzheimer's Disease Neuroimaging Initiative (60 million USD), a multi-center MRI study of 800 patients who will be followed during several years. The aim is to establish new surrogate end-points from the automated analysis of temporal sequences, which is a challenging goal for researchers in Computational Anatomy. The data is to made available to qualified research groups involved or not in the study.

Quite advanced models have already been proposed to study at the molecular, cellular and organ level a number of physiological systems (see for instance [77], [74], [65], [78], [71]). While these models and new ones need to be developed, refined or validated, a grand challenge that we want to address in this project is the automatic adaptation of the model to a given patient by comparing the model with the available biomedical images and signals and possibly also some additional information (e.g. genetic). Building such *patient-specific models* is an ambitious goal, which requires the choice or construction of models with a complexity adapted to the resolution of the accessible measurements and the development of new data assimilation methods coping with massive numbers of measurements and unknowns.

There is a hierarchy of modeling levels for CP models of the human body [66]:

- the first level is mainly geometrical, and addresses the construction of a digital description of the anatomy [61], essentially acquired from medical imagery;
- the second level is physical, involving mainly the biomechanical modeling of various tissues, organs, vessels, muscles and bone structures [72];
- the third level is physiological, involving the modeling of the functions of the major organ systems [73] (e.g. cardiovascular, respiratory, digestive, central or peripheral nervous, muscular, reproductive, hormonal) or some pathological metabolism (e.g. evolution of cancerous or inflammatory lesions, formation of vessel stenoses, etc.); and
- a fourth level is cognitive, modeling the higher functions of the human brain [52].

These different levels of modeling are closely related to each other, and several physiological systems may interact with each other (e.g. the cardiopulmonary interaction [75]). The choice of the resolution at which each level is described is important, and may vary from microscopic to macroscopic, ideally through multiscale descriptions.

Building this complete hierarchy of models is necessary to evolve from a *Visible Human project* (essentially the first level of modeling) to a much more ambitious *Physiological Human project* (see [73], [74]). We will not address all the issues raised by this ambitious project, but instead focus on the topics detailed below. Among them, our objective is to identify some common methods for the resolution of the large inverse problem raised by the coupling of physiological models and medical images for the construction of patient-specific models (e.g. specific variational or sequential methods (EKF), dedicated particle filters). We also plan to develop specific expertise in the extraction of geometrical meshes from medical images for their further use in simulation procedures. Finally, computational models can be used for specific image analysis problems studied in section 3.2 (e.g. segmentation, registration, tracking). Application domains include

1. surgery simulation;
2. cardiac Imaging;
3. brain tumors, neo-angiogenesis, wound healing processes, ovocyte regulation, etc.

3.5. Clinical Validation

If the objective of many of the research activities of the project is the discovery of original methods and algorithms with a proof of its feasibility in a limited number of representative cases (i.e. proofs of concept) and publications in high quality scientific journals, we believe that it is important that a reasonable number of studies include a much more significant validation effort. As the BioMedical Image Analysis discipline becomes more mature, validation is necessary for the transformation of new ideas into clinical tools and/or industrial products. It also helps to get access to larger databases of images and signals, which in turn help to stimulate new ideas and concepts.

4. Highlights of the Year

4.1. Highlights of the Year

4.1.1. *Awards*

- Nina Miolane won the second prize of the competition "My thesis in 180 seconds" at the regional level, among 20 PhD students.

- Xavier Pennec was elected Fellow of the MICCAI scientific Society for "pioneering theoretical contributions grounding the field of computational anatomy, shape statistics and medical image computing".

- Sophie Giffard-Roisin won the best electrophysiology paper award at the Functional Imaging and Modelling of the Heart 2017 conference.

- Matthieu Lê receives the SGBM Research Award for his PhD Thesis.

- Nicholas Ayache was named Chevalier de l'Ordre des Palmes Académiques (Order of Academic Palms), promotion of July 2017.

- Nicholas Ayache was elected member of the Académie Nationale de chirurgie (National Academy of Surgery).

BEST PAPER AWARD:

[37]
S. GIFFARD-ROISIN, H. DELINGETTE, T. JACKSON, L. FOVARGUE, J. LEE, A. RINALDI, N. AYACHE, R. RAZAVI, M. SERMESANT. *Sparse Bayesian Non-linear Regression for Multiple Onsets Estimation in Non-invasive Cardiac Electrophysiology*, in "Functional imaging and modelling of the heart 2017", Toronto, Canada, M. POP (editor), Functional imaging and modelling of the heart 2017, Springer International Publishing, June 2017, pp. 230-238, Best paper award FIMH 2017, category: Electrophysiology [*DOI :* 10.1007/978-3-319-59448-4_22], https://hal.inria.fr/hal-01498602

5. New Software and Platforms

5.1. MedInria

KEYWORDS: Visualization - DWI - Health - Segmentation - Medical imaging
SCIENTIFIC DESCRIPTION: It aims at creating an easily extensible platform for the distribution of research algorithms developed at Inria for medical image processing. This project has been funded by the D2T (ADT MedInria-NT) in 2010, renewed in 2012. A fast-track ADT was awarded in 2017 to transition the software core to more recent dependencies and study the possibility of a consortium creation.The Visages team leads this Inria national project and participates in the development of the common core architecture and features of the software as well as in the development of specific plugins for the team's algorithm.
FUNCTIONAL DESCRIPTION: MedInria is a free software platform dedicated to medical data visualization and processing.

- Participants: Maxime Sermesant, Olivier Commowick and Théodore Papadopoulo

- Partners: HARVARD Medical School - IHU - LIRYC - NIH

- Contact: Olivier Commowick

- URL: http://med.inria.fr

5.2. Music

Multi-modality Platform for Specific Imaging in Cardiology
KEYWORDS: Medical imaging - Cardiac Electrophysiology - Computer-assisted surgery - Cardiac - Health

FUNCTIONAL DESCRIPTION: MUSIC is a software developed by the Asclepios research project in close collaboration with the IHU LIRYC in order to propose functionalities dedicated to cardiac interventional planning and guidance. This includes specific tools (algorithms of segmentation, registration, etc.) as well as pipelines. The software is based on the MedInria platform.

- Participants: Florent Collot, Mathilde Merle and Maxime Sermesant
- Partner: IHU- Bordeau
- Contact: Maxime Sermesant
- URL: https://team.inria.fr/asclepios/software/music/

5.3. SOFA

Simulation Open Framework Architecture
KEYWORDS: Real time - Multi-physics simulation - Medical applications
FUNCTIONAL DESCRIPTION: SOFA is an Open Source framework primarily targeted at real-time simulation, with an emphasis on medical simulation. It is mostly intended for the research community to help develop new algorithms, but can also be used as an efficient prototyping tool. Based on an advanced software architecture, it allows : the creation of complex and evolving simulations by combining new algorithms with algorithms already included in SOFA, the modification of most parameters of the simulation (deformable behavior, surface representation, solver, constraints, collision algorithm, etc.) by simply editing an XML file, the building of complex models from simpler ones using a scene-graph description, the efficient simulation of the dynamics of interacting objects using abstract equation solvers, the reuse and easy comparison of a variety of available methods.

- Participants: Christian Duriez, François Faure, Hervé Delingette and Stéphane Cotin
- Partner: IGG
- Contact: Stéphane Cotin
- URL: http://www.sofa-framework.org

5.4. VP2HF

KEYWORDS: Health - Cardiac - Medical - Image - Processing - Medical imaging
FUNCTIONAL DESCRIPTION: The VP2HF software is developed by the Asclepios team and brings together all the research produced by the VP2HF's partners. It contains MedInria plugins implemented by teams such as UPF Barcelona, KCL, and specific tools provided by Philips (algorithms of segmentation, scar segmentation, ...). It aims at integrating in a single clinical workflow, tools to improve the therapy selection and treatment optimisation for patients suffering from heart failure.

- Participants: Hakim Fadil, Loic Cadour and Maxime Sermesant
- Contact: Maxime Sermesant

5.5. Longitudinal SVF Framework

Longitudinal Stationary Velocity Field (SVF) Framework
KEYWORDS: Image registration - Image analysis - Medical imaging
SCIENTIFIC DESCRIPTION: The pipeline pre-process the images, and then estimates the longitudinal deformation per patient using the log-demons (or more recently the LCC-log-demons), transports the subject-SVF into a common spatial reference and performs group-wise analyses.
FUNCTIONAL DESCRIPTION: The Longitudinal Stationary Velocity Field (SVF) Framework estimates longitudinal brain deformations from image data series, transport them in a common space and perform statistical group-wise analyses.

It is based on freely available softwares and tools, and consists of three main steps: i) Pre-processing, ii) Position correction, iii) Non-linear deformation analysis.

- Authors: Marco Lorenzi, Xavier Pennec, Giovanni Frisoni and Nicholas Ayache
- Partner: IRCCS San Giovanni di Dio Fatebenefratelli
- Contact: Xavier Pennec

5.6. LCC-LogDemons

KEYWORD: Image registration

SCIENTIFIC DESCRIPTION: LCClogDemons is an accurate and robust diffeomorphic registration framework based on the log-Demons. It implements the symmetric Local Correlation Coefficient (LCC) as a similarity measure, and thus it is unbiased with respect to local linear intensity bias of the images.

LCC-LogDemons is suited for both inter and intra-subject registration, and compares well with respect to state-of-art methods. Thanks to the stable and consistent scheme for the computation of the Jacobian determinant of the transformation, LCClogDemons represents a reliable instrument for Tensor Based Morphometry (TBM).

The average registration time for typical 3D images is around 30 minutes for a single core on a Xeon platform 2.66Ghz quad core, 4Gb RAM.

FUNCTIONAL DESCRIPTION: LCClogDemons is an accurate and robust diffeomorphic registration framework based on the log-Demons. It implements the symmetric Local Correlation Coefficient (LCC) as a similarity measure, and thus it is unbiased with respect to local linear intensity bias of the images.

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- Participants: Marco Lorenzi and Xavier Pennec
- Contact: Xavier Pennec
- URL: https://team.inria.fr/asclepios/software/lcclogdemons/

5.7. GP-ProgressionModel

GP progression model

KEYWORDS: Data modeling - Data visualization - Data integration - Machine learning - Biostatistics - Statistical modeling - Medical applications - Evolution - Brain - Uncertainly - Uncertainty quantification - Alzheimer's disease - Probability - Stochastic models - Stochastic process - Trajectory Modeling - Marker selection - Health - Statistic analysis - Statistics - Bayesian estimation

FUNCTIONAL DESCRIPTION: Disease progression modeling (DPM) of Alzheimer's disease (AD) aims at revealing long term pathological trajectories from short term clinical data. Along with the ability of providing a data-driven description of the natural evolution of the pathology, DPM has the potential of representing a valuable clinical instrument for automatic diagnosis, by explicitly describing the biomarker transition from normal to pathological stages along the disease time axis.

In this software we reformulate DPM within a probabilistic setting to quantify the diagnostic uncertainty of individual disease severity in an hypothetical clinical scenario, with respect to missing measurements, biomarkers, and follow-up information. The proposed formulation of DPM provides a statistical reference for the accurate probabilistic assessment of the pathological stage of de-novo individuals, and represents a valuable instrument for quantifying the variability and the diagnostic value of biomarkers across disease stages.

Basic usage:

model = GP_progression_model.GP_progression_model(input_X,input_N,N_random_features)

X and Y should be A list of biomarkers arrays. Each entry "i" of the list is a list of individuals' observations for the biomarker i The monotonicity is enforced by the parameter self.penalty

- The class comes with an external method for transforming a given .csv file in the required input X and Y:

X,Y,list_biomarker = GP_progression_model.convert_csv(file_path)

- The method Save(folder_path) saves the model parameters to an external folder, that can be subsequently read with the method Load(folder_path)

- Optimization can be done with the method Optimize:

model.Optimize()

This software is based on the publication:

Probabilistic disease progression modeling to characterize diagnostic uncertainty: Application to staging and prediction in Alzheimer's disease. Marco Lorenzi, Maurizio Filippone, Daniel C. Alexander, Sebastien Ourselin Neuroimage. 2017 Oct 24. pii: S1053-8119(17)30706-1. doi: 10.1016/j.neuroimage.2017.08.059. HAL Id : hal-01617750 https://hal.archives-ouvertes.fr/hal-01617750/

- Authors: Marco Lorenzi and Maurizio Filippone
- Contact: Marco Lorenzi
- URL: https://team.inria.fr/asclepios/team/marco-lorenzi/

6. New Results

6.1. Medical Image Analysis

6.1.1. *Segmentation and Anatomical Variability of the Cochlea from Medical Images*

Participants: Thomas Demarcy [Correspondant], Hervé Delingette, Charles Raffaelli [CHU, Nice], Clair Vandersteen [IUFC, Nice], Dan Gnansia [Oticon Medical], Nicholas Ayache.

image segmentation ; surgery planning ; shape modelling ; anatomical variability ; cochlear implant ; temporal bone

- We introduced an automated and reproducible framework for cochlear shape analysis [13].
- We introduced a new cochlear segmentation method within a generative probabilistic Bayesian framework for CT images [6].
- We studied the shape variability with a large database of CT images (N = 987) and quantified the bilateral symmetry in cochlear anatomy.
- We provided a proof of concept for the estimation of postoperative cochlear implant electrode-array position from clinical CT (Fig. 1).

6.1.2. *Prediction of Post-Ablation Outcome in Atrial Fibrillation Using Shape Parameterization and Partial Least Squares Regression*

Participants: Shuman Jia [Correspondent], Claudia Camaioni, Marc Michel Rohe, Pierre Jaïs, Xavier Pennec, Hubert Cochet, Maxime Sermesant.
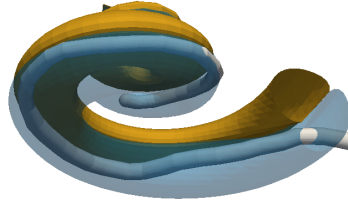
Figure 1. Cochlear implant electrode-array position (white) with respect to scala tympani (blue) and scala vestibuli (orange)

We proposed an application of diffeomorphometry and partial least squares regression to address the problem of post-ablation outcome in atrial fibrillation.

As illustrated in Fig. 2, we computed a template of left atrial shape in control group and then established point-to-point correspondence between patient-specific shapes and the template. The diffeomorphic deformations are encoded and applied in partial least squares regression to predict ablation success, which outperformed the left atrial volume index.
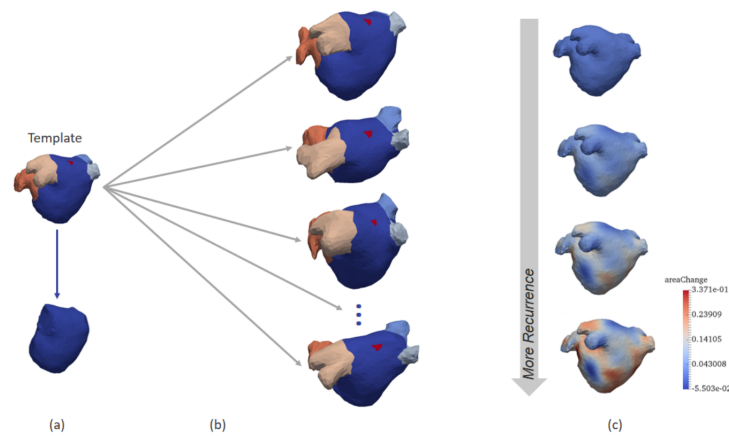
Figure 2. Extraction of remodeling information vs. recurrence. (a) average shape in control group; (b) deformation from the template to patient-specific shapes; (c) deformation mode correlated with recurrence.

6.1.3. Cardiac Imaging and Machine Learning for Electrostructural Tomography

Participants: Tania Marina Bacoyannis [Correspondent], Hubert Cochet [IHU Liryc, Bordeaux], Maxime Sermesant.

This work is funded within the ERC Project ECSTATIC from the IHU Liryc, in Bordeaux.

Machine Learning, Cardiac modeling, Personalised simulation, Inverse problem of ECG, Electrical simulation, Inverse problem.

By using non-invasive electrical data (Body Surface Potential Mapping), we aim to develop a machine learning approach that can improve electrophysiological cardiac modeling in order to improve diagnosis and predict the response to therapy. This project involves measured and simulated data. For example, we processed experimental data provided by the IHU Liryc, gathered during an experiment on an healthy pig's heart (Figure 3). The simulated potentials appeared to be close to the measurements (Figure 4). The short-term goal is to reconstruct semi-automatically the simulated personalized activation maps.
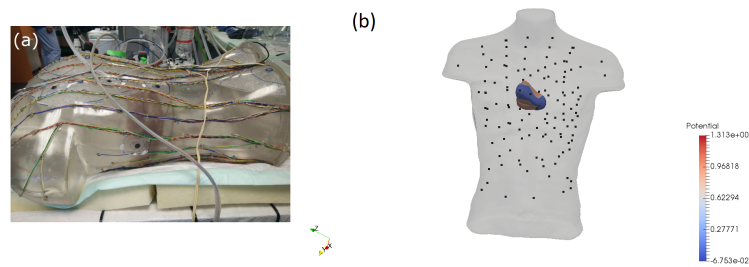
Figure 3. (a) Torso- tank experimental setup with perfused pig heart,(b) Representation of the experimental Torso for BSPM registration of the healthy pig heart, Torso's electrodes and the estimated activation map
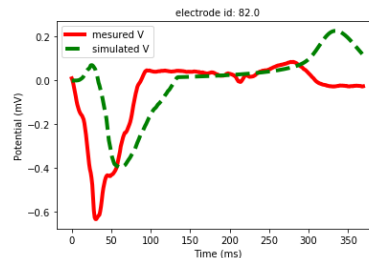
Figure 4. Example of BSPM signals on the Torso's electrode number 82

6.1.4. VT-Scan: image based modelling of cardiac electrophysiology to guide catheter radiofrequency ablation of re-entrant ventricular tachycardia

Participants: Nicolas Cedilnik [Correspondent], Maxime Sermesant, Hubert Cochet, Pierre Jaïs, Frédéric Sacher.

This work was funded by IHU Liryc, Bordeaux.

cardiac electrophysiology modelling, cardiac imaging, ventricular tachycardia, catheter ablation, arrhythmia

- We used cardiac CT images to estimate infarct scar density and location using an automated thickness computation.
- A wavefront propagation speed was derived from this thickness in order to parametrize an Eikonal model of cardiac electrophysiology (see 5).

- We were able to match our simulations to recorded ventricular tachycardia patterns obtained during catheter ablation procedures, on 10 different ventricular tachycardias.
- This work was presented at the Functionnal Imaging and Modelling of the Heart conference in Toronto[34].
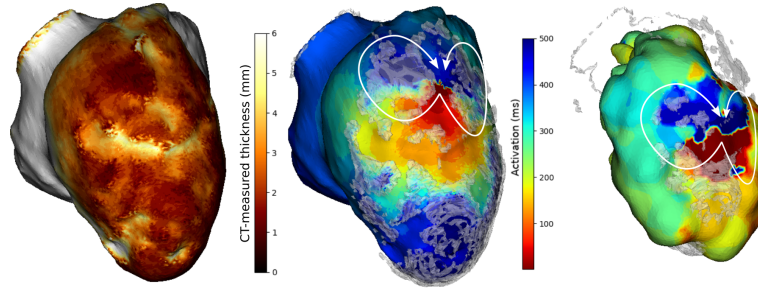
Figure 5. Example of a patient-specific simulation of a proven re-entrant wavefront propagation pattern. [Left] CT-measured myocardial wall thickness, projected on a CT-derived 3D mesh. [Middle] Myocardial activation simulation result using our framework. [Right] Activation recorded during a ventricular tachycardia catheter ablation

6.1.5. Deep Learning for Tumor Segmentation

Participants: Pawel Mlynarski [Correspondent], Nicholas Ayache, Hervé Delingette, Antonio Criminisi [MSR].

This work is funded by Inria-Microsoft joint center and is done in cooperation with Microsoft Research in Cambridge.

deep learning, semi-supervised learning, segmentation, MRI, tumors
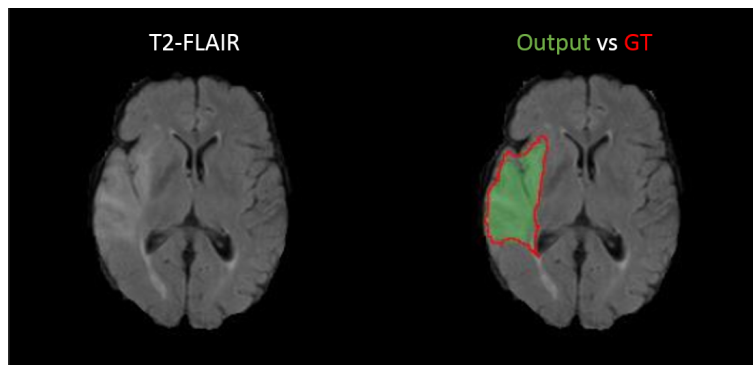
Figure 6. Left: axial slice of a brain MR image presenting a malignant tumor. Right: GT truth (red contour) vs segmentation produced by our semi-supervised method.

- We designed an algorithm for semi-supervised learning of neural nets for segmentation of tumors. The proposed system produces accurate binary segmentations (Figure 6) on unseen images with a limited number of ground truth segmentations used during the training phase.
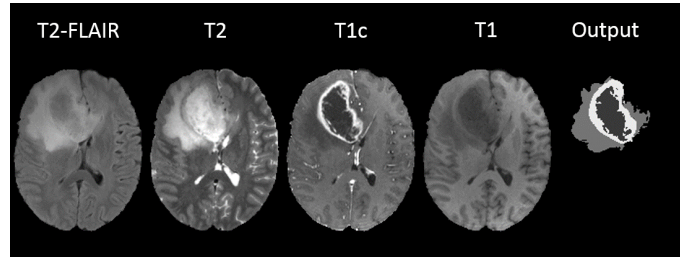
Figure 7. Multimodal MR and the multi-class tumor segmentation produced by our system.

- We proposed an efficient system based on Convolutional Neural Networks for multi-class segmentation of tumors in multimodal MR images (Figure 7). In particular, we proposed a new approach for treating different MR sequences and we introduced a new approach for ensembling 2D and 3D networks. We evaluated our method on the public benchmark of BRATS 2017 challenge and we obtained a top-3 performance among 60 participating teams.

6.1.6. Learning Brain Alterations in Multiple Sclerosis from Multimodal Neuroimaging Data

Participants: Wen Wei [Correspondent], Nicholas Ayache [Inria], Olivier Colliot [ARAMIS].

Multiple Sclerosis, MRI, PET

Multiple sclerosis (MS) is a demyelinating and inflammatory disease of the central nervous system . The goal of this topic is to develop a machine learning approach that can predict different types of PET-derived brain alterations using multiple local and regional MRI measures for MS patients. Figure 8 shows an example of multiple MRI pulse sequences for MS studies.
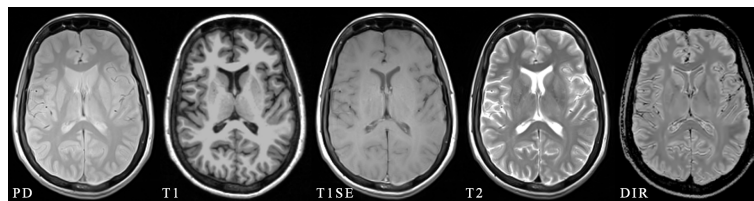
Figure 8. Proton density (PD), T1 spin-echo (T1SE), T1-w, T2-w, double inversion recovery (DIR) weighted images are used for MS studies.

6.1.7. Robust and 3D-Consistent Cardiac Segmentation by Deep Learning

Participants: Qiao Zheng [Correspondent], Hervé Delingette [Inria], Nicolas Duchateau [Université Claude Bernard Lyon 1], Nicholas Ayache [Inria].

Cardiac Segmentation, Deep Learning, MRI, Robustness, Consistency

We propose a method based on deep learning to perform cardiac segmentation on short axis MRI image stacks. An example of segmentation is presented in Figure 9. The method is trained on a large database and then tested on other state-of-the-art cohorts. Results comparable or even better than the state-of-the-art in terms of distance measures are achieved. They prove the contribution of our method to enhance spatial consistency, and its generalization ability to unseen cases even from other databases.
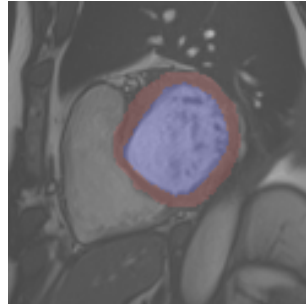
Figure 9. An example of cardiac segmentation.

6.1.8. *Joint analysis of radiomic and metabolomic features to improve diagnosis and therapy in oncology*

Participants: Fanny Orlhac [Correspondent], Charles Bouveyron, Hervé Delingette, Nicholas Ayache, Olivier Humbert [CAL], Jacques Darcourt [CAL], Thierry Pourcher [CEA], Fanny Vandenbos [CHU Nice].

Inria postdoctoral fellowship for 16 months

Radiomics, Metabolomics, Statistical learning

This work is done in collaboration with the Centre Antoine Lacassagne and the TIRO team (Transporter in Imagery and Radiotherapy for Oncology, CEA-UNS) located in Nice.

- The project consists to jointly analyze histogram, shape and textural features extracted from medical images (radiomics) and metabolomic data in oncology (see Figure 10).
- The goal is to better characterize tumor heterogeneity from both data sources in order to provide a personalized patient management.
- The work focuses on two pathologies: breast cancer and glioblastoma.
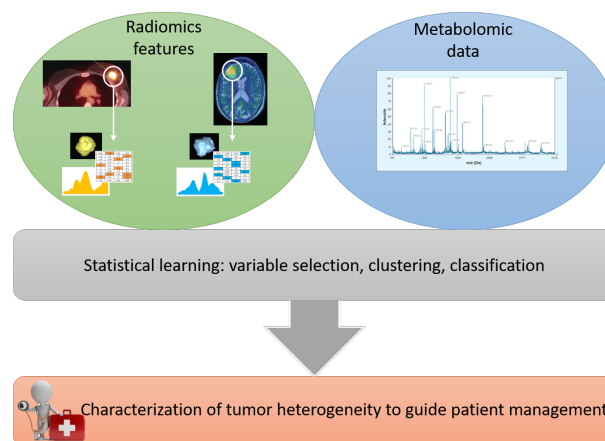
Figure 10. Joint analysis of radiomic and metabolomic features.

6.1.9. Heart & Brain: discovering the link between cardiovascular pathologies and neurodegeneration through biophysical and statistical models of cardiac and brain images.

Participants: Jaume Banús Cobo [Correspondent], Maxime Sermesant, Marco Lorenzi.

Uinversité Côte d'Azur (UCA)

Lumped models - Medical Imaging - Biophysical simulation - Machine learning

The project aims at developing a computational model of the relationship between cardiac function and brain damage from large-scale clinical databases of multi-modal and multi-organ medical images. We will use advanced statistical learning tools for discovering relevant imaging features related to cardiac dysfunction and brain damage from large datasets of medical images and clinical information; these measurements will be combined within a unified mechanistic framework to understand and validate the relationship between cardiac function, vascular pathology and brain damage. The goal is to provide an unprecedented instrument for the in-vivo assessment of latent neurodegenerative conditions in the general population, and will be validated with respect to established indices of cognitive decline and to specific sub-population for which the ground truth is known.
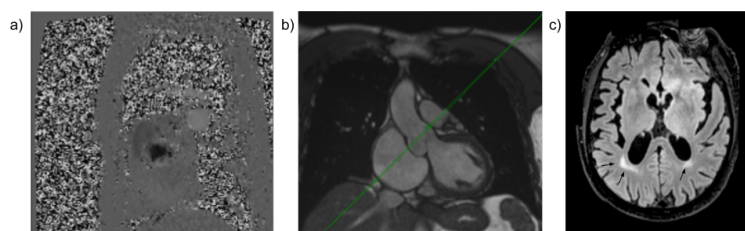
Figure 11. a) Aortic valve flow imaging, view obtained from the plane represented in the left ventricular outflow tract (LVOT) cine b); c) T2 FLAIR image in which white matter hyperintensities (WMHs) are visible.

6.1.10. Statistical learning on large databases of heterogeneous imaging, cognitive and behavioural data

Participants: Luigi Antelmi [Correspondant], Marco Lorenzi, Nicholas Ayache, Valeria Manera, Philippe Robert.

statistical learning, neuroimaging, big data, multimodal

The aim of our work is to develop scalable learning models for the joint analysis of heterogeneous biomedical data. The project will be applied to the investigation of neurological disorders from collections of brain imaging, body sensors, biological and clinical data available in current large-scale health databases. The resulting methodological framework will be tested on the UK Biobank, as well as on pathology-specific clinical data, as provided by the ADNI [4], or INSIGHT [5] initiatives.

From the methodological perspective, the project will focus on the development of computationally efficient formulations of probabilistic latent variable models. These approaches will highlight meaningful relationship among biomarkers that will be used to develop optimal strategies for disease quantification and prediction (Fig. 12).

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[4] http://adni.loni.usc.edu/
[5] http://alzheimer-recherche.org/9248/etude-insight/

The research is within the MNC3 initiative (Médecine Numérique: Cerveau, Cognition, Comportement) funded by Université Côte d'Azur (UCA), and will be performed in collaboration with the Institut Claude Pompidou (CHU of Nice).
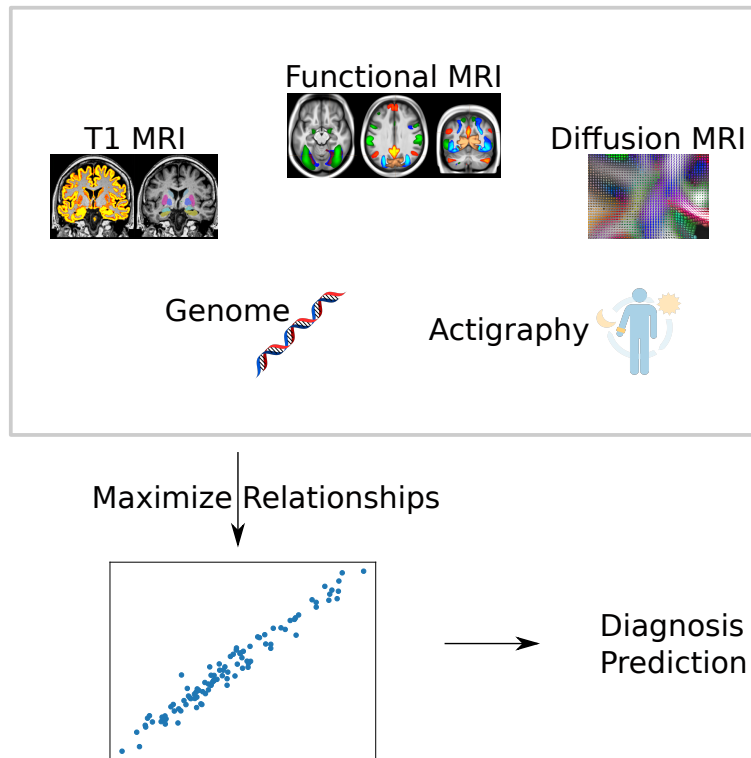
Figure 12. Adopted framework: development of computationally efficient formulations of probabilistic latent variable models to highlight meaningful relationship among biomarkers for disease quantification and prediction.

6.1.11. *Robust non-rigid registration through agent-based action learning*

Participants: Julian Krebs [Correspondent], Hervé Delingette, Tommaso Mansi [Siemens [Siemens Healthineers, Medical Imaging Technologies], Nicholas Ayache.

This PhD is carried out between the Asclepios research group, Inria Sophia Antipolis and Medical Imaging Technologies, Siemens Healthineers, Princeton, New Jersey, USA.

Deformable Registration, Deep Learning, Reinforcement Learning

We developed a deep learning-based approach for organ-specific deformable registration in 3-D [39] by:

- reformulating deformable registration as an agent-based learning problem (Fig. 13)
- using a low-parametric parametric statistical deformation model
- applying a novel ground truth generator which allows generating millions of synthetically deformed training samples requiring only a few real deformation estimations

Improved performance has been demonstrated with respect to traditional algorithms.
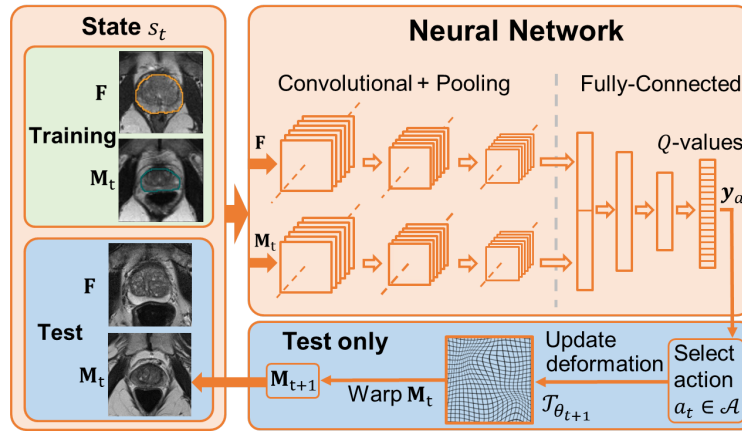
Figure 13. Dual-stream network used for the agent's action estimations including single-stage Markov Decision Process for testing (blue background).

6.2. Computational Anatomy

6.2.1. Inconsistency of Template Estimation in Quotient Spaces

Participants: Loïc Devilliers [Correspondent], Stéphanie Allassonnière [Université Paris-Descartes], Alain Trouvé [ENS Paris-Saclay], Xavier Pennec.

Inria postdoctoral fellowship for 16 months

Template estimation, Fréchet Mean, Quotient Spaces, Inconsistency, Consistency Bias

- A central issue in Computational Anatomy is to compute an unbiased template prototype of our data images (the template) in the presence of two effects: the noise in the ambient space and the unknown registration of the data. The template estimation is usually performed by minimizing the discrepancy after registration (and iterating), which corresponds geometrically to the computation of the Fréchet mean in the quotient space. So far, it was generally believed that the template estimation with this method was unbiased.

- We show in this work that inconsistency is in fact the general situation when the ambient space is an infinite dimensional linear space. In [15] we prove that this method is generally inconsistent when the action is isometric. Moreover the consistency bias has been quantified [35] thanks to a Taylor expansion in the noise level. Besides, we provide proofs of inconsistency for non isometric action [15] when the noise level is large enough.

6.2.2. Geometric statistics for Computational Anatomy

Participants: Nina Miolane [Correspondent], Xavier Pennec.

This work is conducted jointly with the Department of Statistics of Stanford, in the context of the associated team GeomStats of the program Inria@SiliconValley.

Statistics, Computational Anatomy, Differential Geometry, Template shape, asymptotic bias

The usual algorithm of brain template estimation is asymptotically biased, therefore inconsistent: even with an infinite number of brain images in the database, the template estimate may not converge to the brain anatomy it is meant to estimate. In [22]:

- we present a methodology that quantifies spatially the brain template's asymptotic bias, see Figure 14,

- we propose a topologically constrained adaptation of the template computation, that constructs a hierarchical template with bounded bias, and we apply it to the Open Access Series of Imaging Studies (OASIS) database.
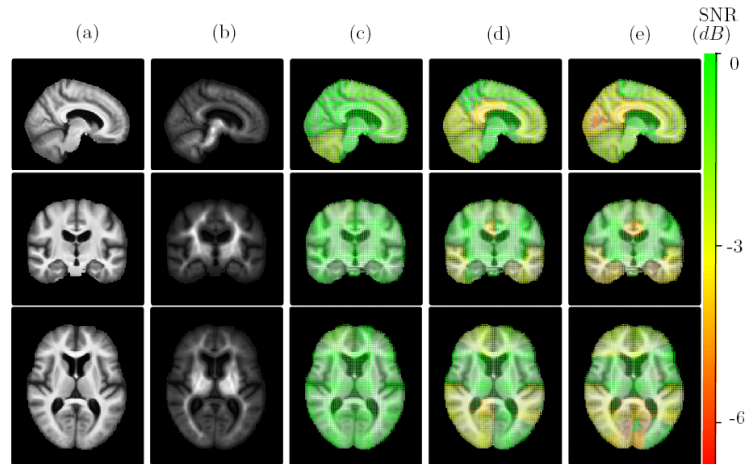
Figure 14. Here we investigate the brain template's consistency as an estimator of a unique anatomy, with respect to the signal-over-noise ratio (SNR) of different regions. The SNR is related to the ratio of the maximum difference in intensity of the region, on the intensity variability averaged on corresponding registered subjects. (a) Template, (b) Template whitened by the intersubject variability, (c) Region-wise inconsistency for a SNR threshold = 1.3, (d) for threshold = 2, (e) for threshold = 4 (dimensionless).

6.2.3. SVF-Net: Learning Deformable Registration Using Shape Matching

Participants: Marc Michel Rohe [Correspondent], Xavier Pennec, Maxime Sermesant.

Registration, Deep Learning, Shape Matching

We propose an innovative approach for registration based on the deterministic prediction of the parameters from both images instead of the optimization of a energy criteria [44]. The method relies on a fully convolutional network (see Fig. 15). Whereas convolutional networks have seen a widespread expansion and have been already applied to many medical imaging problems such as segmentation and classification, its application to registration has so far faced the challenge of defining ground truth data on which to train the algorithm. Here, we present a novel training strategy to build reference deformations which rely on the registration of segmented regions of interest. The speed and robustness of this registration algorithm make it a strong candidate within a multi-atlas segmentation pipeline [45].

6.2.4. Reduced Representation of Segmentation and Tracking in Cardiac Images for Group-Wise Longitudinal Analysis

Participants: Marc Michel Rohe [Correspondant], Xavier Pennec, Maxime Sermesant.
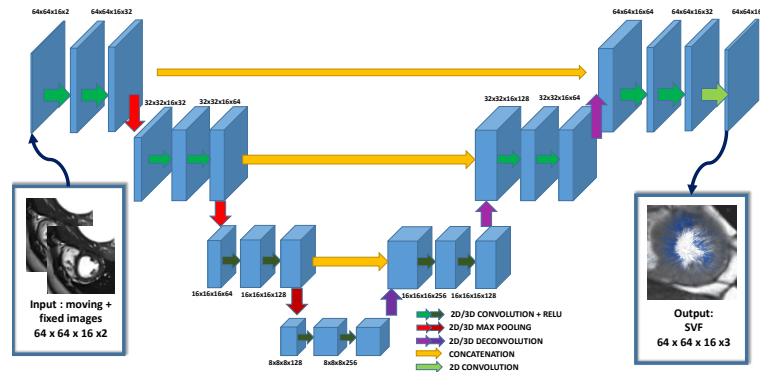
Figure 15. Fully convolutional neural networks for 3D registration: The inputs are the fixed and the moving 3D images. The output is a dense SVF symmetrically mapping the two images defined on the initial image grid.

Medical image analysis, Non-rigid registration, Deep learning, Statistical model reduction, Longitudinal analysis

We study image-based methods for the analysis of cardiac motion to enable group-wise statistics, automatic diagnosis and longitudinal study [10]. This is achieved by combining advanced medical image processing with machine learning methods and statistical modelling. The first axis of this work is to define an automatic method for the segmentation of the myocardium. The second axis of this work is focused on the improvement of cardiac motion tracking methods in order to define relevant low-dimensional representations. Finally, in the last axis, we apply the previously defined representation to the problem of diagnosis and longitudinal analysis. These three axes form an end to end framework for the study of cardiac motion starting from the acquisition of the medical images to their automatic analysis. Such a framework could be used for diagnosis and therapy planning in order to improve the clinical decision making with a more personalised computer-aided medicine.

6.2.5. *A model of brain morphological evolution*

Participants: Raphaël Sivera [Correspondent], Hervé Delingette, Marco Lorenzi, Xavier Pennec, Nicholas Ayache.

Longitudinal modeling, deformation framework, brain morphology, Alzheimer's disease, aging.

We proposed a deformation-based generative model of the brain morphological evolution that can joinly describes the effect of aging and Alzheimer's disease. It relies on longitudinal description of the aging and disease consequences and can be use to compute image-based cross-sectional progression markers (see Figure 16). This approach is able to propose a description of the disease evolution, population and subject-wise.

6.2.6. *Statistical Learning of Heterogeneous Data in Large-Scale Clinical Databases*

Participants: Clement Abi Nader [Correspondent], Nicholas Ayache, Marco Lorenzi.

The research takes place within the MNC3 initiative (Médecine Numérique: Cerveau, Cognition, Comportement) funded by Université Côte d'Azur (UCA), and is performed in collaboration with the Institut Claude Pompidou (CHU of Nice).

Longitudinal modeling, brain structure, Alzheimer's disease, aging, Gaussian processes, ICA.
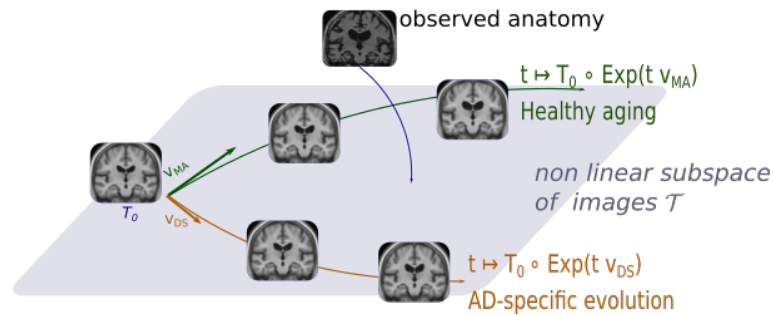
Figure 16. Left: z-values associated with group-wise differences between controls and Alzheimer-diagnosed subjects. Right: Areas of statistically significant differences.

Through this project we aim at developing novel scalable spatio-temporal analysis tools to identify clinical and biological modulators of structural and functional brain changes across time. The project relies on the extension of current un-/semi-supervised image analysis approaches (such as independent component analysis, ICA) to encode priors on spatial and temporal properties of the signal measured in brain images. The application to currently available large-scale biomedical datasets (such as the UK Biobank) will be addressed by focusing on scalable and distributed learning methods.
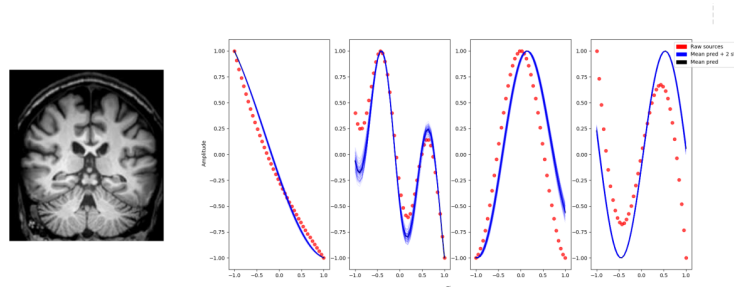
Figure 17. On the left, a coronal slice of a T1 weighted brain MRI. On the right we observe the temporal trajectories that best explain the evolution of the observed brain MRI times series from the UKBIOBANK study. Each trajectory representing the evolution of a meaningful biological and clinical sub-structure of the brain.

6.3. Computational Physiology

6.3.1. *Non-invasive personalisation of a cardiac electrophysiology model from body surface potential mapping*

Participants: Sophie Giffard Roisin [Correspondent], Maxime Sermesant, Nicholas Ayache, Hervé Delingette.

This work has been supported by the European Project FP7 under grant agreement VP2HF (no 611823) and the Marie Curie Actions European Industrial Doctorate CardioFunXion project (with Universitat Pompeu Fabra and Philips as partners).

Cardiac Modelling, Personalised Simulation, Inverse Problem of ECG, Electrical Simulation

Within the VP2HF project, non-invasive cardiac electrical data has been acquired at St Thomas' Hospital, London. It consists in Body Surface Potential Mapping (BSPM), which are recordings of the electrical potential on several locations on the surface of the torso. In [37], we use non-invasive data (body surface potential mapping, BSPM) to personalise complex cardiac electrical activation patterns such as multiple onset activation locations. We have used a relevance vector regression (see Figure 18) and we have evaluated our method on clinical datasets.
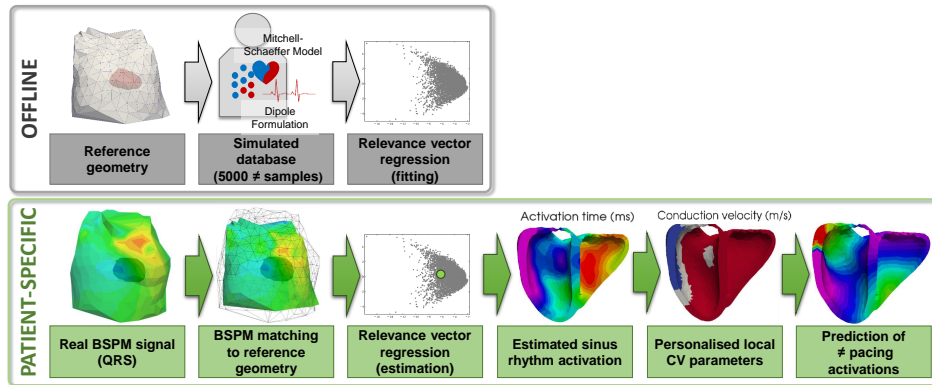
Figure 18. Pipeline of the non-invasive model personalisation

6.3.2. *Mulfidelity-CMA Personalisation Algorithm and Personalised 3D Modeling for Longitudinal Analysis*

Participants: Roch Philippe Molléro [Correspondent], Xavier Pennec, Hervé Delingette, Alan Garny, Nicholas Ayache, Maxime Sermesant.

Cardiac Modelling, Personalised Simulation, Longitudinal Analysis, Parameter Estimation, Finite Element Mechanical Modelling

- We extended the multiscale 0D/3D personalisation approach previously published to build a fast, flexible and computationally efficient *multifidelity personalisation*. This algorithm called **Multifidelity-CMA** can be used to personalise hundreds of cases per day without specific manual supervision, fine-tuning of the algorithm or precomputation. The method was published in a scientific journal [24].

- We built more than **140 personalised 3D simulations** in the context of two longitudinal studies. We first used personalised parameters to model short-term transient effects in digestion ([33] and a poster presentation at FIMH Conference 2016), then to analyze long-term evolution of the cardiac function in cardiomyopathies ([42] and a poster presentation at MICCAI Conference 2017). In particular we showed that the use of priors reduces considerably the variance in the population of estimated parameters leading a better conditionning of parameter values whose variability in the population only reflects physiological properties of the cases. In particular we projected personalised parameters onto the axis of a classifier which discriminates between a cohort of healthy and diseased cases, and showed that the evolution of parameter values suggests an improvement of the cardiac function under therapy since the parameters of the follow-up acquisition are closer to the *healthy side* of the classifier (see Figure 19).
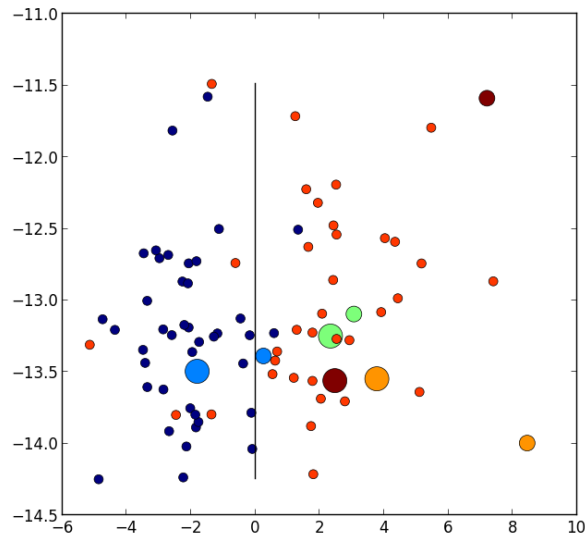
*Figure 19. Projection of personalised parameters on the main direction of a LDA classifier between the healthy
cases (dark blue dots) and cardiomyopathy (other dots) cases (x-axis) and an principal orthogonal direction of this
vector (y-axis). The dots in light blue, brown, orange and green correspond to 4 patients for which the data was
available both at baseline (small dot) and follow-up (larger dot).*

7. Bilateral Contracts and Grants with Industry

7.1. Bilateral Contracts with Industry

7.1.1. CIFRE PhD Fellowships

7.1.1.1. Neurelec/Oticon Medical

Participants: Thomas Demarcy [correspondent], Hervé Delingette, Nicholas Ayache, Dan Gnansia [Oticon
Medical].

The work of Thomas Demarcy, *Segmentation and anatomic variability of the cochlea and other temporal
bone structures from medical images*, is supported by a PhD fellowship from the Neurelec/Oticon Medical
company.

7.1.2. Microsoft Research

Microsoft Research is funding through the Inria-Microsoft joint lab the projects "4D Cardiac MR Images" [6]
and "Medilearn" [7] which aim at analyzing large databases of cardiac images to help the diagnosis of cardiac
diseases and planning of therapy. This project involves A. Crimisi from MSR and partially funds the PhDs of
Pawel Mlynarski.

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[6]http://www.msr-inria.fr/projects/4d-cardiac-mr-images
[7]http://www.msr-inria.fr/projects/medilearn

7.1.3. Spin-off company Therapixel

Therapixel[8] is a spin-off of the Asclepios (Inria Sophia Antipolis) and Parietal (Inria Saclay) project teams founded in 2013. Therapixel makes surgical information systems. It relies on depth sensing, advanced software processing and innovative user interfaces to provide touchless control of the computer. This technology allows for a direct control of the computer, which sterility constraints made impractical in the past. In 2015, Therapixel obtained the CE marking of its product on touchless visualization of medical images.

7.1.4. Spin-off company inHEART

inHEART[9] is a spin-off of the Asclepios team and IHU Liryc founded in 2017. inHEART provides a service to generate detailed anatomical and structural meshes from medical images, that can be used during ablation interventions. inHEART received 2 awards, one from Aquitaine region and one i-LAB form the BPI.

7.1.5. Siemens HealthCare

Siemens Healthcare, Medical Imaging Technologies, Princeton, NJ (U.S.A). is funding the Phd work of Julian Krebs which aims at developing robust medical image registration methods

8. Partnerships and Cooperations

8.1. Regional Initiatives

- Marco Lorenzi is principal investigator of the project Big Data for Brain Research, funded in 2017 by the Department des Alpes Maritimes (AAP Santé 2017). The project aims at creating a computing platform within the facility of Inria Sophia Antipolis dedicated to the analysis of large biomedical datasets. The realization of the data management system and computational platform will be achieved through the collaboration with the Maison de la Modélisation, de la Simulation et des Interactions (MSI) of the Université Côte d'Azur.

- N. Ayache and P. Robert are principal invesgators of the project MNC3 (Médecine Numérique, Cerveau, Cognition, Comportement) financé par l'Idex Jedi du UCA (2017-2021, 450k€). M. Lorenzi (Inria) actively participates to the supervision of this project with the help of V. Manera (ICP).

8.2. National Initiatives

8.2.1. Consulting for Industry

Nicholas Ayache is a scientific consultant for the company Mauna Kea Technologies (Paris).

8.2.2. Collaboration with national hospitals

The Asclepios-project team collaborates with the following 3 French IHU (University Hospital Institute): the IHU-Strasbourg (Pr J. Marescaux and L. Soler) on image-guided surgery, the IHU-Bordeaux (Pr M. Haïssaguere and Pr P. Jaïs) on cardiac imaging and modeling and the IHU-Pitié Salpétrière (Dr. O. Colliot and S. Durrleman) on neuroimaging.

We also have long term collaborations with the CHU Nice and Centre Antoine Lacassagne in Nice.

The Asclepios-project team is part of the EQUIPEX MUSIC consortium with Bordeaux University Hospital, which aim is to exploit an XMR interventional room equipped with a MUSIC workstation.

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[8]http://www.therapixel.com/
[9]http://www.inheart.fr/

8.3. European Initiatives

8.3.1. FP7 & H2020 Projects

8.3.1.1. ECSTATIC

Title: Electrostructural Tomography – Towards Multiparametric Imaging of Cardiac Electrical Disorders

Programm: H2020

Type: ERC

Duration: 2017 - 2022

Coordinator: U. Bordeaux

Inria contact: Maxime Sermesant

Cardiac electrical diseases are directly responsible for sudden cardiac death, heart failure and stroke. They result from a complex interplay between myocardial electrical activation and structural heterogeneity. Current diagnostic strategy based on separate electrocardiographic and imaging assessment is unable to grasp both these aspects. Improvements in personalised diagnostics are urgently needed as existing curative or preventive therapies (catheter ablation, multisite pacing, and implantable defibrillators) cannot be offered until patients are correctly recognised.

ECSTATIC aims at achieving a major advance in the way cardiac electrical diseases are characterised and thus diagnosed and treated, through the development of a novel non-invasive modality (Electrostructural Tomography), combining magnetic resonance imaging (MRI) and non-invasive cardiac mapping (NIM) technologies.

The approach will consist of: (1) hybridising NIM and MRI technologies to enable the joint acquisition of magnetic resonance images of the heart and torso and of a large array of body surface potentials within a single environment; (2) personalising the inverse problem of electrocardiography based on MRI characteristics within the heart and torso, to enable accurate reconstruction of cardiac electrophysiological maps from body surface potentials within the 3D cardiac tissue; and (3) developing a novel disease characterisation framework based on registered non-invasive imaging and electrophysiological data, and propose novel diagnostic and prognostic markers.

This project will dramatically impact the tailored management of cardiac electrical disorders, with applications for diagnosis, risk stratification/patient selection and guidance of pacing and catheter ablation therapies. It will bridge two medical fields (cardiac electrophysiology and imaging), thereby creating a new research area and a novel semiology with the potential to modify the existing classification of cardiac electrical diseases.

8.3.1.2. MD PAEDIGREE

Title: Model-Driven European Paediatric Digital Repository

Programm: FP7

Duration: March 2013 - February 2017

Coordinator: Ospedale Pediatrico Bambini Gesù, Rome.

Partners:

Athena Research and Innovation Center in Information Communication & Knowledge Technologies (Greece)

Biomolecular Research Genomics (Italy)

Deutsches Herzzentrum Berlin (Germany)

Empirica Gesellschaft für Kommunikations- und Technologie Forschung Mbh (Germany)

Fraunhofer-Gesellschaft Zur Foerderung Der Angewandten Forschung E.V (Germany)

Haute Ecole Specialisée de Suisse Occidentale (Switzerland)

Istituto Giannina Gaslini (Italy)

Katholieke Universiteit Leuven (Belgium)

Lynkeus (Italy)

Motek Medical B.V. (Netherlands)

Ospedale Pediatrico Bambino Gesu (Italy)

Siemens Aktiengesellschaft (Germany)

Siemens Corporation (United States)

Technische Universiteit Delft (Netherlands)

University College London (United Kingdom)

Universitair Medisch Centrum Utrecht (Netherlands)

Universita Degli Studi di Roma Lapienza (Italy)

The University of Sheffield (United Kingdom)

Universitatea Transilvania Din Brasov (Romania)

Stichting Vu-Vumc (Netherlands)

Maat Francerl (France)

Inria contact: Xavier Pennec

MD-Paedigree is a clinically-led VPH project that addresses both the first and the second actions of part B of Objective ICT-2011.5.2:

1. it enhances existing disease models stemming from former EC-funded research (Health-e-Child and Sim-e-Child) and from industry and academia, by developing robust and reusable multi-scale models for more predictive, individualised, effective and safer health-care in several disease areas;

2. it builds on the eHealth platform already developed for Health-e-Child and Sim-e-Child to establish a worldwide advanced paediatric digital repository. Integrating the point of care through state-of-the-art and fast response interfaces, MD-Paedigree services a broad range of off-the-shelf models and simulations to support physicians and clinical researchers in their daily work. MD-Paedigree vertically integrates data, information and knowledge of incoming patients, in participating hospitals from across Europe and the USA, and provides innovative tools to define new workflows of models towards personalised predictive medicine. Conceived of as a part of the 'VPH Infostructure' described in the ARGOS, MD-Paedigree encompasses a set of services for storage, sharing, similarity search, outcome analysis, risk stratification, and personalised decision support in paediatrics within its innovative model-driven data and workflow-based digital repository. As a specific implementation of the VPH-Share project, MD-Paedigree fully interoperates with it. It has the ambition to be the dominant tool within its purview. MD-Paedigree integrates methodological approaches from the targeted specialties and consequently analyzes biomedical data derived from a multiplicity of heterogeneous sources (from clinical, genetic and metagenomic analysis, to MRI and US image analytics, to haemodynamics, to real-time processing of musculoskeletal parameters and fibres biomechanical data, and others), as well as specialised biomechanical and imaging VPH simulation models.

8.3.1.3. MedYMA

Title: Biophysical Modeling and Analysis of Dynamic Medical Images

Programme: FP7

Type: ERC

Period: April 2012 - March 2017

Coordinator: Inria

Inria contact: Nicholas Ayache

During the past decades, exceptional progress was made with in vivo medical imaging technologies to capture the anatomical, structural and physiological properties of tissues and organs in patients, with an ever increasing spatial and temporal resolution. Physicians are now faced with a formidable overflow of information, especially when a time dimension is added to the already hard to integrate 3-D spatial, multimodal and multiscale dimensions of modern medical images. This increasingly hampers the early detection and understanding of subtle image modifications, which can have a vital impact on the patient's health. To change this situation, a new generation of computational models for the simulation and analysis of dynamic medical images is introduced. Thanks to their generative nature, they will allow the construction of databases of synthetic and realistic medical image sequences simulating various evolving diseases, producing an invaluable new resource for training and benchmarking. Leveraging on their principled biophysical and statistical foundations, these new models will bring an added clinical value once they have been personalized with innovative methods to fit the medical images of any specific patient. By explicitly revealing the underlying evolving biophysical processes observable in the images, this approach will yield new groundbreaking image processing tools to correctly interpret the patient's condition (computer aided diagnosis), to accurately predict the future evolution (computer aided prognosis), and to precisely simulate and monitor an optimal and personalized therapeutic strategy (computer aided therapy). First applications concern high impact diseases including brain tumors, Alzheimer's disease, heart failure and cardiac arrhythmia and will open new horizons in computational medical imaging.

8.4. International Initiatives

8.4.1. Inria International Labs

8.4.1.1. Inria Associate Team GeomStats (part of Inria@SiliconValley)

Title: Geometric Statistics in Computational Anatomy: Non-linear Subspace Learning Beyond the Riemannian Structure

International Partner (Institution - Laboratory - Researcher):

Stanford (United States) - Department of Statistics - Susan Holmes

Start year: 2015

See also: http://www-sop.inria.fr/asclepios/projects/GeomStats/

The scientific goal of the associated team is to develop the field of geometric statistics with key applications in computational anatomy.

Computational anatomy is an emerging discipline at the interface of geometry, statistics, image analysis and medicine that aims at analyzing and modeling the biological variability of the organs shapes at the population level. An important application in neuroimaging is the spatial normalization of subjects which is necessary to compare anatomies and functions through images in populations with different clinical conditions.

The research directions have been broken into three axes, the first two being methodologically driven and the last one being application driven. The first axis aims at generalizing the statistical framework from Riemannian to more general geometric structures and even non-manifold spaces (e.g. stratified spaces). The goal is to understand what is gained or lost using each geometric structure. The second axis aims at developing subspace learning methods in non-linear manifolds. This objective contrasts with most manifold learning methods which assumes that subspaces are embedded in a large enough Euclidean space. The third scientific direction is application driven with cross-sectional and longitudinal brain neuroimaging studies. The goal will be to extract reduced models of the brain anatomy that best describe and discriminate the populations under study. One intend for instance to show where is impact of a treatment for traumatic brain injuries.

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

8.4.2.1. PERSOCARDIOLEARN

>Title: Personalization of Cardiac Models using Experimental Data and Machine Learning

>International Partner (Institution - Laboratory - Researcher):

>>University of Toronto (Canada) - Sunnybrook Research Institute - Mihaela Pop

>Start year: 2017

>See also: https://team.inria.fr/asclepios/research/associated-team-persocardiolearn/

>Multi-scale computer modelling is a powerful tool that could be used to simulate in silico cardiac electrical activity and biomechanical function of individual heart. Imaging and 3D heart models built from images can help us understand the basis of structurally-diseased hearts at organ level and to predict in silico the changes in electro-mechanical function as a consequence of muscle remodelling in pathologic state (e.g. chronic infarction, a major cause of death). We hypothesize that MRI-based predictive models can help us identify new opportunities to intervene or to predict the outcome of ablation therapy, which currently has low clinical success. However, these predictive models need to be validated and thoroughly tested in preclinical experiments prior to their integration into the clinical stage. Hence, the next logical step for our joint Inria-SB efforts is to expand our experimental-theoretical framework and to personalize fast 3D heart models from in vivo MR-EP data. This translational step involves numerous challenging tasks from the modelling perspective since the in vivo imaging and physiological signals are rather noisy and obtained at a poor spatial resolution, potentially leading to erroneous customization of mathematical model parameters. However, this collaboration employs a rare combination of experiments and modelling specialists. Moreover, the originality of the proposed approach is to build upon machine-learning techniques rather than on data assimilation methods that are more explored in the literature but have inherent limitations (robustness to noise, local minima. . .).

8.4.3. Inria International Partners

8.4.3.1. Informal International Partners

8.4.3.1.1. St Thomas' Hospital, King's College London, United Kingdom

>Maxime Sermesant is a visiting lecturer in the Division of Imaging Sciences and Biomedical Engineering, St Thomas' Hospital, King's College London lead by Pr Reza Razavi. The XMR facility within this hospital is a unique opportunity to validate and exploit the cardiovascular modelling work.

8.4.3.1.2. Massachusetts General Hospital, Boston

>A collaboration with Dr Jan Unklebach, Assistant Professor of Radiation Oncology and Dr Jayashree Kalpathy-Cramer, radiology instructor was initiated in 2013 around the topics of tumor growth modeling, radiotherapy planning and edema characterization from MRI.

8.4.3.1.3. University College London (UCL), London, UK

>Marco Lorenzi is collaborator of the Translational Imaging Group of UCL, led by Prof. Sebastien Ourselin. His collaboration is around the topic of spatio-temporal analysis of medical images, with special focus on brain imaging analysis and biomarker development in Alzheim disease. He is also collaborating with the "Progression Over Neurodegenerative Disorders" (POND) group (Prof. Daniel Alexander) for developing new computational models and techniques for learning characteristic patterns of disease progression using large longitudinal clinical data sets, with special focus on dementias.

8.4.3.1.4. Imaging Genetics Center (IGC), University of Southern California (USC), CA, USA

>Marco Lorenzi is currently collaborator with the IGC for the investigation of the complex relationship between brain atrophy and genetics in Alzheimer's disease, in particular for demonstrating the effectiveness of multivariate statistical models in providing a meaningful description of the relationship between genotype and brain phenotype.

8.4.3.1.5. Other International Hospitals

Collaborations with several other European hospitals have been established through the European projects VP2HF and MD PAEDIGREE.

9. Dissemination

9.1. Promoting Scientific Activities

9.1.1. Scientific Events Organisation

9.1.1.1. Member of the Organizing Committees

- X. Pennec was co-chair of the MICCAI 2017 workshop on Mathematical Foundations of Computational Anatomy MFCA 2017 which was held in Quebec, Canada on September 14, 2017 and co-organiser of the Conference on Topological and Geometrical Structure of Information, held at CIRM Luminy (FR) on Aug.28 - Sept. 1 2017.

- M. Sermesant was a co-chair of the MICCAI 2017 Workshop Statistical Atlases and Computational Models of the Heart (STACOM 2017), which was held in Quebec City, Octobre 10, 2017.

- H. Delingette was a member of the organizing committee of the two scientific days at Inria Sophia Antipolis (July 6th and Dec 4th) presenting the activities of the UCA academy on "Networks, Information and Digital Society".

9.1.2. Scientific Events Selection

9.1.2.1. Member of the Conference Program Committees

- X. Pennec was a member of the paper selection committe of the Conference Information processing in Medical Images (IPMI 2017) held at Boone, NC, USA, June 25-30 2017; area chair of the International Symposium on Biomedical Imaging ISBI 2017; member of the scientific committee of the 3rd conference on Geometric Science of Information GSI2017, Novembre 7-9 2017, Paris (France).

- H. Delingette was program committee member of the conference on the MICCAI 2017 workshop on Simulation and Synthesis of Medical Imaging (SASHIMI'17).

9.1.2.2. Reviewer

- M. Lorenzi was a reviewer for the conferences Neural Information Processing Systems (NIPS 2017), Medical Image Computing and Computer Aided Intervention (MICCAI 2017), International Conference on Learning Representations (ICLR 2018), IEEE International Symposium of Biomedical Imaging (ISBI 2017-18), Information Processing in Medical Imaging (IPMI 2017).

- X. Pennec was a reviewer for the ICCV International Workshop on Manifold Learning: from Euclid to Riemann (MANIFLEARN2017) and the 3rd CVPR International Workshop on DIFFerential Geometry in Computer Vision and Machine Learning (DIFF-CVML 2017).

- H. Delingette was a reviewer for the International Symposium on Biomedical Imaging (ISBI'17), the international conference Functional Imaging and Modeling of the Heart (FIMH 2017),the international conference on computer-aided interventions (IPCAI'17), the conference on Medical Image Computing and Computer Assisted Intervention (MICCAI 2017), the International Conference on Computer Vision and Pattern Recognition (CVPR 2017).

- M. Sermesant was a reviewer for the MICCAI 2017 and FIMH 2017 conferences.

9.1.3. Journal

9.1.3.1. Member of the Editorial Boards

- N. Ayache is the co-founder and the Co-Editor in Chief with J. Duncan (Professor at Yale) of Medical Image Analysis journal. This scientific journal was created in 1996 and is published by Elsevier.

- N. Ayache is a member of the editorial board of the following journals: Medical Image Technology (Japanese journal) and Journal of Computer Assisted Surgery (Wiley).

- H. Delingette is a member of the editorial board of the journal Medical Image Analysis (Elsevier).

- I. Strobant is editorial coordinator for Medical Image Analysis, Elsevier (since october 2001).

- X. Pennec is a member of the editorial board of the journal Medical Image Analysis (Elsevier), of the International Journal of Computer Vision (Springer), of the SIAM Journal on Imaging Sciences (SIIMS), and of the Journal of Mathematical Imaging and Vision (JMIV).

- M. Lorenzi is a member of the editorial board of the journal Scientific Reports (Nature Publishing Group); he is also member of the Board of Statisticians of the Journal of Alzheimer's Disease (IOS Press).

9.1.3.2. Reviewer - Reviewing Activities

- M. Lorenzi was a reviewer for the following journals: Neurobiology of Aging, Alzheimer's and Dementia, Journal of Alzheimer's Disease, Medical Image Analysis, IEEE Transactions on Medical Imaging, NeuroImage, International Journal of Computer Vision, Journal of Mathematical Image and Vision, IEEE Transactions on Biomedical Engineering, Human Brain Mapping, Scientific Reports, Neural Computation.

- X. Pennec was a reviewer for the following journals: Proceedings on the London Mathematical Society (PLMS), Journal of mathematical imaging and vision (JMIV), Journal of Machine Learning Research (JMLR), NeuroImage (NIMG), Foundations of Computational Mathematics (FoCM), International Journal of Computer Vision (IJCV), SIAM journal on Imaging Sciences (SIIMS), Medical Image Analysis (MedIA).

- H. Delingette was a reviewer for the following journals: Medical Image Analysis (Elsevier), IEEE Transactions in Medical Imaging, IEEE Transactions in Biomedical Engineering, Biomedical Engineering, Computers in Biology and Medicine.

- M. Sermesant was a reviewer for the following journals: Journal of the American College of Cardiology, IEEE Transactions on Medical Imaging, IEEE Transactions on Biomedical Engineering, Medical Image Analysis and Computers in Biology and Medecine.

9.1.4. Invited Talks

- **M. Lorenzi** was invited as lecturer at the Mathematical Models In Biomedical Imaging Summer School, organized by the University of Granada, Spain, on July 2017.

- **X. Pennec** was a keynote speaker of the 3rd Int. W on Differential geometry in Comp. Vis. and Machine Learning (DIFF-CVML), Hawaii, USA, 21 July 2017 and at the Computational Brain Connectivity Mapping Winter School Workshop CoBCoM, November 20-24 2017, Juan-les-Pins, France. He was also invited to the MIT CSAIL Seminar series, Cambridge, MA, September 8 2017 and an Imaging Genetics Center Seminar at USC, Marina del Rey, Los Angeles, CA, USA, 19 July 2017.

- **H. Delingette** was a keynote speaker at the Euromech conference in Lille, an invited speaker at the GDR Mamovi in Lyon, at the Computer Vision Seminar at UPF in Barcelona.

- **M. Sermesant** was a keynote speaker at the FIMH conference in Toronto, and an invited speaker at the VT/VF Symposium in Berlin, and the TRM Forum in Lugano.

- **N. Ayache** gave the following plenary invited talks in 2017:
  - From Cardiac Images to Digital Hearts ; Inria 50th anniversary, Paris
  - From Medical Images to Digital Patients, Inria 50th anniversary, Sophia,
  - Important MICCAI contributions of the past 20 years, MICCAI, Québec,

– Le patient numérique, Académie Nationale de Chirurgie, Paris,

– Images, informatique et médecine : Institut Mondor de recherche biomédicale, Créteil.

9.1.5. Leadership within the Scientific Community

- **H. Delingette** is a member of the MICCAI Society Board of Directors.
- **Nicholas Ayache** is a member of the French Academy of Sciences in the section of Mechanics and Informatics. He was elected a free member of the French Academy of Surgery on 6 Dec. 2017. He became an officer of the order of the "Palmes Académiques" on 14 Jul. 2017.

9.1.6. Scientific Expertise

- **Xavier Pennec** was an evaluator for the European Research Concil (ERC) and the French Agence Nationale pour la Recherche (ANR).
- **M. Lorenzi** was reviewer of the granting agencies ANR (Agence Nationale de la Recherche, France) and EPSRC (Engineering and Physical Sciences Research Council, UK).
- **H. Delingette** was an evaluator for the European Research Concil, for the Research Council of KU Leuven.
- M. Sermesant was an evaluator for the Aquitaine region, the Dutch adn the Swiss research councils.
- **Nicholas Ayache** is a member of the scientific council of the Ile de France region since 2016.

9.1.7. Research Administration

- **Xavier Pennec** is co-director and at the board of the Ecole doctorale STIC of Université Côte d'Azur. He is a member of the Doctoral follow-up Committee (CSD) at Inria Sophia Antipolis, of the the "Comité de la Recherche Biomédicale en Santé Publique (CRBSP)" of the Nice hospitals and in charge of the relationships of Inria-Sophia with the Nice University Hospital (CHU).
- **Marco Lorenzi** is is a member of the local steering committee of the technological platforms (Comités Scientifiques de Pilotage des Plateformes) in charge of Cluster, Grid, Cloud, and HPC technologies.
- **Hervé Delingette** is a member of the local committee in charge of the scientific selection of visiting scientists (Comité NICE) and the local committee on the immersive platform. He is the coordinator of the Academy of excellence on "Networks, Information and Digital Society" at the Université Côte d'Azur.

9.2. Teaching - Supervision - Juries

9.2.1. Teaching

Master: H. Delingette and X. Pennec, Introduction to Medical Image Analysis, 21h course (28.5 ETD), Master 2 MVA, ENS Cachan, France.

Master: X. Pennec and H. Delingette, Advanced Medical Imaging, 21h course (28.5 ETD), Master 2 MVA and École Centrale de Paris, France.

Master: X. Pennec and H. Delingette, Computational Anatomy and Physiology, 21h course (28.5 ETD), Master CBB - Computational Biology and Biomedicine, Univ. Nice-Sophia Antipolis.

Master: M. Sermesant, Computational Anatomy and Physiology, 3h course (4.5 ETD), Master CBB - Computational Biology and Biomedicine, Univ. Nice-Sophia Antipolis.

Master: X. Pennec is co-responsible of the Master CBB - Computational Biology and Biomedicine, Univ. Nice-Sophia Antipolis.

9.2.2. Theses Defended

- Marc-Michel Rohé, Analyse statistique spatio-temporelle des formes, déformations, flots et propriétés physiologiques du cœur, Nice Sophia Antipolis University. Started in 2014. Co-directed by X. Pennec and M. Sermesant. Defended on July 3rd, 2017

- Sophie Giffard-Roisin, Non-invasive Estimation of Cardiac Electrophysiological Parameters, Nice Sophia Antipolis University. Started in 2014. Co-directed by N. Ayache and M. Sermesant. Defended on 11th December 2017
- Roch Molléro, Uncertainty quantification in personalized electromechanical models. Application to cardiomyopathies and obesity, Nice Sophia Antipolis University. Started in 2014. Co-directed by N. Ayache and M. Sermesant. Defended on December 19th, 2017
- Thomas Demarcy, Segmentation and anatomic variability of the cochlea and other temporal bone structures from medical images, Nice Sophia Antipolis University. Started in 2014. Directed by H. Delingette. Defended on July the 4$^{\text{th}}$, 2017
- Loïc Devilliers, Consistency of statistics on infinite dimensional orbifolds – Applications to computational anatomy, Nice Sophia Antipolis University. Started in October 2015. Co-directed by X Pennec and St. Allassonière. Defended on November 20th, 2017

9.2.3. PhD in progress

- Raphaël Sivera, Analyse statistique de l'évolution de structures morphologiques partir de séquences temporelles d'IRM, Nice Sophia Antipolis University. Started in October 2015. Co-directed by N. Ayache and H. Delingette and co-supervised by M. Lorenzi and X. Pennec.
- Pawel Mlynarski, Tumor segmentation based on Random Forests and Convolutional Neural Networks trained on partially annotaded data, Nice Sophia Antipolis University. Started in December 2015. Co-directed by N. Ayache and H. Delingette.
- Qiao Zheng, Deep learning for cardiac image analysis, Nice Sophia Antipolis University. Started in January 2016. Co-directed by N. Ayache and H. Delingette.
- Shuman Jia, Population-based Model of Atrial Fibrillation: from Shape Statistics to Group-wise Physiology, Nice Sophia Antipolis University. Started in 2016. Co-directed by M. Sermesant and X. Pennec.
- Wen Wei, Learning Brain Alterations in Multiple Sclerosis from Multimodal Neuroimaging Data, Nice Sophia Antipolis University. Started in 2016. Co-directed by N.Ayache and O.Colliot.
- Julian Krebs, Robust image registration based on machine learning, Nice Sophia Antipolis University. Started in 2016. Co-directed by H. Delingette and N. Ayache.
- Luigi Antelmi, Statistical learning on large databases of heterogeneous imaging, cognitive and behavioural data, Nice Sophia Antipolis University. Started in 2017. Co-directed by P. Robert and N. Ayache and supervised by M. Lorenzi.
- Clément Abi-Nader, Statistical Learning of Heterogeneous Data in Large-Scale Clinical Databases, Nice Sophia Antipolis University. Started in 2017. Co-directed by P. Robert and N. Ayache and supervised by M. Lorenzi.
- Jaume Banús Cobo, Heart & Brain: discovering the link between cardiovascular pathologies and neurodegeneration through biophysical and statistical models of cardiac and brain images., Nice Sophia Antipolis University. Started in 2017. Directed by M. Sermesant and co-supervised by Marco Lorenzi.
- Tania-Marina Bacoyannis, Cardiac Imaging and Machine Learning for Electrostructural Tomography, Nice Sophia Antipolis University. Started in 2017. Co-directed by M. Sermesant and H. Cochet.
- Pamela Moceri, From normal right ventricle to pathology: shape and function analysis with different loading conditions using imaging and modelling. Started in 2015. Directed by M. Sermesant.

9.2.4. Juries

- Xavier Pennec was supervisor or co-supervisor of the PhD theses of Loïc Devilliers (Univ. of Nice Sophia Antipolis), Marc-Michel Rohé (Univ. of Nice Sophia Antipolis) and Roch Molléro (Univ. of Nice Sophia Antipolis). He was also reviewer and member of the jury of the HDR of Joan Alexis Glaunes (Université Paris Descartes), reviewer and member of the jury of the PhDs of Remi Agier (INSA Lyon) and Alice Le Bruiguant (Univ. Bordeaux) and member of the PhD jury of Jean-Baptiste Schiratti (Ecole Polytechnique).

- Marco Lorenzi was jury member for the PhD probation exam (in April 2017) of Kurt Kutajar and Remi Domingues, students of the EURECOM research institute, France.

- Hervé Delingette was co-supervisor of the PhD thesis of T. Demarcy (Univ. of Nice Sophia Antipolis). He was a reviewer in the PhD thesis committee of C. Paulus (Univ. of Strasbourg), of Mikael Agn (Danish Technical University, Lingby, Danemark), of N. Mangado (Univ. Pompeu Fabra, Barcelone), of M. Hafri (Univ. Orléans). He was a member of the PhD thesis committee of Sophie Giffard-Roisin (Univ. of Nice Sophia Antipolis), and Roch Philippe Mollero (Univ. of Nice Sophia Antipolis).

- Maxime Sermesant was a reviewer and a member of the PhD jury of Corentin Dallet, Bordeaux University (Nov 23) and of the HDR jury of Ed Vigmond, Bordeaux University (Jan 13).

9.3. Popularization

M. Lorenzi gave a general audience lecture during the "Semaine du Cerveau" at the CHU of Nice (March 2017).

Nina Miolane participated to the following popularization events:

- Speaker at Unesco France's Ceremony for 70th Anniversary.

- Speaker at the Women Forum Global Meeting 2016. How to bring more women in the sci-tech workforce?

- Speaker at the L'Oreal-Unesco Prizes Ceremony 2016.

- Journal regional de France 3 Azur (Oct. 31 2016)

- Invited on "Le Club de la Tete au Carre". France Inter (National Radio), Oct. 14 2016.

10. Bibliography

Major publications by the team in recent years

[1] S. GIFFARD-ROISIN, T. JACKSON, L. FOVARGUE, J. LEE, H. DELINGETTE, R. RAZAVI, N. AYACHE, M. SERMESANT. *Non-Invasive Personalisation of a Cardiac Electrophysiology Model from Body Surface Potential Mapping*, in "IEEE Transactions on Biomedical Engineering", September 2017, vol. 64, n⁰ 9, pp. 2206 - 2218 [*DOI : 10.1109/TBME.2016.2629849*]

[2] B. KHANAL, N. AYACHE, X. PENNEC. *Simulating Longitudinal Brain MRIs with known Volume Changes and Realistic Variations in Image Intensity*, in "Frontiers in Neuroscience", February 2017, vol. 11, n⁰ Article 132, 18 p. [*DOI : 10.3389/FNINS.2017.00132*]

[3] L. LE FOLGOC, H. DELINGETTE, A. CRIMINISI, N. AYACHE. *Sparse Bayesian registration of medical images for self-tuning of parameters and spatially adaptive parametrization of displacements*, in "Medical Image Analysis", February 2017, vol. 36, pp. 79 - 97 [*DOI : 10.1016/J.MEDIA.2016.09.008*]

[4] M. LORENZI, X. PENNEC. *Geodesics, Parallel Transport & One-parameter Subgroups for Diffeomorphic Image Registration*, in "International Journal of Computer Vision", November 2013, vol. 105, n⁰ 2, pp. 111-127 [*DOI : 10.1007/S11263-012-0598-4*]

[5] M. LÊ, H. DELINGETTE, J. KALPATHY-CRAMER, E. R. GERSTNER, T. BATCHELOR, J. UNKELBACH, N. AYACHE. *MRI Based Bayesian Personalization of a Tumor Growth Model*, in "IEEE Transactions on Medical Imaging", April 2016, vol. 35, n⁰ 10, pp. 2329-2339 [*DOI : 10.1109/TMI.2016.2561098*]

Publications of the year

Doctoral Dissertations and Habilitation Theses

[6] T. DEMARCY. *Segmentation and study of anatomical variability of the cochlea from medical images*, Université Côte d'Azur, July 2017, https://tel.archives-ouvertes.fr/tel-01609910

[7] L. DEVILLIERS. *Consistency of statistics in infinite dimensional quotient spaces*, Université Côte d'Azur, November 2017, https://hal.inria.fr/tel-01683607

[8] S. GIFFARD-ROISIN. *Non-invasive Personalisation of Cardiac Electrophysiological Models from Surface Electrograms*, Université côte d'azur, December 2017, https://hal.inria.fr/tel-01658489

[9] R. MOLLÉRO. *Robust Personalisation of 3D Electromechanical Cardiac Models. Application to Heterogeneous and Longitudinal Clinical Databases*, Université Nice Côte d'Azur, December 2017, https://hal.inria.fr/tel-01656290

[10] M.-M. ROHÉ. *Reduced representation of segmentation and tracking in cardiac images for group-wise longitudinal analysis*, Université Côte d'Azur, July 2017, https://hal.inria.fr/tel-01575292

Articles in International Peer-Reviewed Journals

[11] J. L. BRUSE, A. KHUSHNOOD, K. MCLEOD, G. BIGLINO, M. SERMESANT, X. PENNEC, A. M. TAYLOR, T.-Y. HSIA, S. SCHIEVANO. *How successful is successful? Aortic arch shape after successful aortic coarctation repair correlates with left ventricular function*, in "Journal of Thoracic and Cardiovascular Surgery", February 2017, vol. 153, no 2, pp. 418 - 427 [*DOI :* 10.1016/J.JTCVS.2016.09.018], https://hal.inria.fr/hal-01387297

[12] J. L. BRUSE, M. A. ZULUAGA, A. KHUSHNOOD, K. MCLEOD, H. N. NTSINJANA, T.-Y. HSIA, M. SERMESANT, X. PENNEC, A. M. TAYLOR, S. SCHIEVANO. *Detecting clinically meaningful shape clusters in medical image data: metrics analysis for hierarchical clustering applied to healthy and pathological aortic arches*, in "IEEE Transactions on Biomedical Engineering", February 2017, pp. 1 - 13 [*DOI :* 10.1109/TBME.2017.2655364], https://hal.inria.fr/hal-01421202

[13] T. DEMARCY, C. VANDERSTEEN, N. GUEVARA, C. RAFFAELLI, D. GNANSIA, N. AYACHE, H. DELINGETTE. *Automated analysis of human cochlea shape variability from segmented μCT images*, in "Computerized Medical Imaging and Graphics", 2017, vol. 59, nO July 2017, pp. 1 - 12 [*DOI :* 10.1016/J.COMPMEDIMAG.2017.04.002], https://hal.inria.fr/hal-01528489

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