INRIA

INSTITUT NATIONAL DE RECHERCHE EN INFORMATIQUE ET EN AUTOMATIQUE

Project-Team Asclepios

Analysis and Simulation of Biomedical Images

Sophia Antipolis - Méditerranée

THEME BIO

Table of contents

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2. Overall Objectives

2.1. Introduction

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 a more central role everyday, as well as the exploitation of the genetic information attached to each patient.

Facing the need of 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 to extract 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.

2.2. Highlights of the year

The team has received several prizes (see section 8.5), including

- the 2008 Microsoft Award of the Royal Society and the French Academy of Sciences for Nicholas Ayache;
- the "Young Investigator Award 2008" in the category "Shape and Statistical Analysis" at MICCAI 2008 conference for Stanley Durrleman;
- the first prize of the "Multiple Sclerosis Lesion Segmentation Challenge" organized by the MICCAI satellite workshop "3D Segmentation in the Clinic: A Grand Challenge II" for Jean-Christophe Souplet; and
- a special mention for best PhD in Biomedical Engineering from the SFGBM-IEEE France Section for Olivier Clatz.

3. Scientific Foundations

3.1. Introduction

Tremendous progress has been made in the automated analysis of biomedical images during the past two decades [112]. Readers who are neophyte to the field of medical imaging will find an interesting presentation of acquisition techniques of the main medical imaging modalities in [104], [102]. Regarding the target applications, a good review of the state of the art can be found in the book *Computer Integrated Surgery* [100], in N. Ayache's article [107] and in the more recent syntheses [112] [79]. The scientific journals *Medical Image Analysis* [96], *Transactions on Medical Imaging* [101], and *Computer Assisted Surgery* [103] are also good reference material. One can have a good vision of the state of the art with the proceedings of the most recent conferences MICCAI'2008 (Medical Image Computing and Computer Assisted Intervention) [98], [99] or ISBI'2008 (Int. Symp. on Biomedical Imaging) [97].

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 [113], [133]. It is also possible to obtain from a Magnetic Resonance Image (MRI) of the head a reasonable segmentation into skull tissues, white matter, grey matter, and cerebro-spinal fluid [138], or to measure some functional properties of the heart from dynamic sequences of Magnetic Resonance [106], Ultrasound or Nuclear Medicine images [114].

Despite these advances and successes, one can notice that statistical models of the 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 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 comprehension of the observed images and signals, but also more efficient tools to detect anomalies, predict evolutions, simulate and assess 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 the images are multidimensional (3 spatial coordinates and possibly one temporal dimension), but medical protocols tend to include multi-sequence (or multi-parametric)[1] and multi-modal images[2] for each single patient.

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 on the physics of image acquisition and observed tissues, as well as on 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 3.4 and 3.5.

We plan to pursue our efforts on the following problems:

1. multi-dimensional, multi-sequence and multi-modal image segmentation,
2. Image Registration/Fusion,

3.3. Biological Image Analysis

In Biology, a huge number of images of living systems are produced every day to study the basic mechanisms of life and pathologies. If some bio-imaging *principles* are the same as the ones used for medical applications (e.g. MR, CT, US, Pet or SPECT), the bio-imaging *devices* are usually customized to produce images of higher resolution[3] for the observation of small animals (typically rodents). In addition, Optical Imaging techniques and biophotonics are developing very fast. This includes traditional or Confocal Microscopy (CM), multi-photon confocal microscopy, Optical Coherent Tomography (OCT), near-infrared imaging, diffuse optical imaging, phased array imaging, etc. A very new and promising development concerns micro-endoscopy, which allows cellular imaging at the end of a very small optical fiber [119].

[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 Magnetic Resonance Imaging (MRI), patients followed for multiple sclerosis may undergo every six months a 3-D 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 acquisition (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 to measure for instance the direction of white matter fibers in the brain (same principle can be used to measure the direction of muscular fibers in the heart). Functional MR images 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 subtle higher T2* signal which can be detected with sophisticated image processing techniques.

[2] Multimodal acquisition consists in acquiring on the same patient images from 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, MR providing contrast within soft tissues of different nature) while SPECT and PET images may provide functional information by measuring a local level of metabolic activity.

[3] This is the case with micro-MRI, Micro-CT, Micro-US devices, and to a less extent with Micro-SPECT and Micro-PET devices.

Most of these imaging techniques can be used for *Molecular Imaging*, an activity aiming at the *in vivo* characterization and measurement of biological processes at cellular and molecular level. With optical techniques, molecular imaging makes an extensive use of the fluorescent properties of certain molecules (in particular proteins, e.g. GFP[4]) for imaging of gene expression *in vivo*. With other modalities (like PET, SPECT, MR, CT and even US), molecular imaging can use specific contrast agents or radioactive molecules. For clinical applications, the ultimate goal of molecular imaging is to find the ways to probe much earlier the molecular anomalies that are the basis of a disease rather than to image only its end effects [140].

Some of the recent advances made in Medical Image Analysis could be directly applied (or easily adapted) to Biological Image Analysis. However, the specific nature of biological images (higher resolution, different anatomy and functions, different contrast agents, etc.), requires specific image analysis methods (one can refer to the recent tutorial [128] and to the Mouse Brain Atlas Project [105]. This is particularly true when dealing with *in vivo* microscopic images of cells and vessels.

Our research efforts will be focused to the following generic problems applied to *in vivo* microscopic images:

1. quantitative analysis of microscopic images,
2. detection and quantification of variations in temporal sequences,
3. construction of multiscale representations (from micro to macro).

3.4. Computational Anatomy

The objective of Computational Anatomy (CA) is the modeling and analysis of 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[5] [124].

Studying the variability of biological shapes is an old problem (cf. the remarkable book "On Shape and Growth" by D'Arcy Thompson [135]). Significant efforts have been made since that time to develop a theory for statistical shape analysis (one can refer to [111] for a good synthesis, and to the special issue of Neuroimage [134] for recent developments). Despite all these efforts, there is a number of challenging mathematical issues which remain largely unsolved in general. A particular issue is the computation of statistics on manifolds which can be of infinite dimension (e.g the group of diffeomorphisms).

There is a classical stratification of the problems into the following 3 levels [121]: 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 to the following problems:

1. Statistics on anatomical manifolds,
2. Propagation of variability from anatomical manifolds,
3. Linking anatomical variability to image analysis algorithms,
4. Grid-Computing Strategies to exploit large databases.

3.5. 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 and biology, where CP can be used for instance to better understand the basic processes leading to the apparition of a pathology, to model its probable evolution and to plan, simulate, and monitor its therapy.

[4] Green Fluorescent Protein.

[5] The NIH has lauched 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 objective will be to establish new surrogate end-points from the automated analysis of temporal sequences. This is a challenging objective for researchers in Computational Anatomy. The data will be 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 organic level a number of physiological systems (see for instance [127], [117], [109], [130], [115]). 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 confronting the model with the available biomedical images and signals and possibly also from 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 (e.g. [132], [123] 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:

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

These different levels of modeling are closely related to each other, and several physiological systems may interact together (e.g. the cardiopulmonary interaction [120]). 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 first level of modeling) to a much more ambitious *Physiological Human project* (see [116], [117]). We will not address all the issues raised by this ambitious project, but instead focus on topics detailed below. Among them, our objective is to identify some common methods for the resolution of the large inverse problems raised by the coupling of physiological models to biological images for the construction of patient-specific models (e.g. specific variational or sequential methods (EKF), dedicated particle filters, etc.). We also plan to develop a specific expertise on 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, etc.). Application domains include

1. Surgery Simulation,
2. Cardiac Imaging,
3. Brain tumors, neo-angiogenesis, wound healing processes, ovocyte regulation, ...

3.6. Clinical and Biological Validation

If the objective of many of the research activities of the project is the discovery of original methods and algorithms with a demonstration of feasibility on a limited number of representative examples (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, this is a necessary condition to see new ideas transformed into clinical tools and/or industrial products. It is also often the occasion to get access to larger databases of images and signals which in turn participate to the stimulation of new ideas and concepts.

4. Software

4.1. vtkINRIA3D

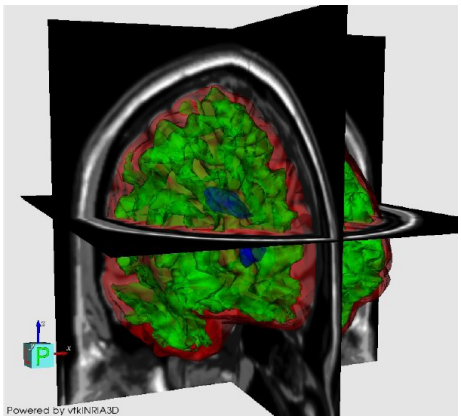
Keywords: *DICOM*, *Data Management*, *ITK*, *Mesh*, *Spatiotemporal Data*, *Synchronization*, *Time Sequence*, *VTK*, *medical imaging*.

Participants: Nicolas Toussaint [Correspondant], Pierre Fillard, Tommaso Mansi.

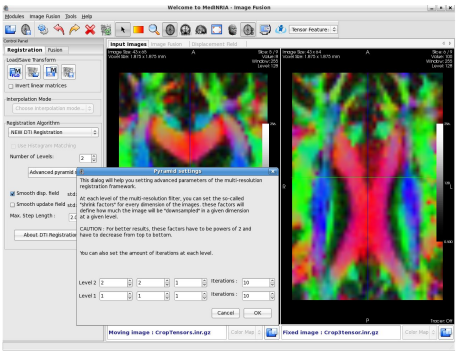
http://www.inria.fr/sophia/asclepios/software/vtkINRIA3D

vtkINRIA3D is an open source set of C++ libraries [136], extending the Visualization ToolKit VTK (http://www.vtk.org). It was initiated to gather the developement efforts in terms of data visualization and synchronization.

In particular, an ITK-based framework for image registration is proposed. The contribution in this framework is to gather different ITK state-of-the-art image registration methods in a single "console". Furthermore, we propose to store the successive registrations between input images in order to easily go back and force in the global alignement process.



a- vtkINRIA3D



b- MedINRIA

Figure 1. (a) vtkINRIA3D also provides developer-friendly API for synchronizing data. In this figure, segmentation results are shown as overlying the input MRI image. (b) MedINRIA: the visual comparison between tensor field is done by extracting features from the tensor fields such as the Color Fractional Anisotropy (FA) maps as shown here.

4.2. MedINRIA

Keywords: *DT-MRI*, *Fiber Tracking*, *Log-Euclidian Metrics*, *MRI*, *Registration*, *Tensor Estimation*, *Tensor Registration*, *f-MRI*.

Participants: Nicolas Toussaint [Correspondant], Pierre Fillard, Daniel Barbeau, Tommaso Mansi.

http://www.inria.fr/sophia/asclepios/software/MedINRIA

MedINRIA is a free collection of softwares developed within the Asclepios research project [137]. It aims at providing to clinicians state-of-the-art algorithms dedicated to medical image processing and visualization. MedINRIA is freely available.

In particular MedINRIA proposes new image registration techniques embedded in a friendly user interface. Block-Matching rigid registration [129] has been integrated and provides robust processing method for image alignement. Moreover, a tensor registration framework that uses Exact Finite-Strain Differential [75] gives the possibility to fully use the tensor information in the registration process.

4.3. CardioViz3D

Keywords: *Cardiac Imaging*, *Cardiac Simulation*, *CardioSense3D*, *DICOM*, *KWWidgets*, *Mesh Projection*, *Software*, *Time Sequence*, *vtkINRIA3D*.

Participants: Nicolas Toussaint [Correspondant], Jean-Marc Peyrat, Tommaso Mansi, Maxime Sermesant, Hervé Delingette.

http://www.inria.fr/sophia/asclepios/software/CardioViz3D

CardioViz3D is a freely available platform dedicated to dynamic cardiac simulation and processing [71]. It uses advanced and interactive frameworks to provide researchers and clinicians with adapted tools for pre-processing dynamic cardiac data, from the segmentation of the myocardium to the delineation of pathological regions, resulting in a patient-specific anatomical and geometrical model of the heart. Moreover, simulation results can be intuitively evaluated and compared to initial clinical data.

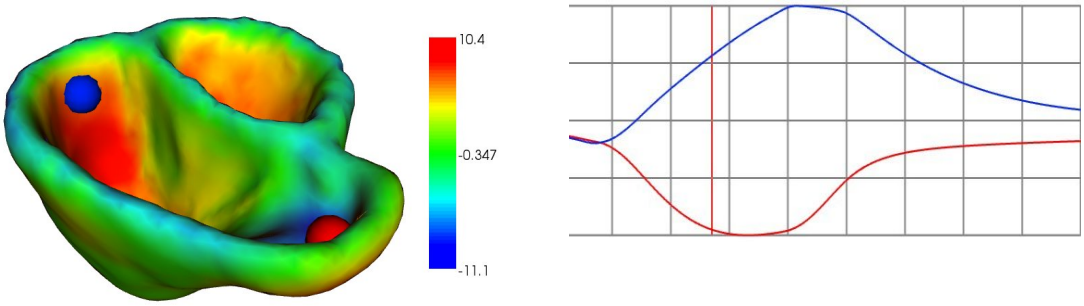


Figure 2. CardioViz3D allows to follow the evolution of scalar information at a specific location in the myocardium. Left: The vertex displacements (in mm) along the surface normal (with respect to a rest position) is shown. Two landmarks have been placed respectively in the healthy part (in blue) and the dyskinetic area (in red) of the right ventricle (patient with a RV overload). Right: Graphs representing the evolution of the displacement among the sequence for both landmark locations, showing a significant difference of curve patterns.

4.4. SepINRIA

Participants: Jean-Christophe Souplet [Correspondant], Erik Pernod, Nicolas Toussaint, Grégoire Malandain.

http://www.inria.fr/sophia/asclepios/software/SepINRIA

SepINRIA [91], [95], [94], [90] is a software offering visualisation, comparison and analysis of Multiple Sclerosis (MS) brain MRI. Its aim is to provide clinicians with a tool allowing to quantify lesion burden and atrophy.

SepINRIA works on a convenient database in which new DICOM files can be added. Images can be visualised in 2D or 3D. Two images (either of the same or different sequences) can be aligned and visualised in the same window (side to side or by image fusion).

Lesion segmentation can be obtained manually, semi-automatically or fully-automatically from T1, T2, PD and T2-FLAIR sequences. Quantitative values (number of lesions, volume, ...) are then computed. Manual and semi-automatic modes can be used to perform a segmentation of reference. In this case, a quantitative comparison of the segmentations can be realized.

Manual and automatic brain atrophy evaluations are available too. In the manual method, specific points have to be identified. Then distances between these points are computed and give linear measures (width of brain, lateral ventricles and third ventricle). In the automatic method, the brain parenchymal fraction (BPF) is computed from an automatic segmentation of the brain based on T1, T2 and DP sequences and taking into consideration partial volume effects. This is done simultaneously for each date of exam. Evolution of the BPF reflects the atrophy.

4.5. Diffeomorphic Image Registration Software

Keywords: *DTI*, *Image registration*, *demons algorithm*, *diffeomorphisms*, *spherical images*.

Participants: Olivier Clatz [Correspondant], Pierre Fillard, Nicolas Toussaint, Tom Vercauteren, B. T. Thomas Yeo.

This work is done in collaboration with Mauna Kea Technologies, Paris, France, http://www.maunakeatech.com and partly with the group of Polina Golland at MIT CSAIL, Cambridge, MA, people.csail.mit.edu/polina/.

Based on the diffeomorphic demons framework, three softwares have been made publicly available:

- Diffeomorphic Demons [51] is an efficient algorithm for the diffeomorphic registration of N dimensional images. Typical 256x256x181 3D medical images can be registered in less than three minutes on a 2 x 2.8 GHz quad-core Intel Xeon Apple Mac pro computer. The source code has been integrated into ITK, http://www.itk.org. A user-interface is now included in MedINRIA's image fusion module.
- Spherical Demons [74] is an algorithm that registers spherical images. Registration between a 160k vertices subject mesh and an atlas takes less than 5 mins on a Xeon 3.2GHz single processor machine, which is more than 10 times faster than the popular, freely-available FreeSurfer. Experiments also show that Spherical Demons is at least as accurate as FreeSurfer. Spherical Demons is available at http://yeoyeo02.googlepages.com/sphericaldemonsrelease.
- Diffusion Tensor Registration with Exact Finite Strain Differential (DT-REFinD) [75] is an algorithm that registers diffusion tensor images using full tensor information. Registration of a pair of 128x128x60 diffusion tensor volumes takes 15 minutes on a Xeon 3.2GHz single processor machine, which is faster than many non-linear scalar image registration algorithms. DT-REFinD is now included in MedINRIA's image fusion module.

4.6. Isis

Keywords: *anatomical volume reconstruction*, *image registration*.

Participants: Daniel Barbeau [Correspondant], Grégoire Malandain, David Rey.

Isis is a software designed to strictly do volume reconstruction from serial cross sections. It uses in-house algorithms developped at Asclepios as well as the Insight Toolkit from Kitware.

In biology, histological observation is considered ground truth compared to observation of images acquired by CT-scans or MRI. It provides direct observation of the anatomical structures themselves. These histological cross-sections can be digitised and therefore allow for observation and processing at often higher resolutions than CT or MRI. When an anatomical structure is cut into a series of thin slices which are digitised, it is possible to reconstruct the volume and explore the structures in 3D rather than in 2D. However, during the data acquisition, the spatial consistency between slices might be lost and, before the data is usable, it must be restored through a two-by-two registration of the digitized slices. Currently, that operation, the reconstruction of the volume, can be cumbersome for clinicians. Researchers rely on hand-made scripts to do it as there can be hundreds of images for one anatomical volume.

Isis is meant to make the reconstruction of anatomical volumes from serial slices easier for both clinicians and researchers. Ideally, clinicians need to be able to just load their images, do a registration of the whole stack of images, control the quality of the reconstruction and correct the errors locally or globally. Researchers need to have access to finer controls to the registration algorithms or process images before registration. The output of Isis is a volume image and the geometrical transformations between each image.

The work concerning Isis at the end of 2007 and during 2008 covers the definition of its use cases, its functional and technical specifications.

4.7. Simulation Open Framework Architecture (SOFA)

Keywords: *medical simulation*, *surgery simulation*.

Participants: Barbara André, Erik Pernod, Hervé Delingette [Correspondant].

Web site: http://www.sofa-framework.org/ Gforge link: http://gforge.inria.fr/projects/sofa/

SOFA is an Open Source framework for the real-time simulation of deformable structures, particularly for medical simulation and planning. Three INRIA research teams are currently contributing to development of the SOFA platforms: the project team Alcove in Lille, Asclepios in Sophia-Antipolis and Evasion in Grenoble. The simulation group of the CIMIT (affiliated to MIT / Harvard / Massachussets General Hospital) has also strongly supported its development. This international open source platform is mostly intended for the research community to help the development of new algorithms, but it can also be used as a prototyping tool thanks to its modular architecture.

The involvement of the Asclepios team has been mostly focused on a new design that allows each SOFA component to cope with topological changes. Indeed, when simulating the surgical resection or suturing of an organ, it is necessary to update the data structure associated with the mesh of the organ but also the sparse matrices used in the computation of the mass and stiffness of the material. Propagating those topological changes to all components in a modular and generic way is a challenging task but provides a significant added value to all SOFA users.

An additional objective include the definition of scalar fields (like pressure, electric potential fields) on surface or volumetric meshes in order to implement physiological models. Our mid-term goal is to develop in SOFA a real-time simulator of radiofrequency ablation involving haptic devices which is suitable to train cardialogist for this endovascular procedure.

4.8. Other softwares

Baladin, MIPS, Pasha, Prospect, Runa, smDeform, simuDeform, and Yasmina have been described in previous activity reports.

5. New Results

5.1. Medical Image Analysis

5.1.1. Biomechanical modeling of the knee joint

Keywords: *Biomechanics*, *knee*, *simulation*.

Participants: Tobias Heimann [Correspondant], Francois Chung, Olivier Clatz, Hervé Delingette.

Within the EU project 3D Anatomical Human, our goal is the construction of subject-specific models of the knee joint to predict exact movement patterns for the lower limbs. As a first step towards this endeavor, we implemented non-linear biomechanical models for simulating tendons and ligaments as simple line elements. Using these models and high resolution MRI data, we built a subject-specific knee model (see Fig. 3) and integrated it into the open source framework SOFA. A preliminary validation by simulating a single-leg landing experiment yielded encouraging results.

5.1.2. Atlas-based segmentation in the context of head and neck tumor radiotherapy

Keywords: *Average contours building*, *atlas-based segmentation*, *head and neck region*, *kappa statistics*, *radiotherapy planning*.

Participants: Liliane Ramus [Correspondant], Grégoire Malandain.

This work is done in collaboration with DOSIsoft S.A., Cachan and Université Catholique de Louvain.

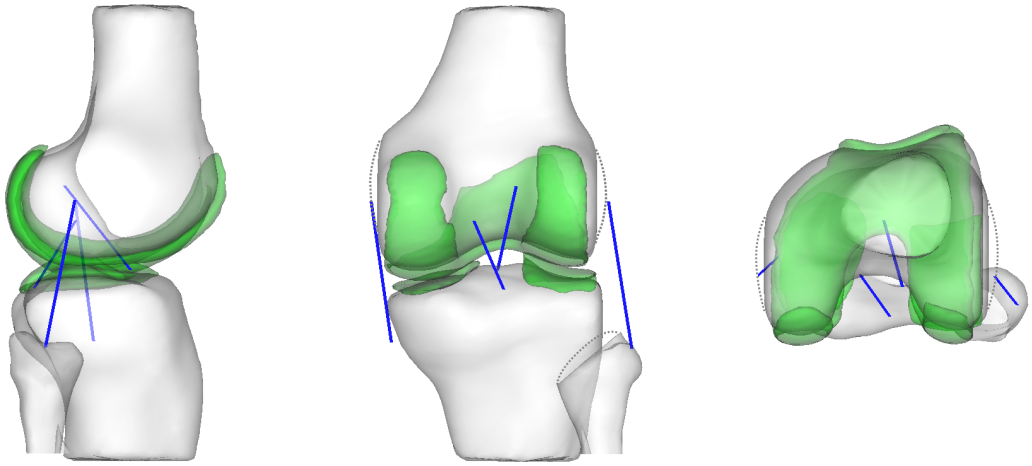


Figure 3. Model of the knee joint with cruciate and collateral ligaments in sagittal, coronal, and transversal view.

Atlas-based segmentation is used in radiotherapy planning to automatically delineate organs at risks in the head and neck region. An atlas is defined as an image (e.g. CT or MRI) with its segmentation. To build an head-and-neck atlas, we propose to average first the CT images of a database, and then the associated contours. For this last step, we use the STAPLE algorithm [139]. However, the obtained atlas suffer from a global trend for over-segmentation that may be due to the combination of differents types of variabilities:

- anatomical inter-patient variability (corpulence, neck flexion)
- registration discrepancies
- inter-expert and intra-expert variability in the manual delineations

To overcome this effect, we first have designed a protocol to define the optimal erosion (a mathematical morphology operation) for each delineated structure. Then we propose to use Kappa statistics, and Cohen's kappa [110] in particular, to build agreement maps that characterize the inter-contours variability. Regional maxima extraction and watershed transform allow then to obtain a binary segmentation for the concerning anatomical structure.

Fig.4 compares, for two patients, the qualitative results obtained using our approach with those obtained using standard atlas-based segmentation described in previous work [38]. A quantitative analysis on the 105 patients of our database showed that our approach provides a greater specificity than standard atlas-based segmentation, confirming that it enables to reduce over-segmentation.

5.1.3. Efficient diffeomorphic image registration

Keywords: *DTI*, *Image registration*, *demons algorithm*, *diffeomorphisms*, *spherical images*.

Participants: Olivier Clatz [Correspondant], Nicholas Ayache, Pierre Fillard, Xavier Pennec, Tom Vercauteren [Mauna Kea Technologies], B. T. Thomas Yeo.

This work is done in collaboration with Mauna Kea Technologies, Paris, France, http://www.maunakeatech.com and partly with the group of Polina Golland ar MIT CSAIL, Cambridge, MA, http://people.csail.mit.edu/polina/.

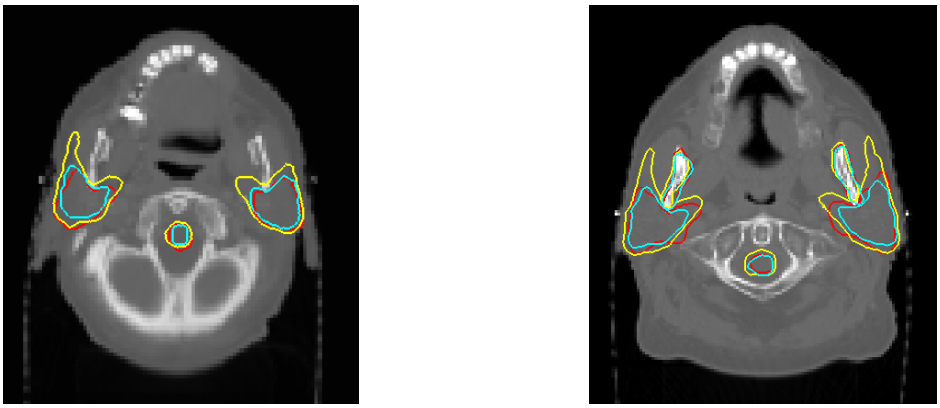


Figure 4. Qualitative results of atlas-based segmentation using kappa maps compared to standard atlas-based segmentation results (axial sections of CT images). Manual segmentation in red, Standard atlas-based segmentation in yellow, and Atlas-based segmentation using kappa maps in blue.

In 2007, we proposed a fast non-parametric diffeomorphic image registration scheme based on Thirion's demons algorithm. The theoretical roots of the algorithm have been expanded in [29], [51] and some applications were presented in [81] and [118]. In [73], we extended our diffeomorphic demons framework to propose a fast symmetric image registration scheme.

This work had initially been focused on 2D and 3D scalar image registration. In [75], we showed that an efficient scheme for diffusion tensor images reagistration could be build on top of the diffeomorphic demons. For that matter we showed that a closed-form expression of the finite-strain differential could be used. Finally, in [74], the diffeomorphic demons framework was used to propose a fast diffeomorphic landmark-free surface registration scheme for 2D closed surfaces.

5.1.4. Analysis of multiple sclerosis cerebral MRI

Keywords: *MRI*, *Multiple Sclerosis*, *Segmentation*, *SepINRIA*.

Participants: Jean-Christophe Souplet [Correspondant], Mikael Cohen [Pasteur hospital], Christine Lebrun [Pasteur hospital], Grégoire Malandain.

Studies have shown that brain atrophy seems to be better correlated with patients handicap. However, the different actual atrophy measurement methods' results can be conflicting. In a first step, an automatic method to compute the brain parenchymal fraction has been developed [93], [70]. First, the three MRI sequences (T1, T2, PD) of each time point are co-registered on the T2 sequence of the first timepoint. Then, these images are cropped, spatially unbiased and skull-stripped. A segmentation of the brain taking into consideration longitudinal information is performed. The White Matter, Grey Matter and Cerebro-Spinal Fluid volumes are computed at each time points. The brain parenchymal fraction (BPF) is obtained from these volumes at each time point. Evolution of the BPF between the different time points reflects the brain atrophy. In a second step, the results of this method have been compared to other methods' results [92].

5.1.5. Multiple sclerosis cerebral MRI segmentation workflow deployment on the EGEE grid

Keywords: *EGEE*, *Multiple Sclerosis*, *NeuroLOG*, *grid*, *workflow*.

Participants: Erik Pernod [Correspondant], Jean-Christophe Souplet, Xavier Pennec, Javier Rojas Balderrama [I3S], Diane Lingrand [I3S], Johan Montagnat [I3S].

This work is funded by the French National Research Agency NeuroLOG project (ANR-06-TLOG-024).

The segmentation of lesions on brain MRI is required for diagnosis purpose in multiple Sclerosis (MS). Moreover, the lesion burden is also used in MS patients' follow-up and in MS clinical researches. Different methods of lesions segmentation are available in the literature [52]. Most of them are based on complex algorithms which are useful but computationally intensive tools in medical image computing. Deploying them on grid infrastructures can provide an efficient resource for data handling and computing power.

In this context, an efficient implementation of a brain MRI segmentation method through a grid-interfaced workflow enactor has been done [67]. All the work has been done in cooperation with I3S within the framework of the NeuroLOG project (section 7.2.2). Indeed, used tools, like the grid-interfaced workflow enactor MOTEUR, and knowledge on grid were brought by this team.

To deploy this kind of application on a computational grid, the first step is to describe our pipeline as a workflow. Concretely, the pipeline has to be splitted into services (independent black boxes described by an additional XML file). Then, on described the links and the iteration strategies between services. Finally, the services are executed on the EGEE grid through the MOTEUR engine, hiding to the user the complexity of individual services submissions and management.

Experiments demonstrate that this brain lesion segmentation application is well adapted to grids and provide a sizeable gain of time in multiple executions. Moreover, the careful modeling of services allows to easily reuse them in more complex workflows, for instance meta-workflows comparing different segmentation strategies.

5.1.6. Versatile design of changing mesh topologies for surgery simulation

Keywords: *Mesh Topology*, *Real-Time Simulation*, *Topological Change*, *User-defined Data Structure*.

Participants: Barbara André, Hervé Delingette [Correspondant], Erik Pernod.

In the context of surgery simulation, we have developed a generic and efficient solution to handle topological changes on deformable meshes under real-time constraints implemented in the SOFA (section 4.7) platform [53]. The mesh topology is described by a topological component which also provides algorithms for performing topological changes (cutting, refinement). An important aspect of the design is that mesh related data is not centralized in the mesh data structure but stored in each dedicated component. Furthermore, topological changes are handled in a transparent way for the user through a mechanism of propagation of topological events from the topological components toward other components. Finally, the previous concepts have been extended to provide multiple topologies for the same degrees of freedom. Examples of cataract surgery simulation based on this versatile design have been demonstrated.

5.2. Biological Image Analysis

5.2.1. Confocal microscopic image restoration using matching and fusion

Keywords: *fusion*, *image restoration*, *matching*, *partial volume effect*.

Participants: Romain Fernandez [Correspondant], Grégoire Malandain, Christophe Godin [Virtual Plants], Jean-Luc Verdeil [CIRAD], Jan Traas [UMR5667], Pradeep Das [UMR5667].

Images acquired by confocal laser-scanning imaging systems suffer from the shadowing effect on cell walls that are parallel to the focal plane. We designed a restoration method and an acquisition protocol that produce high-quality and isotropic images of meristems, using matching and fusion of stacks of the same meristem acquired under different orientations. The cell walls parallel to the focal plane are up to 30 % brighter after the fusion than before. This method provides images with a sufficient quality, which can be processed by automatic algorithms with few errors (cell segmentation average error ratio is close to 5 %).

5.2.2. Cell tracking in time-series acquisition of confocal microscopic images

Keywords: *Confocal microscopy*, *cell tracking*, *meristem*.

Participants: Romain Fernandez [Correspondant], Grégoire Malandain, Christophe Godin [Virtual Plants], Jean-Luc Verdeil [CIRAD], Jan Traas [UMR5667], Pradeep Das [UMR5667].

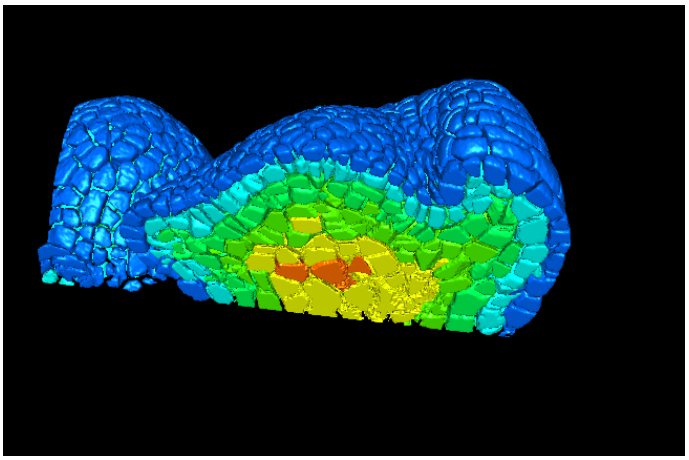


Figure 5. Segmentation of an apical meristem, with colorization of the different cell layers.

In order to understand the dynamics of the meristems, we studied the tracking of meristem cells using time-lapse confocal microscopy acquisition on early stages flowers of Arabidopsis shoot apical meristems. We designed a tracking algorithm in order to map two segmentations of the same meristem at different times. We declined it under two versions, according to the manner that the tracking problem is solved:

- An heuristic method, that iteratively selects and locks the better correspondance between a cell of the first image and one or more cells of the second image, using a maximum likelihood criterion.
- A global method, that solves the tracking problem using min-cost flow algorithm.

Visual inspection by biologists showed good results. The comparison against a ground truth segmentation will allow a quantitative assessment of these methods.

5.2.3. Image registration and mosaicing for dynamic in vivo fibered confocal microscopy

Keywords: *Cellvizio*, *Mosaicing*, *fibered confocal microscopy*, *image registration*.

Participants: Tom Vercauteren [Mauna Kea Technologies], Aymeric Perchant [Mauna Kea Technologies], Nicholas Ayache.

This work is done in collaboration with Mauna Kea Technologies, Paris, France, http://www.maunakeatech.com.

Fibered confocal microscopy (FCM), and especially Cellvizio® by Mauna Kea Technologies, is a potential tool for *in vivo* and *in situ* optical biopsy. In [72], we presented a real-time extension of our previous work on image sequence mosaicing for FCM. Mosaicing techniques are used to widen the field of view (FOV) and enhance the possibilities offered by FCM. This work has been reviewed in [29], [83].

5.3. Computational Anatomy

5.3.1. Registration of 4D time-series of cardiac images

Keywords: *4D*, *Demons*, *cardiac*, *heart*, *multichannel*, *registration*, *sequence*, *time-series*, *tracking*, *trajectory*.

Participants: Jean-Marc Peyrat [Correspondant], Hervé Delingette, Maxime Sermesant, Xavier Pennec, Chenyang Xu [Siemens SCR], Nicholas Ayache.

This work is funded by Siemens Corporate Research (NJ, USA).

In the case of spatio-temporal registration of two 4D sequences, we proposed a general framework [68] defined by mapping trajectories of physical points as opposed to spatial registration that solely aims at mapping homologous points. To ensure a mapping of the same physical points over the entire sequence, the transformation has to be temporally consistent with the motion occurring in both sequences and needs to, hence, map homologous trajectories. Including *trajectory constraints*, 4D registration can be formulated as a multichannel 3D registration which simplifies the optimization problem by parameterizing the time-dependent spatial transformations by a single spatial transformation. To solve the multichannel 3D registration problem, we proposed a novel 3D vector-valued version of the Diffeomorphic Demons preserving the coupling between each channel. This framework has been applied to the inter-subject non-linear registration of 4D cardiac CT sequences and showed a better consistency of the spatial transformations over time.

5.3.2. Statistical modeling of the scoliotic spine

Keywords: *Anatomical Variability*, *Articulated models*, *Orthopedic Treatments*, *Scoliosis*, *Spine*.

Participants: Jonathan Boisvert [Correspondant], Xavier Pennec, Farida Chériet [Polytechnic School of Montreal], Nicholas Ayache.

This project is part of a partnership between the Asclepios team, the Montreal's Sainte-Justine hospital and the Polytechnic School of Montreal.

The spine it is a flexible structure which is piecewise rigid. Thus, an articulated model encoding the articulations of neighboring vertebrae naturally accounts for the specific nature of the spine deformations in order to create statistical models of its shape. As such articulated models naturally belong to a Riemannian manifold and not to a vector space, we first used a statistical analysis on manifolds to analyze a large group of scoliotic patients. This revealed that the spine shape variability is inhomogeneous and anisotropic, and that it is possible to localize the vertebral levels that are significantly altered by an orthopedic treatment [33]. A more detailed analysis where the model is improved to take into account the local shape of each vertebra showed that the principal deformation modes uncovered clinically relevant patterns when applied to scoliotic patients [34]. Besides the understanding and classification of the pathologies, this statistical model can be used as a prior in a Maximum a posteriori (MAP) estimation procedure to reconstruct 3D spine models from partial radiological data or from 2D landmarks identified on radiographs. Our results indicate that the proposed method outperforms the most commonly used 3D reconstruction method and that a reconstruction error of less than 2mm was obtained when at least 25% of the data were available [32]. The results of all these studies, detailed in [26], indicate that a statistical model of the whole spine geometry, based on an articulated description of the spine, leads to clinically interpretable descriptive statistics and to algorithms that can reconstruct 3D spine models in circumstances where this was previously impossible.

5.3.3. Point-based statistical models without correspondences

Keywords: *statistical model*, *surfaces*, *template*.

Participants: Heike Hufnagel [Correspondant], Xavier Pennec.

This work takes place in a cooperation with the medical imaging group of the university Hamburg-Eppendorf.

The construction of statistical shape model (SSM) based on unstructured point sets without correspondences was continued this year. Estimating the SSM parameters from a set of observations is an inverse problem which we solve using an efficient Maximum a posteriori (MAP) framework involving an Expected-Maximization step. Experimental results on brain structure data sets demonstrate the efficiency and well-posedness of the approach [63], [45]. We are now coupling this statistical shape model with segmentation algorithms in order to robustify the automatic extraction of organs delineation.

5.3.4. Tensor based morphometry of the brain

Keywords: *deformation*, *statistical shape analysis*, *tensors*.

Participants: Xavier Pennec [Correspondant], Caroline Brun [LONI, UCLA], Natasha Lepore [LONI, UCLA], Paul Thompson [LONI, UCLA].

Tensor-based morphometry (TBM) is an increasingly popular method to study differences in brain anatomy statistically based on a local statistical analysis of the deformation (usually the determinant of the Jacobian matrix) aligning a set of images to a common template space. We have previously proposed to use statistics on the more complete strain tensor instead to better capture differences between populations.

In 2008, we firstly studied the influence of the choice of template on the TBM results [66]. Using 3D brain MR images from 10 monozygotic twin pairs, we defined a tensor-based distance between each image pair in the study. Relative to this metric, twin pairs were found to be closer to each other on average than random pairings, consistent with evidence that brain structure is under strong genetic control. The mean template was defined as the brain that minimizes the log-Euclidean deformation cost. This avoids the blurring caused by creating a synthetic image from a population, and when selected from a large population, avoids bias by being geometrically centered, in a metric that is sensitive enough to anatomical similarity that it can even detect genetic affinity among anatomies.

The development of a fluid registration consistent with TBM statistics was also continued. We defined for that a new regularizer that is a fluid extension of the Riemannian elasticity, which assures diffeomorphic transformations. We applied our method to an MRI dataset from 40 fraternal and identical twins, to reveal voxelwise measures of average volumetric differences in brain structure for subjects with different degrees of genetic resemblance. On the average, the difference in brain structure volumes was found to be less in identical (MZ) than fraternal (DZ) twins [56], [76], which is consistent with the degree of genetic similarity. To go one step further, we mapped in [55] the heritability of brain morphology. The performance of the Riemannian fluid registration algorithm was compared to a more standard fluid registration algorithm. The consistency between TBM registration and statistics should improve the detection power , which is paramount in epidemological studies or drug trials. Results showed that 3D maps from both registration techniques displayed similar heritability patterns throughout the brain. However, by comparing the cumulative distribution functions of the p-values from both methods, the Riemannian algorithm was shown to outperformed the standard fluid registration in terms of statistical power.

5.3.5. Template estimation from sets of curves and surfaces

Keywords: *current*, *curves*, *statistical atlas*, *surfaces*, *template*.

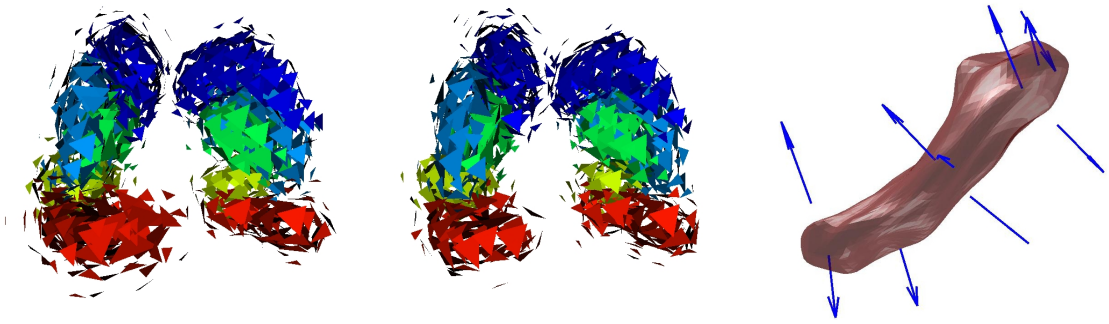
Participants: Stanley Durrleman [Correspondant], Xavier Pennec, Alain Trouvé, Nicholas Ayache.

Following our earlier work [40], we embed curves and surfaces into the space of currents. This modeling does not require any condition on the sampling of the data, and does not rely on point correspondences between shapes. As the space of current is a vector and a Hilbert space, we can define a Gaussian noise processes and compute the likelihood of the observations given a template. This generative statistical modeling is called 'forward model' by contrast to the 'backward model' that estimates a template by averaging deformations of the observations toward an unknown common reference frame. In practice, the maximum likelihood template is computed with a gradient descent scheme that requires a fast and robust deconvolution scheme, such as the one we develop in [60]. To characterize differences between populations, we first estimate a common template for the two populations of curves or surfaces and we infer the parameters of independent Gaussian covariance models for each population via PCA on the deformations of the template to the data of each population. The complete procedure is explained in [59]. Thanks to the generative model, we can also visualize the principal modes of deformation within each population, which helps interpreting the discriminative differences. An example of a resulting template in shown in figure 6.

5.3.6. Watershed and statistical atlases for brain DTI analysis

Keywords: *Diffusion Tensors Images*, *Region Merging*, *Statistical Atlases*, *Watershed*.

Participants: Jean Cousty [Correspondant], Pierre Fillard, Xavier Pennec.



a- Autistics b- Controls c- Difference on hippocampus

Figure 6. Estimated templates from 25 autistics (a) and 7 controls (b) for 10 sub-cortical structures (Caudate, Putamen, Globus Pallidus, Amygdala and Hippocampus). In (c), the blue arrows approximate the difference between autistics and controls' template, superimposed with the hippocampus of a control. Data courtesy of Prof. Guido Gerig (University of Utah).

This work was supported by ARC BrainVar.

In the context of the BrainVar ARC, we propose a segmentation framework for DTIs. It relies on watershed cuts, a new watershed notion for edge-weighted graphs, and on the Log-Euclidean distance between tensors. To merge the oversegmented watershed regions, we proposed an interactive procedure where the regions are sequentially merged according to user given (inside/outside) labels. Based on these manully edited segmentation, we built a statistical atlas that is then used to perform an automatic labeling and segmentation. Results on 10 DTIs show that the accuracy of interactive and automated methods are equivalent.

5.4. Computational Physiology

5.4.1. Cardiac motion recovery by coupling an electromechanical model and cine MRI data

Keywords: *data assimilation*, *deformable model*, *electromechanical models*, *heart simulation*, *pro-active model*.

Participants: Florence Billet [Correspondant], Maxime Sermesant, Hervé Delingette, Nicholas Ayache.

This work is funded by the CardioSense3D project.

We proposed a new method to estimate the state of an electromechanical model from cine MR images which is inspired from the deformable model framework used in medical image analysis [54]. This method is similar to a pro-active deformable model described in [131]. We showed the formal equivalence between this method and a data assimilation method proposed by Moireau et al. [122]. The theoretical equivalence between the deformable model approach proposed here and this filtering approach leads to a better understanding of the trade-off between the electromechanical model and the image data.

Fig. 7 shows the MR images at some instant of the cardiac cycle. The surimposed lines represent the endocardium and epicardium surfaces of the estimated mesh with these cine MRI data. Colours correspond to the intensity of the images forces.

5.4.2. Planning of cardiac radiofrequency ablation therapy

Keywords: *cardiac*, *electrophysiology*, *radio-frequency ablation*, *simulation*.

Participants: Jatin Relan [Correspondant], Hervé Delingette, Maxime Sermesant, Nicholas Ayache.

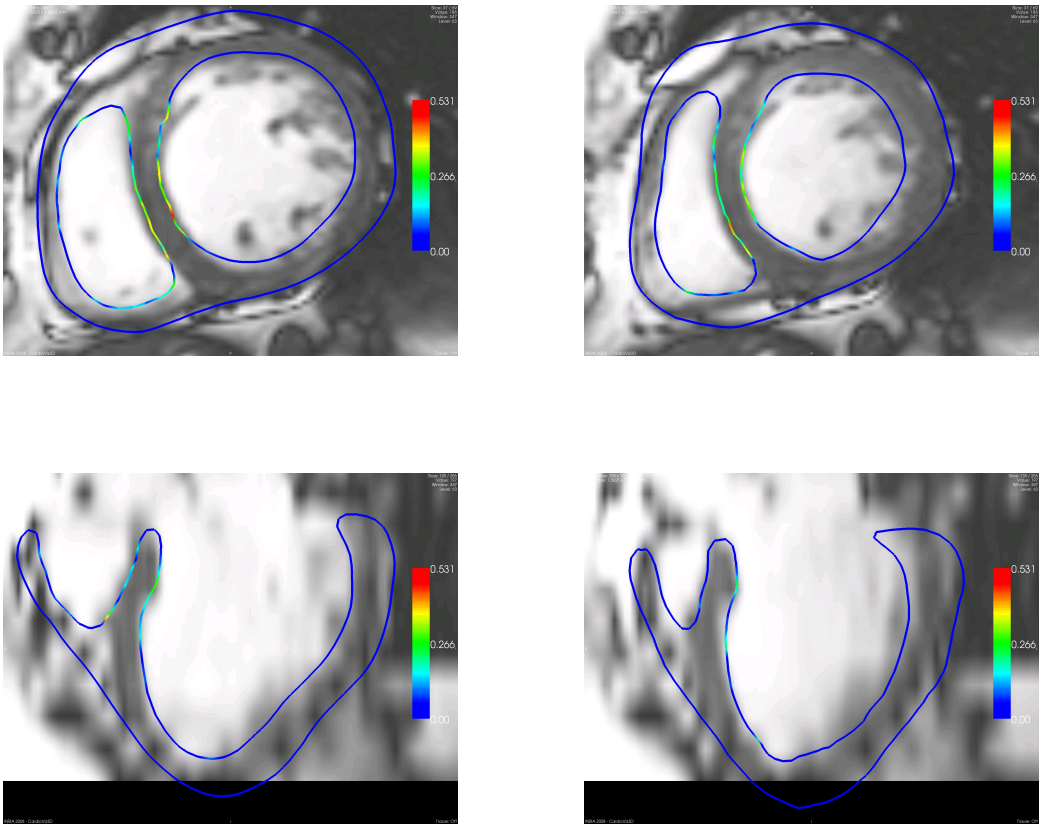


Figure 7. Results of the motion tracking: delineation of the estimated mesh surimposed with cine MRI at end-diastole (left column) and end-systole (right column). Colours encode the intensity of the image forces (blue: small, red: large).

This work is funded by the FP7 European Project euHeart.

This work is a part of work package WP6 "Cardiac Radiofrequency Ablation" of an European project "euHeart: Personalised & Integrated Cardiac Care: Patient-specific Cardiovascular Modelling and Simulation for In Silico Disease Understanding & Management and for Medical Device Evaluation & Optimization". The objective of this work package is to use personalized biophysical models of the cardiac electrophysiology and electro-mechanics in order to improve the planning and guidance of radiofrequency ablation therapies on patients suffering from Atrial Fibrillation (AF) and Ventricular Tachycardia (VT).

5.4.3. Virtual pulmonary valve replacement interventions with a personalised cardiac electromechanical model

Keywords: *electromechanical models*, *health-e-child*, *paediatric diseases*, *personalised heart simulation*, *soft-tissue intervention simulation*, *tetralogy of Fallot*.

Participants: Tommaso Mansi [Correspondant], Barbara André, Maxime Sermesant, Hervé Delingette, Xavier Pennec, Nicholas Ayache.

Part of this work is funded by the FP6 European Project Health-e-CHild.

In this work we investigated the use of a personalised electromechanical model of the heart with a soft-tissue intervention platform to help the cardiologist in choosing the right therapy for patients suffering from chronic pulmonary valve regurgitations, such as in repaired Tetralogy of Fallot. Pulmonary valve replacement (PVR) is becoming a pivotal treatment and, recently, two techniques are becoming prevalent: a minimally invasive approach and an open-heart surgery with direct right ventricle volume reduction. However, there is no common agreement about the postoperative outcomes of these PVR techniques, which makes the choice of the therapy a clinical challenge.

An electromechanical model of the heart was personalised to simulate the cardiac function of a real patient. Minimally-invasive pulmonary valve replacement was simulated by stopping the regurgitations in the model, whereas a soft-tissue intervention platform, SOFA[6] was adapted and used to simulate the surgical intervention in real-time. The user can interactively cut, move and join parts of the anatomical model to resect myocardium regions that appear lesional (fibrosis, scars, etc.).

The framework was tested on a real case. The results were promising and suggested that such framework may be used to evaluate the effects of pulmonary valve replacement upon the cardiac function of a patient. In this way, current work aims now at validating the framework on other cases and simulate the natural myocardium remodelling to predict long term effects of these two therapies.

5.4.4. Extrapolating glioma invasion margin in brain magnetic resonance images: suggesting new irradiation margins

Keywords: *Eikonal equations*, *Tumor growth*, *asymptotic approximations*, *extrapolation*, *glioblastoma multiforme*, *gliomas*, *irradiation*, *radiotherapy*, *reaction-diffusion*.

Participants: Ender Konukoglu [Correspondant], Olivier Clatz, Pierre-Yves Bondiau, Hervé Delingette, Nicholas Ayache.

Radiotherapy for brain gliomas treatment relies on magnetic resonance (MR) and computed tomography (CT) images. They provide information on the spatial extent of the tumor, but can only visualize parts of the tumor where cancerous cells are dense enough, masking the low density infiltration. In radiotherapy, a 2 cm constant margin around the tumor is taken to account for this uncertainty. This approach however, does not consider the growth dynamics of gliomas, particularly the differential motility of tumor cells in the white and in the gray matter. In this work, we propose a novel method for estimating the full extent of the tumor infiltration starting from its visible mass in the patients' MR images. This problem of estimating the tumor cell distribution beyond the visible tumor mass in an image is a time independent extrapolation problem where we do not have information about the temporal evolution of the pathology or the initial conditions.

[6] http://www.sofa-framework.org/

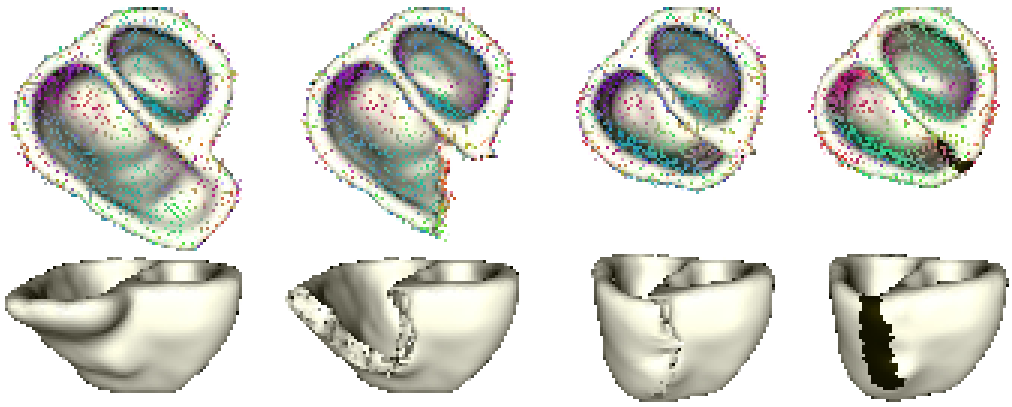


Figure 8. Overview of the complete cardiac surgery pipeline. From left to right: original mesh, after resection, during attachment, final mesh. Colour lines: fibre orientations. Black area: postoperative scar.

Based on the reaction-diffusion models widely used in the literature, we derive our approximation method to solve this extrapolation problem. Previously we have already addressed this problem, during the last year we have returned to the method and improved our approximation technique. The method relied on global linearization of the reaction-diffusion equation as a first order crude approximation. We have found that local linearization combined with spatial integration yields a much better approximation remaining still first order. After improving our technique, we use this formulation to tailor new tumor specific variable irradiation margins. We perform geometrical comparisons between the conventional constant and the proposed variable margins through determining the amount of targeted tumor cells and healthy tissue in the case of synthetic tumors. Results of these experiments suggest that the variable margin could be more effective at targeting cancerous cells and preserving healthy tissue.

5.4.5. Image guided personalization of reaction-diffusion type tumor growth models using modified anisotropic eikonal equations

Keywords: *Eikonal equations*, *Tumor growth*, *glioblastoma multiforme*, *gliomas*, *inverse problems*, *parameter estimation*, *reaction-diffusion*.

Participants: Ender Konukoglu [Correspondant], Olivier Clatz, Bjoern H. Menze, Marc-André Weber, Bram Stieltjes, Emmanuel Mandonnet, Hervé Delingette, Nicholas Ayache.

Reaction-diffusion based tumor growth models have been widely used in the literature for modeling the growth of brain gliomas. Lately, recent models have started integrating medical images in their formulation. Including different tissue types, geometry of the brain and the directions of white matter fiber tracts improved the spatial accuracy of reaction-diffusion models. The adaptation of the general model to the specific patient cases on the other hand have not been studied thoroughly yet.

In this work, conducted in the context of the CompuTumor associated team (see section 7.4), we address this adaptation. We propose a parameter estimation method for reaction-diffusion tumor growth models using time series of medical (Magnetic Resonance) images. This method estimates the patient specific parameters of the model using the images of the patient taken at different successive time instances. The proposed method formulates the evolution of the tumor delineation visible in the images based on the reaction-diffusion dynamics therefore it remains consistent with the information available. As a result of the described derivation we show that the reaction-diffusion dynamics can be well approximated by a certain modified anisotropic Eikonal equation. We perform thorough analysis of the method using synthetic tumors and show important

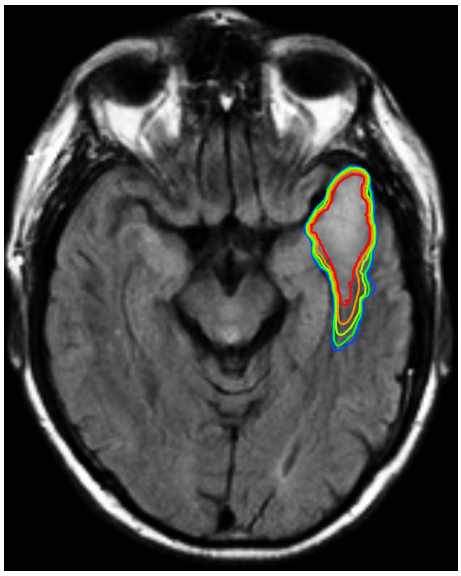


Figure 9. Prediction of tumor infiltration.

couplings between parameters of the reaction-diffusion model. We show that several parameters can be uniquely identified in the case of fixing one parameter, namely the proliferation rate of tumor cells. Moreover, regardeless of the value the proliferation rate is fixed to, the speed of growth of the tumor can be estimated with accuracy. Finally we apply our method to a few real cases and show promising preliminary results.

5.4.6. Monitoring slowly evolving tumors

Keywords: *deformation analysis*, *follow-up*, *intensity analysis*, *meningiomas*, *pathologies*, *slowly growing*, *tumor*, *volume comparison*.

Participants: Ender Konukoglu [Correspondant], William M. Wells, Sébastien Novellas [Archet II hospital], Nicholas Ayache, Ron Kikinis, Peter M. Black, Kilian M. Pohl.

Change detection is a critical task in the diagnosis of many slowly evolving pathologies. This work describes an approach that semi-automatically performs this task using longitudinal medical images. We are specifically interested in meningiomas, which experts often find difficult to monitor as the tumor evolution can be obscured by image artifacts. We test the method on synthetic data with known tumor growth as well as ten clinical data sets. We show that the results of our approach highly correlate with expert findings but seem to be less impacted by inter- and intra-rater variability [64].

6. Contracts and Grants with Industry

6.1. European Marie Curie project "3D Anatomical Human"

Participants: François Chung, Olivier Clatz, Hervé Delingette [correspondant], Tobias Heimann.

The Research Training Network "3D Anatomical Human" (MRTN-CT-2006-035763 , http://3dah.miralab.unige.ch/) is a European project aiming at developing realistic functional three-dimensional models for the human musculoskeletal system, the methodology being demonstrated on the lower limb. François Chung has been hired as ESR (Early Staged Researcher) and Tobias Heimann as ER (Experienced Researcher). In this context, INRIA has collaborated with UCL (UK) and University of Geneva for the acquisition and segmentation of the MR images of the lower limbs and with Istituti Ortopedici Rizzoli (Italy) and EPFL (Switzerland) for the biomechanical modeling of the knee. Other research groups include the Vrije Universiteit Brussel (Belgium), Aalborg University (Denmark) and CRS4 (Italy). Within this project, three plenary meetings, one workshop and one summer school have been organized in 2008 as well as several exchanges of students.

6.2. "Virtual Physiological Human" Network of Excellence

Participants: Nicholas Ayache, Olivier Clatz, Hervé Delingette, Florence Dru, Maxime Sermesant [Correspondant].

The "Virtual Physiological Human" Network of Excellence (VPH NoE) is a EU Seventh Framework funded project, working to connect and support researchers in the VPH field within Europe and beyond. INRIA is one of the core members, and is more dedicated, through Asclepios, to the data fusion part of the VPH toolkit. The consortium members are: University CollegeLondon, University of Oxford, University of Nottingham, University of Sheffield, UK; CNRS, the French National Institute for Research in Computer Science and Control (INRIA), France; Université Libre de Bruxelles, Belgium; University Pompeu Fabra, Institut Municipal dâAssistència Sanitària, Spain; University of Auckland, New Zealand; European Molecular Biology Laboratory, Germany; Karolinska Institutet, Sweden; GEIE ERCIM.

6.3. PASSPORT

Participant: Hervé Delingette [Correspondant].

The PASSPORT project (Ref 223894, http://www.passport-liver.eu/) is a 3-year (2008-2011) STREPS European project which aims at developing patient-specific models of the liver. Those models should integrate anatomical, functional, mechanical, appearance, and biological descriptions of the liver. More precisely, it is expected to simulate the liver deformation due to breathing as well as the liver regeneration after hepatectomy.

INRIA is involved in this project through the teams Alcove, Evasion and Asclepios and around the software platform SOFA which will serve as the integration plartform for the project. IRCAD (Strasbourg) is the project leader which also gathers TUM (Munich, Germany), UCL (London, UK), ETH (Zurich, Switzerland), ICL (London, UK), INSERM (Paris), ULP (Strasbourg), IZBI (Leipzig, Germany). One plenary meeting have been organized in 2008.

6.4. EuHeart

Participants: Nicholas Ayache, Florence Billet, Hervé Delingette [Correspondant], Tommaso Mansi, Adityo Prakosa, Jatin Relan, Maxime Sermesant.

The EuHeart project (Ref 224495, http://www.euheart.eu/) is a 4-year (2008-2012) integrated European project which aims at developing personalized, and clinically validated multi-physics, multi-level models of the heart and great vessels. Those models need to be tightly integrated with signal and image processing tools in order to assist clinical decision making and to help reducing morbidity and mortality rates associated with cardiovascular diseases.

Asclepios is leading a workpackage on radiofrequency ablation for which electromechanical models of the heart are used to improve the planning of radiofrequency ablation lines for patient suffering from atrial fibrillation and ventricular tachycardia. This project is lead by Philips Research and also involves two other Inria teams (Macs and Reo) as well as Univ. of Oxford (UK), Univ. of Auckland (New Zealand), Univ. of Pompeu Fabra (Barcelone, Spain), Univ. of Karlsruhe (Germany), King's College London (UK), Univ. of Sheffield (UK), Amsterdam Medical Center (The Netherlands). One plenary and two topical meetings have been organized in 2008.

6.5. Health-e-Child

Participants: Xavier Pennec [Correspondant], Nicholas Ayache, Maxime Sermesant, Hervé Delingette, Stanley Durrleman, Ender Konukoglu, Tommaso Mansi.

The European project Health-e-Child (IST 027749, http://www.health-e-child.org/), coordinated by Siemens, Germany, aims to create an IT platform to share paediatric knowledge and clinical data based on grid technologies. The project currently brings together eight European countries and intends to integrate heterogeneous biomedical data from three clinical specialities (cardiology, neurology and rheumatology) coming from three paediatric hospitals in Europe (Hôpital Necker in Paris, France, Giannina Gaslini institute in Genoa, Italy, and Great Ormond Street Hospital in London, Great-Britain). This integration should lead to a better understanding of the pathologies studied, and, in the long term, provide real tools to help paediatricians make the right decisions. In this project, the role of the Asclepios team is to model the congenital heart pathologies of the right ventricle and the grown of brain tumors.

6.6. CIFRE PhD Fellowships

6.6.1. Dosisoft

The work of Liliane Ramus, *Digital anatomical atlases for radiotherapy planning*, is supported by a PhD fellowship from the Dosisoft company.

6.6.2. Mauna Kea Technologies

The work of Barbara André, *Smart Atlas for the Early Diagnosis of Gastrointestinal Cancers from Optical Biopsy Images*, is supported by a PhD fellowship from the Mauna Kea Technologies company.

6.7. Other contracts

The contracts Cancéropôle PACA CPER Telius, Maestro[7], Miniara, and Philips, and Siemens are described in our previous activity report.

7. Other Grants and Activities

7.1. Regional initiatives

7.1.1. Regional PhD fellowships

Ender Konukoglu is partially supported by a "Région Provence-Alpes Côte d'Azur" PhD fellowship.

7.2. National initiatives

7.2.1. INRIA Large Collaborative Effort CARDIOSENSE3D

Participants: Hervé Delingette [coordinator], Nicholas Ayache, Maxime Sermesant, Florence Billet, Tommaso Mansi, Adityo Prakosa, Nicolas Toussaint, Damien Lepiller, Jatin Relan, Jean-Marc Peyrat.

The action CARDIOSENSE3D is a 4-year large initiative action (2005-2009) on the topic of cardiac simulation. This action gathers the expertise of four INRIA research teams (Asclepios, Macs, Reo and Sysiphe) on this multi-disciplinary research topic. CardioSense3D has three main objectives:

1. to build a cardiac simulator that couples four different physiological phenomena,
2. to estimate patient specific parameters and state variables from observations (images, electrophysiology mappings) of the cardiac activity,
3. to build several applications to solve clinical problems related to the diagnosis or therapy of cardiac pathologies.

[7] http://www.maestro-research.org/

H. Delingette is in charge of the coordination of this action. More information can be found at the following web site http://www.inria.fr/CardioSense3D/

7.2.2. RNTL NeuroLOG

Participants: Xavier Pennec [correspondant], Erik Pernod, Grégoire Malandain, Jean-Christophe Souplet.

The French National Research funded project NeuroLOG http://neurolog.polytech.unice.fr/ (ANR-06-TLOG-024) is addressing software technologies for the integration of processes, data and knowledge in neurological medical imaging:

- Management and access of partly structured data, heterogeneous and distributed in an open environment.
- Access control and protection of private medical data.
- Control of workflows implied in complex computing process on grid infrastructures.
- Extraction and quantification of relevant parameters for three different pathologies: multiple sclerosis, brain vascular stroke and brain tumors.

This is a multi-disciplinary project which associates partners in software technologies (I3S at Sophia-Antipolis, LRI in Orsay), databases (Business Objects, LaRIA, Visages at IRISA-Rennes) and medical imaging (Visages at IRISA-Rennes, Visioscopie, U594, IFR49, Asclepios at INRIA-Sophia).

7.2.3. INRIA Cooperative Research Initiative BrainVar

Participants: Xavier Pennec [coordinator], Stanley Durrleman, Pierre Fillard.

Understanding and modelling the individual anatomy of the brain and its variability across a population is made difficult by the absence of meaningful physical models for comparing different subjects, the complexity of shapes, and the high number of degrees of freedom implied.

Each research team is currently investigating independently particular aspects of the general problem and is proposing different but often complementary approaches. The goal of this INRIA cooperative research initiative is to federate the efforts of several groups in France (Asclepios, INRIA Sophia Antipolis; LNAO Neurospin, CEA - DSV - DRM- SHFJ; Neurospin, INRIA Futurs; MMiXT, CNRS UPR640 LENA, Pitié-Salpétrière; VisAGeS, IRISA Rennes; LSIS, UMR 6168, LXAO team, Marseille; CMLA, ENS Cachan) to identify the challenges for a future potential neuro-anatomic plateform. The general research themes are related to anatomical and functional neuroimaging on one hand and on computational anatomy on the other hand.

7 scientific meeting sessions were organized during the 2 years with about 6 to 8 presentations and 20 participants at each meeting. Results are detailed on the BrainVar web page http://www-sop.inria.fr/asclepios/projects/ARCBrainVar/.

7.2.4. Other Initiatives

The ATP CIRAD Meristem Grant and QUALICORE are described in our previous activity report.

7.2.5. Consulting for Industry

- Nicholas Ayache is scientific consultant for the company Mauna Kea Technologies (Paris).
- Hervé Delingette is a scientific consultant for the company Median and a member of the scientific council of the company QuantifiCare.
- Grégoire Malandain is a member of the technical council of the company Dosisoft (Paris), a subsidiary from the Gustave Roussy Institute and the Curie Institute (Paris).

7.2.6. Collaboration with national hospitals

Here we provide a list of research centers in national hospitals with whom we collaborate in common research projects.

7.2.6.1. IRCAD, hôpitaux de Strasbourg

Pr. Marescaux and L. Soler : hepatic surgery simulation segmentation of abdominal structures from CT scan images and augmented reality for guidance in hepatic surgery [125], [126].

7.2.6.2. Hôpital de la Pitié-Salpétrière, Paris

Dr. J. Yelnik (INSERM U.289), Pr. D. Dormont, and E. Bardinet (CNRS) are our partners in a collaboration with Medtronic [108].

7.2.6.3. Centre anti-cancer Antoine Lacassagne, Hôpital Pasteur, Nice

Dr. Bondiau participates in our research on atlas registration for radiotherapy planning and on tumour growth simulation.

7.2.6.4. CHU de Nice, Hôpital Pasteur

We continue our collaboration with Dr. C. Lebrun-Frenay of the neurology department, and with Dr. Chanalet of the radiology department, within the framework of a study on the temporal evolution of MS lesion load.

7.2.7. Collaboration with international hospitals

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

Maxime Sermesant is a part-time lecturer in the Interdisciplinary Medical Imaging Group, Division of Imaging Sciences, St Thomas' Hospital, King's College London. The XMR facility within this hospital is a unique possibility to validate and exploit the cardiovascular modelling work.

7.3. Foreign Associated Team: Brain Atlas

Participants: Xavier Pennec [Correspondant], Stanley Durrleman, Pierre Fillard, Nicholas Ayache, Caroline Brun [LONI, UCLA], Natasha Lepore [LONI, UCLA], Paul Thompson [LONI, UCLA].

Since its creation in September 2001, the associated team program between the Asclepios laboratory at INRIA and the laboratory of NeuroImaging at the UCLA School of Medicine has enabled an active collaboration between both structures, with the objective of comparing and analyzing the performances and behaviors of image processing algorithms devoted to the building of brain atlases.

In 2008, the theoretical work on the statistical modeling of curves by S. Durrleman was continued and extended to surfaces. This is described in section 5.3.5. The noted presentation at the MICCAI conference [60] was awarded the "Young Investigator Award 2008" in the category "Shape and Statistical Analysis". The work that we initiated last year on tensor-based morphometry was continued by studying the influence of the choice of template, and by developing a fluid registration method that computes the mappings and performs TBM statistics in a consistent way. These results are described in Sections 5.3.4.

With the additional help of the NSF-INRIA REUSSI internship program, we hosted the visit of C. Brun (PhD student at UCLA) and L. Lepore (post-doc at UCLA) for three weeks in April/May in the Asclepios team. Symmetrically X. Pennec and S. Durrleman participated to the very successful IPAM summer school on Mathematics in Brain Imaging organized by P. Thompson in July 2008 at UCLA.

7.4. Foreign Associated Team: CompuTumor

Participants: Nicholas Ayache, Olivier Clatz [Correspondant], Pierre Fillard, Polina Golland [CSAIL, MIT], Ender Konukoglu, Xavier Pennec, Tom Vercauteren, Simon Warfield [CRL, Harvard Medical School], William Wells [CSAIL, MIT], Boon Thye Thomas Yeo [CSAIL, MIT].

The CompuTumor associated team has been funded early 2007. This project is dedicated to the study of brain tumor models and their integration with medical images to better assist diagnosis and therapy. The project strongly relies on the current collaborations between INRIA and world leading teams with complementary technical and clinical expertise in Boston and Nice.

In 2008, the work on DTI processing was continued and extended [74], [75]. New algorithms were developped to assess the growth of slowly evolving tumors [64]. Ongoing work aims at coupling models and images to infer quantitative tumor paramters that could be used for therapy planning. This is described in Sections 5.4.4 and 5.4.5.

8. Dissemination

8.1. Promotion of the Scientific Community

8.1.1. Journal editorial boards

N. Ayache is the co-founder and the co-editor in Chief with J. Duncan (Professor at Yale) of **Medical Image Analysis**[8]. This scientific journal was created in 1996 and is published by Elsevier. Its impact factor in 2003 was 4.4, it was 3.2 in 2004, 3.14 in 2005, 3.26 in 2006 and 3.5 in 2008.

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).

N. Ayache is associated editor of **IEEE Transactions on Medical Imaging**[9].

I. Strobant is editorial assistant for Transactions on Medical Image Analysis, IEEE (since october 2001)

N. Ayache is a member of the editorial board of the following journals *Mathematical Modeling and Numerical Analysis (M2N)*, *Medical Image Technology* (Japanese journal) and *Journal of Computer Assisted Surgery* (Wiley). and *Journal of Computer Assisted Surgery* (Wiley).

G. Malandain is a member of the editorial board of the journal *International Journal on Computer Vision* (Kluwer).

X. Pennec is a member of the editorial board of the journal *Medical Image Analysis* (Elsevier).

8.1.2. Participation in the organization of conferences

N. Ayache was co-chair for industrial relationships of the International Symposium on Biomedical Imaging (ISBI'08).

H. Delingette was a member of the program committee of the International Conference on Computer Vision and Pattern Recognition (CVPR08),Medical, European Conference on Computer Vision (ECCV'08), the International Symposium on Biomedical Simulation (ISBMS'08), Virtual Reality Interactions and Physical Simulation (VRIPHYS'08), the workshop on 3D Physiological Human (3DPH'08), MICCAI Workshop on Functional Medical Image Analy sis, and a member of the review committees of the International Symposium on Biomedical Imaging (ISBI'08).

G. Malandain was a member of the program committee of the International Conference on Medical Image Computing and Computer Assisted Intervention (MICCAI'08), and a member of the review committees of the International Symposium on Biomedical Imaging (ISBI'08), MICCAI workshop on "Medical Image Analysis on Multiple Sclerosis" (MIAMS'08), workshop on Computational Topology in Image Context (CTIC'08), Colloque Africain sur la Recherche en Informatique et en Mathématiques Appliquées (CARI'08), and the Journées d'Études Algéro-Française en Imagerie Médicale (JETIM'08).

[8] http://www.elsevier.com/wps/find/journaleditorialboard.cws_home/620983/editorialboard
[9] http://www.ieee-tmi.org/

X. Pennec organized and chaired the 2nd workshop "Mathematical Foundations of Computational Anatomy (MFCA'08)" http://www-sop.inria.fr/asclepios/events/MFCA08/ associated to MICCAI on Sept. 6, 2008 in New York which gathered more than 60 participants.

He was also a member of the program committees of: Computational Diffusion MRI Workshop (CDMRI'08), MICCAI workshop on Medical imaging on grids: achievements and perspectives (MICCAI-grid 2008), MICCAI Workshop on Manifold Learning in Medical Imaging 2008, Workshop on Non-Rigid Shape Analysis and Deformable Image Alignment (NORDIA'08), Volume Graphics (VG'08), IEEE Workshop on Mathematical Methods in Biomedical Image Analysis (MMBIA'08); and a member of the review commitees of: International Conference on Medical Image Computing and Computer Assisted Intervention (MICCAI'08) and International Symposium on Biomedical Imaging (ISBI'08).

M. Sermesant was a member of the program committe of the MICCAI 2008 Workshop on the analysis of functional medical images.

8.1.3. Scientific animation

Nicholas Ayache is member of the scientific council of the Institute for Technologies of INSERM. He is also a member of the "comité sectoriel du département Biologie-Santé of the "Agence Nationale pour la Recherche (ANR)", and a member of the "Comité de la Recherche Biomédicale en Santé Publique (CRBSP)" of the Nice hospitals from beginning of 2008.

G. Malandain is chairing the local experimentation and software development committee (CDL).

G. Malandain was an evaluator for Syscomm program of the French National Research Agency, the Fondation "Santé et Radiofréquences", the Cible program of the région Rhône-Alpes,

O. Clatz is a member of the scientific committee and evaluator for the research cluster ISLE of Rhônes-Alpes.

X. Pennec was a member of the working group "Engineer and Computer Sciences" of the national prospective exercice on production grids (gpro-s2i).

H. Delingette was a member of the local committee in charge of the scientific selection of visiting scientists applications (Comité Nice).

M. Sermesant is a member of the INRIA-INSERM reflexion group on "modelling living systems". He is an evaluator for the Biotechnology and Biological Sciences Research Council (BBSRC), and the National Institute for Health Research (NIHR), United Kingdom.

8.2. University teaching

École Centrale de Paris. N. Ayache, H. Delingette and G. Malandain are co-responsible of 2 modules on medical imaging (formation and analysis of medical images) (45 hours of lectures) with the participation of X. Pennec (15 hours). These 2 modules are common to the Master MVA of ENS Cachan "Mathematiques, Vision et Apprentissage", and to the Master IDB of École Centrale de Paris.

Master IGMMV, université de Nice Sophia-Antipolis. G. Malandain is responsible of one module of 15 hours (medical image analysis). H. Delingette is responsible of one module of 15 hours on image segmentation and soft tissue simulation.

Master PENSUM, ENS Lyon / Univ. Nice-Sophia-Antipolis. X. Pennec is responsible of a 24h module on Mathematics for Medical Image processing.

Master Génie biomédical, université de Nice Sophia-Antipolis. G. Malandain is responsible of one module of 48 hours (24 hours of lectures + 24 hours of practical work) with the participation of Jean-Christophe Souplet.

Master IMA, université Pierre et Marie Curie. G. Malandain gave a 3 h course.

Diplôme Inter Universitaire - Radiothérapie externe Haute Technicité. G. Malandain gave a 3 h course.

Spring school on Medical image processing: from voxels to numerical atlases. Strasbourg, June 2-6, 2008. X. Pennec and H. Delingette gave 3h of lecture each.

Summer School Program on Mathematics in Brain Imaging. Institute for Pure and Applied Mathematics (IPAM) / UCLA, July 14-25, 2008. X. Pennec gave a 1 hour lecture.

Applied Mathematics Master, Ecole des Ponts et Chaussées O. Clatz gave a 3h lecture.

Hervé Delingette gave a tutorial presentation at the Summer School on 3D Anatomical Human in Pula (Italy) and at the conference 3D Physiological Human in Zermatt (Switzerland).

8.3. PhD Theses and Internships

8.3.1. PhD defended in 2008

1. Jonathan Boisvert, *Modèles de la variabilité géométrique du rachis scoliotique*. Cotutelle (joint supervision) University of Nice-Sophia-Antipolis / Polytechnique School of Montreal, Canada, March 19, 2008. Committee: F. Guibeault (president), N. Ayache (supervisor), F. Cheriet (co-supervisor), X. Pennec (co-supervisor), M.-O. Berger (reviewer), L. Desbat (reviewer), S. Parent (referee).
2. Jimena Costa, *Segmentation of Anatomical Structures of the Lower Abdomen using 3D Deformable Models* École des Mines de Paris, March 14, 2008. Committee: J. Troccaz (reviewer), M. Revenu (reviewer), N. Ayache (supervisor), H. Delingette (co-supervisor), J.-P. Gérard (president), H. Kafrouni (referee), S. Novellas, P.-Y. Bondiau (invited).
3. Pierre Fillard, *Riemannian Processing of Tensors for Diffusion MRI and Computational Anatomy of the Brain*. Nice-Sophia Antipolis University, February 8, 2008. Committee: N. Ayache (supervisor), X. Pennec (co-supervisor), G. Gerig (reviewer), J.-F. Mangin (reviewer), C. Barillot, R. Deriche, C.-F. Westin (referees), A. Anwander, P. Basser, T. Knösche, P. Thompson (invited).
4. Tom Vercauteren, *Image Registration and Mosaicing for Dynamic In Vivo Fibered Confocal Microscopy*, École des Mines de Paris, January 25, 2008. Committee: O. Faugeras (president), P. Golland (reviewer), N. Navab (reviewer), N. Ayache (supervisor), X. Pennec (co-supervisor), A. Perchant (referee), Mauna Kea Technologies Examinateur V. Becker, S. Loiseau (invited).

8.3.2. Current PhDs

1. Barbara André, *Smart Atlas for the Early Diagnosis of Gastrointestinal Cancers from Optical Biopsy Images*, École des Mines de Paris. Cifre collaboration with Mauna Kea Technologies.
2. Florence Billet, *Analyse de la fonction cardiaque à l'aide d'un modèle électromécanique du cœur*, Nice-Sophia-Antipolis University. Cardiosense3D.
3. François Chung, *Reconstruction et Simulation des muscles et du squelette des membres inférieurs* Nice-Sophia Antipolis University.
4. Stanley Durrleman, *Joint modeling of the brain growth and of the population variability. Application to pediatric brain imaging.* Nice-Sophia Antipolis University. In collaboration with A. Trouvé, CMLA, ENS.
5. Romain Fernandez, *3D segmentation and reconstruction of rice's root meristem from multiphoton microscopic images*, Montpellier university. In collaboration with C. Godin, Virtual Plants.
6. Ezequiel Geremia, *Multi-scale computational models of brain tumors for medical image analysis*, Nice-Sophia Antipolis University.
7. Heike Hufnagel, *Statistical shape analysis of normal and pathological organs within the abdomen*, University of Hamburg. PhD in collaboration with Prof. Dr. Heinz Handels, Institut für Medizinische Informatik, University of Hamburg.

8. Ender Konukoglu, *Modeling and control of tumor growth with medical imaging*. Nice-Sophia Antipolis University.
9. Tommaso Mansi *Modelling of paediatric cardiac pathologies*. École des Mines de Paris
10. Jean-Marc Peyrat, *Electro-mechanical models of the heart activity personalized from medical images*, Nice-Sophia Antipolis University.
11. Adityo Prakosa, *Analysis and Simulation of the heart function from multimodal cardiac images*, Nice-Sophia Antipolis University.
12. Liliane Ramus, *Digital anatomical atlases for radiotherapy planning*, Nice-Sophia Antipolis University. Cifre collaboration with Dosisoft.
13. Jatin Relan, *Planning of radiofrequency ablation of the heart using electromechanical models personnalized from cardiac images and electrophysiological signals*, Ecole des Mines.
14. Jean-Christophe Souplet, *Analysis of Multiple Sclerosis MRI images*. Nice-Sophia-Antipolis University.

8.3.3. Participation to thesis committees

Nicholas Ayache participated as chair of jury for the Habilitation of S. Cotin (Lille), as invited member for the Habilitation of L. Soler (Strasbourg), as supervisor or co-supervisor to the thesis committee of J. Boisvert, J. Costa, P. Fillard and T. Vercauteren.

Hervé Delingette participated as co-supervisor to the PhD thesis of J. Costa (Nice University) as reviewer to the Phd thesis committee of J. Schaerer (Lyon University), M. Bucki (Grenoble University), L. Roose (KUL, Belgium), Mathieu Nesme (Grenoble University), as reviewer to the Habilitation à Diriger les Recherches committee of Emmanuel Promayon (Grenoble University), François Faure (Grenoble University).

Grégoire Malandain participated as president to the PhD thesis committee of B. Perrenot (INSA Lyon), as reviewer to the PhD thesis committee of P. Coupé (Rennes university), A. Dubois (Paris-Sud 11 university), J. Fripp (Queensland university), Y. Gavet (Saint-Etienne university), M. Hachama (Paris 5 university), A. Hostettler (Strasbourg university), as reviewer to the Habilitation à Diriger des Recherches thesis committee of D. Sarrut (Lyon university) and as referee to the PhD thesis committee of B. Scherrer (Grenoble university).

Xavier Pennec participated to the PhD committees of P. Fillard, T. Vercauteren and J. Boisvert as co-supervisor.

8.3.4. Training activities

1. François Hebert, *Segmentation de l'intestin grêle dans le cadre de la maladie de Crohn*, University of Nice-Sophia Antipolis, Master thesis, 2008.
2. Erik Pernod, *Interface Development for Medical Imaging Applications in the framework of the Multiple Sclerosis Disease*, Institut des Sciences de l'Ingénieur de Toulon et du Var, 2008.

8.4. Participation to workshops, conferences, seminars, invitations

We only give here the invited participations. Please refer to general references for the regular participation to conferences with a submission process.

- **Nicholas Ayache** gave invited talks to the Collège de France (Paris), VBM conference (Keynote, Delft), NCRI Cancer Conference (Birmingham), and at Microsoft Research (Cambridge).
- **Olivier Clatz** gave an invited lecture at the "Imaging and Measurements in Biomechanics and Medical Engineering" workshop in Talence and at the "Imaging and Measurements in Biomechanics and Medical Engineering" workshop in Paris.

- **Hervé Delingette** gave an invited lecture at the INRIA Visiting Committee on December 18th, at the conference ICT Bio 2008 at Brussels le 24 octobre 2008, at the Miccai workshop on 3D analysis of cardiac structure and function on Sept. 10th in New-York (USA), at the ENS Cachan symposium on physiopathology modeling on June 16th 2008, at the GID conference in Ibiza (Spain) on May 8th 2008.
- **Grégoire Malandain** gave invited lectures at the Maestro symposium (satellite symposium of the European Society for Therapeutic Radiology and Oncology (ESTRO) conference), SY-STEM Meeting on modelling in plant science, “Association de Recherche contre la Sclérose En Plaques” (ARSEP) workshop, workshop on “mouvements respiratoires”,
- **Xavier Pennec** gave invited plenary talks at: the Mathematical meeting "Statistical modeling of images" at Luminy on Mai 5-9; the Interdisciplinary Workshop on 3D Paleo-Anthropology, Anatomy, Computer Science & Engineering - Synergies for the Future, Toulouse, June 19-20; the Journés MAS de la SMAI (french applied and industrial mathematical society). Rennes, August 29; the MICCAI tutorial on Advances in Diffusion MRI Analysis, Ney-York, USA, September 6; the Emerging Trends in Visual Computing (ETVC’08) colloquium at Ecole Polytechnique on November 18th-20th.

  He also gave invited seminars at: the Probability and Statistics Lab (LSP), Toulouse, February 19; the Biomedical Imaging and Analysis seminar series, CSAIL, MIT, September 12; the join GdR Isis / GdR Stic-Sante meeting day on diffusion imaging, ENST, Paris, December 9.
- **Maxime Sermesant** gave an invited lecture at the meeting "Première rencontre CRM-INRIA-MITACS", Montréal, Canada, at the mini-symposium "Numerical simulation of cardiac bioelectric activity" during The European Consortium For Mathematics In Industry, London, UK, and at the "Salon professionel télésanté, éthique, robotisation médicale et hôpitaux numériques", Agora Einstein, Sophia Antipolis, France.
- **Stanley Durrleman** gave an invited presentation at the Workshop “Geometry and Statistics of Shapes” held at the Hausdorff Center for Mathematics in Bonn (Germany) on June 9th, organized by D. Cremers, D. Mumford, A. Trouvé and M. Rumpf.
- **Stanley Durrleman** gave a presentation at the workshop “Déformations et Statistiques en Imagerie Médicale” organized by the Groupe de Recherche “Stats et Santé” at Université Descartes, Paris 5 on Avril 7 ; at the workshop “Rencontres de Modélisation en Physiop athologie” at ENS de Cachan on June 17 , and at the seminar “Probabilités, Statistique, Image” at University Paris 13, on December 17.

8.5. Nominations and prizes

- **Nicholas Ayache** is the winner of the 2008 Microsoft Award of the Royal Society and the French Academy of Sciences
- The following awards have been received in the context of MICCAI 2008 conference in New-York, USA:
  - **Stanley Durrleman** received the "Young Investigator Award 2008" in the category "Shape and Statistical Analysis" for his paper "Sparse Approximations of Currents for Statistics on Curves and Surfaces", that was a collaboration between the CMLA at Cachan (A. Trouve) and INR IA (S. Durrleman, X. Pennec and N. Ayache).
  - **Jean-Christophe Souplet** won the "Multiple Sclerosis Lesion Segmentation Challenge" organized in the context of the MICCAI satellite workshop "3D Segmentation in the Clinic: A Grand Challenge II".
  - **B. T. Thomas Yeo** was nominated for a Young Researcher award for his article "Spherical Demons: Fast Surface Registration", that was a collaborative research between MIT (B.T. Thomas Yeo, Mert Sabuncu, Bruce Fischl and Polina Golland) and INRIA (Tom Vercauteren and Nichol as Ayache).

  - **Damien Lepiller** was nominated for a Young Researcher award for his article "Cardiac Electrophysiology Model Adjustment Using the Fusion of MR and Optical Imaging" that was a collaborative research between the Sunnybrook Health Sciences Center (Mihaela Pop and Graham Wrig ht) and INRIA (Damien Lepiller, Maxime Sermesant, Hervé Delingette and Nicholas Ayache).
  - **Nicholas Ayache** received the "Significant Researcher Award", for his contributions to the MICCAI conference and Society.

- **Tommaso Mansi** received the Best Poster Award at the 8th IEEE EMBS Summer School, Berder (France).
- **Tommaso Mansi** received a Special Award from the Sociétés Françaises Médico-Chirurgicales Pédiatriques, Nantes, June 6.
- **Olivier Clatz** was awarded a special mention for best PhD in Biomedical Engineering from the SFGBM-IEEE France Section, Paris, May 28.
- **Jean-Christophe Souplet** received the Best Poster Award (Prix Etienne Roulet) at the Journées de Neurologie de Langue Française, April, Bordeaux (France).
- The EU-funded project Health-e-Child has won the "Best Exhibition Award - 1st Prize" at the biggest European conference of the year on Information and Communication Technologies, *i.e.* ICT2008 in Lyon in France (November 2008),

9. Bibliography

Major publications by the team in recent years

[1] N. AYACHE (editor). *Computational Models for the Human Body*, Handbook of Numerical Analysis (Ph. Ciarlet series editor), Elsevier, 2004.

[2] N. AYACHE, H. DELINGETTE (editors). *Proceedings of the International Symposium on Surgery Simulation and Soft Tissue Modeling*, Lecture Notes in Computer Science, vol. LNCS 2673, Springer-Verlag, Juan-les-Pins, France, June 2003.

[3] V. ARSIGNY, P. FILLARD, X. PENNEC, N. AYACHE. *Log-Euclidean Metrics for Fast and Simple Calculus on Diffusion Tensors*, in "Magnetic Resonance in Medicine", PMID: 16788917, vol. 56, n^{o} 2, August 2006, p. 411-421, ftp://ftp-sop.inria.fr/epidaure/Publications/Arsigny/arsigny_mrm_2006.pdf.

[4] N. AYACHE. *Epidaure: a Research Project in Medical Image Analysis, Simulation and Robotics at INRIA*, in "IEEE Trans. on Medical Imaging", vol. 22, n^{o} 10, October 2003, p. 1185–1201, ftp://ftp-sop.inria.fr/epidaure/Publications/Ayache/Ayache-editorial-ieee-tmi.pdf.

[5] N. AYACHE. *L'analyse automatique des images medicales, etat de l'art et perspectives*, in "Annales de l'Institut Pasteur", Numero special sur les progres recents de l'imagerie medicale, vol. 9, n^{o} 1, avril-juin 1998, p. 13-21.

[6] N. AYACHE, O. CLATZ, H. DELINGETTE, G. MALANDAIN, X. PENNEC, M. SERMESANT. *Asclepios: a Research Project-Team at INRIA for the Analysis and Simulation of Biomedical Images*, in "From semantics to computer science: essays in honor of Gilles Kahn", Cambridge University Press, 2008, http://www.inria.fr/sophia/asclepios/Publications/Nicholas.Ayache/Colloquium-Gilles-Kahn-NA-2007-v5.pdf.

[7] C. BLONDEL, R. VAILLANT, G. MALANDAIN, N. AYACHE. *3-D tomographic reconstruction of coronary arteries using a precomputed 4-D motion field*, in "Physics in Medicine and Biology", vol. 49, n^{o} 11, 2004, p. 2197–2208, ftp://ftp-sop.inria.fr/epidaure/Publications/Malandain/blondel-pmb-2004.pdf.

[8] P. CACHIER, É. BARDINET, D. DORMONT, X. PENNEC, N. AYACHE. *Iconic Feature Based Nonrigid Registration: The PASHA Algorithm*, in "CVIU — Special Issue on Nonrigid Registration", vol. 89, n^{o} 2-3, Feb.-march 2003, p. 272–298, ftp://ftp-sop.inria.fr/epidaure/Publications/Cachier/Cachier_CVIU_2003.pdf.

[9] O. CLATZ, M. SERMESANT, P.-Y. BONDIAU, H. DELINGETTE, S. K. WARFIELD, G. MALANDAIN, N. AYACHE. *Realistic Simulation of the 3D Growth of Brain Tumors in MR Images Coupling Diffusion with Mass Effect*, in "IEEE Transactions on Medical Imaging", vol. 24, n^{o} 10, October 2005, p. 1334-1346, ftp://ftp-sop.inria.fr/epidaure/Publications/Clatz/TMI_GBM_clatz.pdf.

[10] H. DELINGETTE, N. AYACHE. *Soft Tissue Modeling for Surgery Simulation*, in "Computational Models for the Human Body", N. AYACHE (editor), Handbook of Numerical Analysis (Ed : Ph. Ciarlet), Elsevier, 2004, ftp://ftp-sop.inria.fr/epidaure/Publications/Delingette/hna-delingette.pdf.

[11] H. DELINGETTE. *General Object Reconstruction based on Simplex Meshes*, in "International Journal of Computer Vision", vol. 32, n^{o} 2, 1999, p. 111-146.

[12] J. DUNCAN, N. AYACHE. *Medical Image Analysis: Progress over two decades and the challenges ahead*, in "IEEE Transactions on Pattern Analysis and Machine Intelligence", vol. 22, n^{o} 1, 2000, p. 85-106.

[13] M. Á. GONZÁLEZ BALLESTER, X. PENNEC, M. G. LINGURARU, N. AYACHE. *Generalized Image Models and Their Application as Statistical Models of Images*, in "Medical Image Analysis", MICCAI 2003 Special Issue, vol. 8, n^{o} 3, September 2004, p. 361–369, ftp://ftp-sop.inria.fr/epidaure/Publications/Gonzalez/Gonzalez:MedIA:2004.pdf.

[14] K. KRISSIAN, G. MALANDAIN, N. AYACHE, R. VAILLANT, Y. TROUSSET. *Model-Based Detection of Tubular Structures in 3D Images*, in "Computer Vision and Image Understanding", vol. 80, n^{o} 2, 2000, p. 130–171, ftp://ftp-sop.inria.fr/epidaure/Publications/Malandain/krissian-cviu-2000.pdf.

[15] G. MALANDAIN, É. BARDINET, K. NELISSEN, W. VANDUFFEL. *Fusion of autoradiographs with an MR volume using 2-D and 3-D linear transformations*, in "NeuroImage", vol. 23, n^{o} 1, September 2004, p. 111–127, ftp://ftp-sop.inria.fr/epidaure/Publications/Malandain/malandain-neuroimage-2004.pdf.

[16] J. MONTAGNAT, H. DELINGETTE. *4D Deformable Models with temporal constraints : application to 4D cardiac image segmentation*, in "Medical Image Analysis", vol. 9, n^{o} 1, February 2005, p. 87–100, ftp://ftp-sop.inria.fr/epidaure/Publications/Delingette/montagnat-Media04.pdf.

[17] X. PENNEC, N. AYACHE, J.-P. THIRION. *Landmark-based registration using features identified through differential geometry*, in "Handbook of Medical Imaging", I. BANKMAN (editor), chap. 31, Academic Press, September 2000, p. 499-513, ftp://ftp-sop/epidaure/Publications/Pennec/Pennec.HMIP.pdf.

[18] X. PENNEC, P. CACHIER, N. AYACHE. *Tracking Brain Deformations in Time-Sequences of 3D US Images*, in "Pattern Recognition Letters - Special Issue on Ultrasonic Image Processing and Analysis", vol. 24, n^{o} 4-5, February 2003, p. 801–813, ftp://ftp-sop.inria.fr/epidaure/Publications/Pennec/Pennec.Cachier.Ayache.PattRecLetters02.pdf.

[19] G. PICINBONO, H. DELINGETTE, N. AYACHE. *Non-Linear Anisotropic Elasticity for Real-Time Surgery Simulation*, in "Graphical Models", vol. 65, n^{o} 5, September 2003, p. 305–321, ftp://ftp-sop.inria.fr/epidaure/Publications/Delingette/Picinbono-GM03.pdf.

[20] S. PRIMA, S. OURSELIN, N. AYACHE. *Computation of the Mid-Sagittal Plane in 3D Brain Images*, in "IEEE Transaction on Medical Imaging", vol. 21, n^{o} 2, February 2002, p. 122–138, ftp://ftp-sop.inria.fr/epidaure/Publications/Prima/tmi.final.pdf.

[21] D. REY, G. SUBSOL, H. DELINGETTE, N. AYACHE. *Automatic Detection and Segmentation of Evolving Processes in 3D Medical Images: Application to Multiple Sclerosis*, in "Medical Image Analysis", vol. 6, n^{o} 2, June 2002, p. 163-179, ftp://ftp-sop.inria.fr/epidaure/Publications/Rey/rey-media-2002.pdf.

[22] A. ROCHE, G. MALANDAIN, N. AYACHE. *Unifying Maximum Likelihood Approaches in Medical Image Registration*, in "International Journal of Imaging Systems and Technology: Special Issue on 3D Imaging", vol. 11, n^{o} 1, 2000, p. 71–80, ftp://ftp-sop.inria.fr/epidaure/Publications/Roche/ijist00.pdf.

[23] A. ROCHE, X. PENNEC, G. MALANDAIN, N. AYACHE. *Rigid Registration of 3D Ultrasound with MR Images: a New Approach Combining Intensity and Gradient Information*, in "IEEE Transactions on Medical Imaging", vol. 20, n^{o} 10, October 2001, p. 1038–1049, ftp://ftp-sop.inria.fr/epidaure/Publications/Roche/Roche_MR_US_TMI_2001.pdf.

[24] M. SERMESANT, H. DELINGETTE, N. AYACHE. *An Electromechanical Model of the Heart for Image Analysis and Simulation*, in "IEEE Transactions in Medical Imaging", vol. 25, n^{o} 5, 2007, p. 612–625, ftp://ftp-sop.inria.fr/asclepios/Publications/Maxime.Sermesant/TMI2006Sermesant.pdf.

[25] M. SERMESANT, C. FOREST, X. PENNEC, H. DELINGETTE, N. AYACHE. *Deformable biomechanical models: Application to 4D cardiac image analysis*, in "Medical Image Analysis", vol. 7, n^{o} 4, December 2003, p. 475–488, http://authors.elsevier.com/sd/article/S1361841503000689.

Year Publications

Doctoral Dissertations and Habilitation Theses

[26] J. BOISVERT. *Modèles de la variabilité géométrique du rachis scoliotique*, PhD thesis, Université de Nice-Sophia Antipolis (France) and École Polytechnique de Montréal (Canada), March 2008, http://www.inria.fr/sophia/asclepios/Publications/Jonathan.Boisvert/PhD_Boisvert.pdf.

[27] J. COSTA. *Segmentation of Anatomical Structures of the Lower Abdomen using 3D Deformable Models*, PhD Thesis, École Nationale Supérieure des Mines de Paris, March 2008, http://www.inria.fr/sophia/asclepios/Publications/Costa/These.pdf.

[28] P. FILLARD. *Riemannian Processing of Tensors for Diffusion MRI and Computational Anatomy of the Brain*, PhD Thesis, University of Nice-Sophia Antipolis, February 2008, http://www.inria.fr/sophia/asclepios/Publications/Pierre.Fillard/ThesisPFillard.pdf.

[29] T. VERCAUTEREN. *Image Registration and Mosaicing for Dynamic In Vivo Fibered Confocal Microscopy*, PhD Thesis, École Nationale Supérieure des Mines de Paris, January 2008, http://www.inria.fr/sophia/asclepios/Publications/Tom.Vercauteren/PhDThesis-TomVercauteren.pdf.

Articles in International Peer-Reviewed Journal

[30] N. ARCHIP, O. CLATZ, S. WHALEN, S. DIMAIO, P. BLACK, A. GOLBY, F. JOLESZ, S. K. WARFIELD. *Compensation of geometric distortion effects on intraoperative magnetic resonance imaging for enhanced visualization in image-guided neurosurgery.*, in "Neurosurgery", vol. 62, n^{o} 3 supl. 1, Mar 2008, p. 209-15.

[31] É. BARDINET, M. BHATTACHARJEE, D. DORMONT, B. PIDOUX, G. MALANDAIN, M. SCHUPBACH, N. AYACHE, P. CORNU, Y. AGID, J. YELNIK. *A three-dimensional histological atlas of the human basal ganglia. II. Atlas deformation strategy and evaluation in deep brain stimulation for Parkinson disease*, in "Journal of neurosurgery", October 2008, http://www.inria.fr/sophia/asclepios/Publications/Bardinet/bardinet-jn-2008.pdf.

[32] J. BOISVERT, F. CHERIET, X. PENNEC, H. LABELLE, N. AYACHE. *Articulated Spine Models for 3D Reconstruction from Partial Radiographic Data*, in "IEEE Transactions on Biomedical Engineering", PMID: 18990626, vol. 55, n^{o} 11, November 2008, p. 2565–2574, http://www.inria.fr/sophia/asclepios/Publications/Xavier.Pennec/Boisvert-TBME08.pdf.

[33] J. BOISVERT, F. CHERIET, X. PENNEC, H. LABELLE, N. AYACHE. *Geometric Variability of the Scoliotic Spine using Statistics on Articulated Shape Models*, in "IEEE Transactions on Medical Imaging", PMID: 18390352, vol. 27, n^{o} 4, 2008, p. 557–568, http://www.inria.fr/sophia/asclepios/Publications/Xavier.Pennec/Boisvert.TMI08.pdf.

[34] J. BOISVERT, F. CHERIET, X. PENNEC, H. LABELLE, N. AYACHE. *Principal Deformations Modes of Articulated Models for the Analysis of 3D Spine Deformities*, in "Electronic Letters on Computer Vision and Image Analysis", vol. 7, n^{o} 4, December 2008, p. 13–31, http://elcvia.cvc.uab.es/index.php/elcvia/article/view/165/202.

[35] P.-Y. BONDIAU, O. CLATZ, M. SERMESANT, P.-Y. MARCY, H. DELINGETTE, M. FRENAY, N. AYACHE. *Biocomputing: numerical simulation of glioblastoma growth using diffusion tensor imaging.*, in "Physics in Medicine and Biology", vol. 53, n^{o} 4, Feb 2008, p. 879-93, http://www.inria.fr/sophia/asclepios/Publications/Maxime.Sermesant/PMB2008Bondiau.pdf.

[36] P. CHINCHAPATNAM, K. RHODE, M. GINKS, C. RINALDI, P. LAMBIASE, R. RAZAVI, S. ARRIDGE, M. SERMESANT. *Model-Based Imaging of Cardiac Apparent Conductivity and Local Conduction Velocity for Diagnosis and Planning of Therapy*, in "IEEE Transactions on Medical Imaging", vol. 27, n^{o} 11, 2008, p. 1631-1642, http://www.inria.fr/sophia/asclepios/Publications/Maxime.Sermesant/TMI2008Phani.pdf.

[37] O. COMMOWICK, V. ARSIGNY, A. ISAMBERT, J. COSTA, F. DHERMAIN, F. BIDAULT, P.-Y. BONDIAU, N. AYACHE, G. MALANDAIN. *An Efficient Locally Affine Framework for the Smooth Registration of Anatomical Structures*, in "Medical Image Analysis", vol. 12, n^{o} 4, 2008, p. 427-441, http://www.inria.fr/sophia/asclepios/Publications/Olivier.Commowick/CommowickMedia2008.pdf.

[38] O. COMMOWICK, V. GRÉGOIRE, G. MALANDAIN. *Atlas-Based Delineation of Lymph Node Levels in Head and Neck Computed Tomography Images*, in "Radiotherapy Oncology", vol. 87, n^{o} 2, 2008, p. 281-289, http://www.inria.fr/sophia/asclepios/Publications/Olivier.Commowick/CommowickRO2008.pdf.

[39] H. DELINGETTE. *Triangular Springs for Modeling Nonlinear Membranes*, in "IEEE Transactions on Visualisation and Computer Graphics", vol. 14, n^{o} 2, March/April 2008, http://www.inria.fr/sophia/asclepios/Publications/Herve.Delingette/tvcg-membrane.pdf.

[40] S. DURRLEMAN, X. PENNEC, A. TROUVÉ, P. M. THOMPSON, N. AYACHE. *Inferring brain variability from diffeomorphic deformations of currents: an integrative approach*, in "Medical Image Analysis", PMID: 18658005, vol. 12/5, n^{o} 12, 2008, p. 626–637, http://www.inria.fr/sophia/asclepios/Publications/Stanley.Durrleman/Durrleman_Media08.pdf.

[41] P. FILLARD, X. PENNEC, P. M. THOMPSON, N. AYACHE. *Evaluating Brain Anatomical Correlations via Canonical Correlation Analysis of Sulcal Lines*, in "NeuroImage", Accepted for publication, 2008, http://www.inria.fr/sophia/asclepios/Publications/Pierre.Fillard/Fillard.Neuroimage.2008.pdf.

[42] T. GLATARD, J. MONTAGNAT, D. EMSELLEM, D. LINGRAND. *A Service-Oriented Architecture enabling dynamic services grouping for optimizing distributed workflows execution*, in "Future Generation Computer Systems", vol. 7, n^{o} 24, July 2008, p. 720–730.

[43] T. GLATARD, J. MONTAGNAT, D. LINGRAND, X. PENNEC. *Flexible and efficient workflow deployment of data-intensive applications on GRIDS with MOTEUR*, in "International Journal of High Performance Computing Applications", Special issue on Workflow Systems in Grid Environments, vol. 3, n^{o} 22, August 2008, p. 347–360, http://www.i3s.unice.fr/~glatard/docs/ijhpca.pdf.

[44] S. HAIK, D. GALANAUD, M. G. LINGURARU, K. PEOC'H, N. PRIVAT, B. FAUCHEUX, N. AYACHE, J. HAUW, D. DORMONT, J. BRANDEL. *In Vivo Detection of Thalamic Gliosis: A Pathoradiologic Demonstration in Familial Fatal Insomnia*, in "Archives of Neurology", vol. 65, n^{o} 4, April 2008, p. 545-549, http://www.inria.fr/sophia/asclepios/Publications/Nicholas.Ayache/HaikAN2008.pdf.

[45] H. HUFNAGEL, X. PENNEC, J. EHRHARDT, N. AYACHE, H. HANDELS. *Generation of a Statistical Shape Model with Probabilistic Point Correspondences and EM-ICP*, in "International Journal for Computer Assisted Radiology and Surgery (IJCARS)", vol. 2, n^{o} 5, March 2008, p. 265–273, http://www.inria.fr/sophia/asclepios/Publications/Heike.Hufnagel/hufnagel_IJCARS.pdf.

[46] A. ISAMBERT, F. DHERMAIN, F. BIDAULT, O. COMMOWICK, P.-Y. BONDIAU, G. MALANDAIN, D. LEFKOPOULOS. *Evaluation of an Atlas-Based Automatic Segmentation Software for the Delineation of Brain Organs at Risk in a Radiation Therapy Clinical Context*, in "Radiotherapy Oncology", vol. 87, n^{o} 1, 2008, p. 93-99.

[47] E. MANDONNET, J. PALLUD, O. CLATZ, H. DUFFAU, L. CAPELLE. *Computational Modelling of the WHO Grade II Glioma Dynamics: Principles and Applications to Surgical Strategy*, in "Neurosurgical Review", vol. 31, n^{o} 3, Jul 2008, p. 263-9.

[48] J. MONTAGNAT, T. GLATARD, I. CAMPOS PLASENCIA, F. CASTEJON, X. PENNEC, G. TAFFONI, V. VOZNESENSKY, C. VUERLI. *Workflow-based data parallel applications on the EGEE production grid infrastructure*, in "Journal of Grid Computing (JGC)", vol. 6, n^{o} 4, December 2008, p. 369-383.

[49] M. POP, M. SERMESANT, D. LEPILLER, M. V. TRUONG, E. MCVEIGH, E. CRYSTAL, A. DICK, H. DELINGETTE, N. AYACHE, G. A. WRIGHT. *Fusion of optical imaging and MRI for the evaluation and adjustment of macroscopic models of cardiac electrophysiology: A feasibility study*, in "Medical Image Analysis", Jul 2008, http://www.inria.fr/sophia/asclepios/Publications/Maxime.Sermesant/MEDIA2008Pop.pdf.

[50] M. SERMESANT, J.-M. PEYRAT, P. CHINCHAPATNAM, F. BILLET, T. MANSI, K. RHODE, H. DELINGETTE, R. RAZAVI, N. AYACHE. *Toward patient-specific myocardial models of the heart*, in "Heart Failure Clin-

ics", vol. 4, n^{o} 3, Jul 2008, p. 289-301, http://www.inria.fr/sophia/asclepios/Publications/Maxime.Sermesant/HFC2008Sermesant.pdf.

[51] T. VERCAUTEREN, X. PENNEC, A. PERCHANT, N. AYACHE. *Diffeomorphic Demons: Efficient Non-parametric Image Registration*, in "NeuroImage", In press. PMID: 19041946, 2008, http://www.inria.fr/sophia/asclepios/Publications/Tom.Vercauteren/DiffeoDemons-NeuroImage08-Vercauteren.pdf.

Articles in National Peer-Reviewed Journal

[52] J.-C. SOUPLET, C. LEBRUN, S. CHANALET, N. AYACHE, G. MALANDAIN. *Revue des approches de segmentation des lésions de sclérose en plaques dans les séquences conventionnelles IRM*, in "Revue Neurologique", Accepted for publication, 2008.

International Peer-Reviewed Conference/Proceedings

[53] B. ANDRÉ, H. DELINGETTE. *Versatile design of changing mesh topologies for surgery simulation*, in "Fourth International Symposium on BioMedical Simulation (ISBMS'08), London, UK", Lecture Notes in Computer Science, vol. 5104, Springer-Verlag, July 2008, p. 147–156.

[54] F. BILLET, M. SERMESANT, H. DELINGETTE, N. AYACHE. *Cardiac Motion Recovery by Coupling an Electromechanical Model and Cine-MRI Data: First Steps*, in "Proc. of the Workshop on Computational Biomechanics for Medicine III. (Workshop MICCAI-2008)", K. MILLER, P. NIELSEN (editors), September 2008, http://www.inria.fr/sophia/asclepios/Publications/Florence.Billet/Billet_MICCAI08.pdf.

[55] C. BRUN, N. LEPORE, X. PENNEC, Y.-Y. CHOU, A. D. LEE, M. BARYSHEVA, G. I. DE ZUBICARAY, M. MEREDITH, K. MCMAHON, M. J. WRIGHT, A. W. TOGA, P. M. THOMPSON. *A tensor-based morphometry study of genetic influences on brain structure using a new fluid registration method*, in "Proc. Medical Image Computing and Computer Assisted Intervention (MICCAI'08), New York, USA", D. METAXAS, L. AXEL (editors), Lecture Notes in Computer Science, PMID: 18982692, vol. 5242, Springer-Verlag, September 2008, p. 914–921, http://www.inria.fr/sophia/asclepios/Publications/Xavier.Pennec/Brun_MICCAI08.pdf.

[56] C. BRUN, N. LEPORE, X. PENNEC, Y.-Y. CHOU, A. D. LEE, G. I. DE ZUBICARAY, K. MCMAHON, M. J. WRIGHT, M. BARYSHEVA, A. W. TOGA, P. M. THOMPSON. *A new registration method based on Log-Euclidean Tensor metrics and its application to genetic studies*, in "Proc. of the 2008 IEEE Int. Symp. on Biomedical Imaging: From Nano to Macro (ISBI'08), Paris, France, May 14-17", 2008, p. 1115-1118.

[57] O. COMMOWICK, P. FILLARD, O. CLATZ, S. K. WARFIELD. *Detection of DTI White Matter Abnormalities in Multiple Sclerosis Patients*, in "Proc. Medical Image Computing and Computer Assisted Intervention (MICCAI'08), New York, USA", D. METAXAS, L. AXEL (editors), Lecture Notes in Computer Science, vol. 5241, Springer-Verlag, September 2008, p. 975-982, http://www.inria.fr/sophia/asclepios/Publications/Olivier.Commowick/CommowickMiccai2008.pdf.

[58] H. DELINGETTE. *Biquadratic and Quadratic Springs for Modeling St Venant Kirchhoff Materials*, in "Fourth International Symposium on BioMedical Simulation (ISBMS'08), London, UK", Lecture Notes in Computer Science, vol. 5104, Springer-Verlag, July 2008, p. 40–48.

[59] S. DURRLEMAN, X. PENNEC, A. TROUVÉ, N. AYACHE. *A Forward Model to Build Unbiased Atlases from Curves and Surfaces*, in "Proc. of the International Workshop on the Mathematical Foundations of Computational Anatomy (MFCA-2008)", X. PENNEC, S. JOSHI (editors), September 2008, http://www.inria.fr/sophia/asclepios/Publications/Stanley.Durrleman/Durrleman_MFCA08.pdf.

[60] S. DURRLEMAN, X. PENNEC, A. TROUVÉ, N. AYACHE. *Sparse Approximation of Currents for Statistics on Curves and Surfaces*, in "Proc. Medical Image Computing and Computer Assisted Intervention (MICCAI'08), Part II, New-York, USA", D. METAXAS, L. AXEL, G. SZÉKELY, G. FICHTINGER (editors), LNCS, PMID: 18982629, vol. 5242, Springer, September 2008, p. 390–398, http://www.inria.fr/sophia/asclepios/Publications/Stanley.Durrleman/Durrleman_MICCAI08.pdf.

[61] T. GLATARD, J. MONTAGNAT, X. PENNEC. *A Probabilistic Model to Analyse Workflow Performance on Production Grids*, in "8th IEEE International Symposium on Cluster Computing and the Grid, 2008. CCGRID '08", IEEE, May 2008, p. 510–517, http://rainbow.polytech.unice.fr/publis/glatard-montagnat-etal:2008b.pdf.

[62] M. HERNANDEZ, S. OLMOS, X. PENNEC. *Comparing algorithms for diffeomorphic registration: Stationary LDDMM and Diffeomorphic Demons*, in "Proc. of the International Workshop on the Mathematical Foundations of Computational Anatomy (MFCA-2008)", X. PENNEC, S. JOSHI (editors), September 2008, http://www.inria.fr/sophia/asclepios/events/MFCA08/Proceedings/mfca08_1_3.pdf.

[63] H. HUFNAGEL, X. PENNEC, J. EHRHARDT, N. AYACHE, H. HANDELS. *Comparison of Statistical Shape Models Built on Correspondence Probabilities and One-to-One Correspondences*, in "Proc. SPIE Symposium on Medical Imaging '08, San Diego, USA", SPIE Conference Series, vol. 6914, February 2008, http://www.inria.fr/sophia/asclepios/Publications/Heike.Hufnagel/hufnagel_SPIO08.pdf.

[64] E. KONUKOGLU, W. M. WELLS, S. NOVELLAS, N. AYACHE, R. KIKINIS, P. BLACK, K. POHL. *Monitoring Slowly Evolving Tumors*, in "In Proceedings of the IEEE Internation Symposium on Biomedical Imaging: From Nano to Macro (ISBI'08), Paris, France", May 2008, http://www.inria.fr/sophia/asclepios/Publications/Ender.Konukoglu/isbi08.pdf.

[65] D. LEPILLER, M. SERMESANT, M. POP, H. DELINGETTE, G. A. WRIGHT, N. AYACHE. *Cardiac Electrophysiology Model Adjustment Using the Fusion of MR and Optical Imaging.*, in "MICCAI", D. METAXAS, L. AXEL, G. FICHTINGER, G. SZÉKELY (editors), Lecture Notes in Computer Science, vol. 5241, Springer, 2008, p. 678-685, http://www.inria.fr/sophia/asclepios/Publications/Maxime.Sermesant/LepillerMICCAI2008.pdf.

[66] N. LEPORE, C. BRUN, Y.-Y. CHOU, A. D. LEE, M. BARYSHEVA, X. PENNEC, K. MCMAHON, M. MEREDITH, G. I. DE ZUBICARAY, M. J. WRIGHT, A. W. TOGA, P. M. THOMPSON. *Best individual template selection from deformation tensor minimization*, in "Proc. of the 2008 IEEE Int. Symp. on Biomedical Imaging: From Nano to Macro (ISBI'08), Paris, France, May 14-17", 2008, p. 460-463.

[67] E. PERNOD, J.-C. SOUPLET, J. ROJAS BALDERRAMA, D. LINGRAND, X. PENNEC. *Multiple Sclerosis Brain MRI Segmentation Workflow deployment on the EGEE Grid*, in "MICCAI-Grid Workshop (MICCAI-Grid), New York, NY, USA", September 2008, p. 55-64, http://www.i3s.unice.fr/~johan/MICCAI-Grid/pdf/MICCAIGproceedings2008.pdf.

[68] J.-M. PEYRAT, H. DELINGETTE, M. SERMESANT, X. PENNEC, C. XU, N. AYACHE. *Registration of 4D Time-Series of Cardiac Images with Multichannel Diffeomorphic Demons*, in "Proc. Medical Image Computing and Computer Assisted Intervention (MICCAI'08), New York, USA", D. METAXAS, L. AXEL, G. FICHTINGER, G. SZÉKELY (editors), Lecture Notes in Computer Science, PMID: 18982699, vol. 5242, Springer-Verlag, September 2008, p. 972–979, http://www.inria.fr/sophia/asclepios/Publications/Jean-Marc.Peyrat/Peyrat_2008_MICCAI.pdf.

[69] A. SANDHOLM, J. SCHMID, F. CHUNG, N. MAGNENAT-THALMANN, D. THALMANN, H. DELINGETTE. *Musculoskeletal simulation model generation from MRI datasets and motion capture data*, in "Workshop on 3D Physiological Human, Zermatt, Switzerland, December 1-4", 2008.

[70] J.-C. SOUPLET, C. LEBRUN, N. AYACHE, G. MALANDAIN. *A New Evaluation Of The Brain Parenchymal Fraction: Application In Multiple Sclerosis Longitudinal Studies*, in "Proceedings of the IEEE International Symposium on Biomedical Imaging: From Nano to Macro (ISBI'08), Paris, France", IEEE, May 2008, p. 65-68.

[71] N. TOUSSAINT, T. MANSI, H. DELINGETTE, N. AYACHE, M. SERMESANT. *An Integrated Platform for Dynamic Cardiac Simulation and Image Processing: Application to Personalised Tetralogy of Fallot Simulation*, in "Proc. Eurographics Workshop on Visual Computing for Biomedicine (VCBM), Delft, The Netherlands", 2008, http://www.inria.fr/sophia/asclepios/Publications/Nicolas.Toussaint/Toussaint.VCBM08.pdf.

[72] T. VERCAUTEREN, A. MEINING, F. LACOMBE, A. PERCHANT. *Real Time Autonomous Video Image Registration for Endomicroscopy: Fighting The Compromises*, in "Proc. SPIE BIOS - Three-Dimensional and Multidimensional Microscopy: Image Acquisition and Processing XV, San Jose, CA, USA", J.-A. CONCHELLO, C. J. COGSWELL, T. WILSON (editors), vol. 6861, SPIE, January 2008, 68610C, http://www.inria.fr/sophia/asclepios/Publications/Tom.Vercauteren/RealTimeMosaicing-SPIEBIOS07-Vercauteren.pdf.

[73] T. VERCAUTEREN, X. PENNEC, A. PERCHANT, N. AYACHE. *Symmetric Log-Domain Diffeomorphic Registration: A Demons-based Approach*, in "Proc. Medical Image Computing and Computer Assisted Intervention (MICCAI'08), Part I, New York, USA", D. METAXAS, L. AXEL, G. FICHTINGER, G. SZÉKELY (editors), Lecture Notes in Computer Science, PMID: 18979814, vol. 5241, Springer-Verlag, September 2008, p. 754–761, http://www.inria.fr/sophia/asclepios/Publications/Tom.Vercauteren/SymLogDemons-MICCAI08-Vercauteren.pdf.

[74] B. T. T. YEO, M. SABUNCU, T. VERCAUTEREN, N. AYACHE, B. FISCHL, P. GOLLAND. *Spherical Demons: Fast Surface Registration*, in "Proc. Medical Image Computing and Computer Assisted Intervention (MICCAI'08), New York, USA", D. METAXAS, L. AXEL, G. FICHTINGER, G. SZÉKELY (editors), Lecture Notes in Computer Science, PMID: 18979813. Source code found here, vol. 5241, Springer-Verlag, September 2008, p. 745-753, http://www.inria.fr/sophia/asclepios/Publications/Tom.Vercauteren/SphericalDemons-MICCAI08-Yeo.pdf.

[75] B. T. T. YEO, T. VERCAUTEREN, P. FILLARD, X. PENNEC, P. GOLLAND, N. AYACHE, O. CLATZ. *DTI Registration with Exact Finite-Strain Differential*, in "Proceedings of the IEEE International Symposium on Biomedical Imaging: From Nano to Macro (ISBI'08), Paris, France", IEEE, May 2008, http://www.inria.fr/sophia/asclepios/Publications/Olivier.Clatz/DTIDiffeomorphicDemons-ISBI08-Yeo.pdf.

Workshops without Proceedings

[76] C. BRUN, N. LEPORE, X. PENNEC, Y.-Y. CHOU, A. D. LEE, M. BARYSHEVA, K. MCMAHON, G. I. DE ZUBICARAY, M. J. WRIGHT, A. W. TOGA, P. M. THOMPSON. *Volumetric Differences in Brain Structure in Identical and Fraternal Twins Computed using Riemannian Tensor-Based Morphometry*, in "13th Annual Meeting of the Organization for Human Brain Mapping (OHBM), June 15-19, Melbourne, Australia", 2008.

[77] J. ROJAS BALDERRAMA, D. LINGRAND, E. PERNOD, J.-C. SOUPLET, X. PENNEC, J. MONTAGNAT. *NeuroLOG: neuroscience application workflows execution on the EGEE grid*, in "Enabling Grid for E-sciencE (EGEE) conference, Istanbul, Turkey", EGEE'08 best paper award, , September 2008.

[78] J.-C. SOUPLET, C. LEBRUN, N. AYACHE, G. MALANDAIN. *An Automatic Segmentation of T2-FLAIR Multiple Sclerosis Lesions*, in "MICCAI-Multiple Sclerosis Lesion Segmentation Challenge Workshop, New York, NY, USA", September 2008.

Scientific Books (or Scientific Book chapters)

[79] N. AYACHE, O. CLATZ, H. DELINGETTE, G. MALANDAIN, X. PENNEC, M. SERMESANT. *Asclepios: a Research Project-Team at INRIA for the Analysis and Simulation of Biomedical Images*, in "From semantics to computer science: essays in honor of Gilles Kahn", Cambridge University Press, 2008, http://www.inria.fr/sophia/asclepios/Publications/Nicholas.Ayache/Colloquium-Gilles-Kahn-NA-2007-v5.pdf.

[80] E. KONUKOGLU, X. PENNEC, O. CLATZ, N. AYACHE. *Tumor Growth Modeling in Oncological Image Analysis*, in "Handbook of Medical Image Processing and Analysis - New edition", I. BANKMAN (editor), ISBN-13: 978-0-12-373904-9, chap. 18, Academic Press, December 2008, p. 297–307.

[81] M. G. LINGURARU, T. VERCAUTEREN, M. REYES AGUIRRE, M. Á. GONZÁLEZ BALLESTER, N. AYACHE. *Intensity-free Segmentation of Brain Internal Nuclei from Deformable Atlases*, in "Brain Mapping Research Trends, New York, NY", Invited – To appear, Nova Science Publishers, 2008.

[82] X. PENNEC, N. AYACHE, J.-P. THIRION. *Landmark-based registration using features identified through differential geometry*, in "Handbook of Medical Image Processing and Analysis - New edition", I. BANKMAN (editor), ISBN-13: 978-0-12-373904-9, chap. 34, Academic Press, December 2008, p. 565–578, http://www.inria.fr/sophia/asclepios/Publications/Xavier.Pennec/Pennec.HMIP08.pdf.

[83] T. VERCAUTEREN, N. AYACHE, N. SAVOIRE, G. MALANDAIN, A. PERCHANT. *Processing of In Vivo Fibered Confocal Microscopy Video Sequences*, in "Microscopic Image Analysis for Life Science Applications", J. RITTSCHER, R. MACHIRAJU, S. T. C. WONG (editors), chap. 19, Artech House, 2008, p. 441–463.

Books or Proceedings Editing

[84] X. PENNEC, S. JOSHI (editors). *Proceedings of the Second International Workshop on Mathematical Foundations of Computational Anatomy - Geometrical and Statistical Methods for Modelling Biological Shape Variability*, September 2008, http://www.inria.fr/sophia/asclepios/events/MFCA08/Proceedings/MFCA08_Proceedings.pdf.

Research Reports

[85] S. DURRLEMAN, X. PENNEC, A. TROUVÉ, N. AYACHE. *Sparse Approximation of Currents for Statistics on Curves and Surfaces*, Research Report RR-6571, INRIA, June 2008, http://hal.inria.fr/inria-00286014/fr/.

Other Publications

[86] F. HEBERT. *Segmentation de l'intestin grêle dans le cadre de la maladie de Crohn*, Master's Thesis, Master IGMMV, Université de Nice Sophia-Antipolis, 2008.

[87] T. MANSI, M. SERMESANT, M. HUBER, A. TAYLOR, G. PONGIGLIONE, X. PENNEC, Y. BOUDJEMLINE. *Modélisation électromécanique du cœur et analyse d'images*, Archives de Pédiatrie 15(5):1032 – Special award for best presentation, February 2008, Archives de Pédiatrie - Congrès des Sociétés Françaises Médico-chirurgicales Pédiatriques.

[88] S. NOVELLAS, G. MALANDAIN, J. COSTA, J.-C. SOUPLET, N. AYACHE, P. CHEVALLIER. *Apport d'un algorithme de segmentation semi-automatique pour analyse des adénopathies médiastinales*, October 2008, Journées Françaises de Radiologie.

[89] E. PERNOD. *Interface Development for Medical Imaging Applications in the framework of the Multiple Sclerosis Disease*, Rapport de fin d'études, Institut des Sciences de l'Ingénieur de Toulon et du Var, 2008.

[90] E. PERNOD, J.-C. SOUPLET, M. COHEN, N. TOUSSAINT, C. LEBRUN, G. MALANDAIN. *SepINRIA v1.7.2: Multiple Sclerosis Brain MRI visualisation, comparison and analysis Software*, , September 2008, World Congress for Treatment and Research in Multiple Sclerosis (WCTRIMS).

[91] J.-C. SOUPLET, P. FILLARD, N. TOUSSAINT, C. LEBRUN, G. MALANDAIN. *SepINRIA: A software to analyse Multiple Sclerosis Brain MRI*, April 2008, 60th American Academy of Neurology Annual Meeting.

[92] J.-C. SOUPLET, C. LEBRUN, P. CLAVELOU, W. CAMU, S. CHANALET, N. AYACHE, G. MALANDAIN. *A Comparative Study of Atrophy Measurements in Multiple Sclerosis*, March 2008, 17th Franco-UK scientific meeting of ARSEP (François Lhermitte Conferences).

[93] J.-C. SOUPLET, C. LEBRUN, P. CLAVELOU, W. CAMU, S. CHANALET, N. AYACHE, G. MALANDAIN. *A New Atrophy Measurement Method dedicated to Multiple Sclerosis*, April 2008, 60th American Academy of Neurology Annual Meeting.

[94] J.-C. SOUPLET, C. LEBRUN, G. MALANDAIN. *SepINRIA v1.7.1: A Free Software for Lesion Segmentation and Atrophy Evaluation dedicated to Multiple Sclerosis Brain MRI*, vol. 255, Springer, Nice, France, June 2008, Journal of Neurology - 18th European Neurological Society Meeting.

[95] J.-C. SOUPLET, C. LEBRUN, G. MALANDAIN. *SepINRIA: Un logiciel gratuit dédié à l'analyse d'Images de Résonance Magnétique cérébrales de patients atteints de sclérose en Plaques*, , Nice, France, apr 2008, Journées de Neurologie de Langue Française.

References in notes

[96] N. AYACHE, J. DUNCAN (editors). *Medical Image Analysis*, Elsevier.

[97] IEEE (editor). *International Symposium on Biomedical Imaging: From Nano to Macro*, IEEE, Paris, France, May 2008.

[98] D. METAXAS, L. AXEL, G. FICHTINGER, G. SZÉKELY (editors). *Medical Image Computing and Computer-Assisted Intervention (MICCAI'08), Part I*, Lecture Notes in Computer Science, vol. 5241, Springer, New York, NY, USA, 2008.

[99] D. METAXAS, L. AXEL, G. FICHTINGER, G. SZÉKELY (editors). *Medical Image Computing and Computer-Assisted Intervention (MICCAI'08), Part II*, Lecture Notes in Computer Science, vol. 5242, Springer, New York, NY, USA, 2008.

[100] R. H. TAYLOR, S. LAVALLÉE, G. S. BURDEA, R. MÖSGES (editors). *Computer-Integrated Surgery: Technology and Clinical Applications*, MIT Press, 1995.

[101] W. VANNIER, M. A. VIERGEVER (editors). *Transactions on Medical Imaging*, IEEE.

[102] S. WEBB (editor). *The Physics of Medical Imaging*, Institute of Physics Publishing, 1988.

[103] *The international journal of Medical Robotics + Computer Assisted Surgery*, Wiley.

[104] R. ACHARYA, R. WASSERMAN, J. STEVENS, C. HINOJOSA. *Biomedical Imaging modalities: a tutorial*, in "Computerized Medical Imaging and Graphics", vol. 19, n^{o} 1, 1995, p. 3–25.

[105] P. ALLEN. *Brain Atlas Project*, 2003, http://brain-map.org/welcome.do;jsessionid=1DB51DDFDE6BEC143CE5005682B62003.

[106] L. AXEL, A. MONTILLO, D. KIM. *Tagged magnetic resonance imaging of the heart: a survey*, in "Medical Image Analysis", vol. 9, n^{o} 4, 2005, p. 376–393.

[107] N. AYACHE. *L'analyse automatique des images médicales, état de l'art et perspectives*, in "Annales de l'Institut Pasteur", numéro spécial sur les progrès récents de l'imagerie médicale, vol. 9, n^{o} 1, avril–juin 1998, p. 13–21.

[108] É. BARDINET, D. DORMONT, G. MALANDAIN, M. BHATTACHARJEE, B. PIDOUX, C. SALEH, P. CORNU, N. AYACHE, Y. AGID, J. YELNIK. *Retrospective cross-evaluation of an histological and deformable 3D atlas of the basal ganglia on series of Parkinsonian patients treated by deep brain stimulation (DBS)*, in "Proceedings of MICCAI'05, Palm Springs, California", J. DUNCAN, G. GERIG (editors), LNCS, vol. 3750, Springer Verlag, 2005, p. 385–393, ftp://ftp-sop.inria.fr/epidaure/Publications/Malandain/bardinet-miccai-2005.pdf.

[109] M. BELIK, T. USYK, A. MCCULLOCH. *Computational Methods for Cardiac Electrophysiology*, in "Computational Models for the Human Body", N. AYACHE (editor), Elsevier, 2004, p. 129–187.

[110] J. COHEN. *A coefficient of agreement for nominal scales*, in "Educational and Psychological Measurement", vol. 20, n^{o} 1, 1960, p. 37-46.

[111] I. L. DRYDEN, K. V. MARDIA. *Statistical Shape Analysis*, John Wiley and Sons, 1998.

[112] J. DUNCAN, N. AYACHE. *Medical Image Analysis: Progress over two decades and the challenges ahead*, in "IEEE Transactions on Pattern Analysis and Machine Intelligence", vol. 22, n^{o} 1, 2000, p. 85–106.

[113] N. C. FOX, J. M. SCHOTT. *Imaging cerebral atrophy: normal ageing to Alzheimer's disease*, in "Lancet", vol. 363, n^{o} 9406, 2004.

[114] A. F. FRANGI, W. J. NIESSEN, M. A. VIERGEVER. *Three-dimensional modeling for functional analysis of cardiac images: a review*, in "IEEE Trans Med Imaging", vol. 20, n^{o} 1, January 2001, p. 2-25.

[115] P. C. FRANZONE, L. GUERRI, M. PENNACHIO, B. TACCARDI. *Spread of excitation in 3-D models of the anisotropic cardiac tissue*, in "Mathematical Biosciences", vol. 151, 1988, p. 51–98.

[116] P. HUNTER, T. BORG. *Integration from proteins to organs: the Physiome project*, in "Nature Reviews - Molecular Cell Biology", vol. 4, 2003, p. 237–243.

[117] P. HUNTER. *Computational Physiology and the Physiome Project*, 2004.

[118] M. G. LINGURARU, T. VERCAUTEREN, M. REYES AGUIRRE, M. Á. GONZÁLEZ BALLESTER, N. AYACHE. *Segmentation Propagation from Deformable Atlases for Brain Mapping and Analysis*, in "Brain Research Journal", vol. 1, n^{o} 4, 2007, p. 269–287, https://www.novapublishers.com/catalog/product_info.php?products_id=7148.

[119] C. MACAULAY, P. LANE, R. RICHARDS-KORTUM. *In vivo pathology: microendoscopy as a new endoscopic imaging modality*, in "Gastrointestinal Endoscopy Clinics of North America", vol. 14, 2004, p. 595–620.

[120] D. METAXAS, J. KAYES, F. PRIMANIO. *A 3-D virtual environment for modeling mechanical cardiopulmonary interactions*, in "Medical Image Analysis", vol. 3, n^{o} 1, 1997, p. 1–26.

[121] M. I. MILLER. *Computational anatomy: shape, growth, and atrophy comparison via diffeomorphisms*, in "NeuroImage", Special Issue : Mathematics in Brain Imaging, vol. 23, n^{o} Supplement 1, 2004, p. S19–S33.

[122] P. MOIREAU, D. CHAPELLE, P. LE TALLEC. *Joint state and parameter estimation for distributed mechanical systems*, in "Computer Methods in Applied Mechanics and Engineering", vol. 197, 2008, p. 659–677.

[123] V. MOREAU-VILLÉGER, H. DELINGETTE, M. SERMESANT, O. FARIS, E. MCVEIGH, N. AYACHE. *Global and Local Parameter Estimation of a Model of the Electrical Activity of the Heart*, Research Report, n^{o} 5269, INRIA, July 2004, http://hal.inria.fr/inria-00070729.

[124] NIH. *Alzheimer's Disease Neuroimaging Initiative*, 2004.

[125] S. NICOLAU, A. GARCIA, X. PENNEC, L. SOLER, N. AYACHE. *An augmented reality system to guide radio-frequency tumour ablation*, in "Computer Animation and Virtual World (previously the Journal of Visualization & Computer Animation)", vol. 16, n^{o} 1, 2005, p. 1–10, ftp://ftp-sop.inria.fr/epidaure/Publications/Pennec/Nicolau.CAVW.pdf.

[126] S. NICOLAU, X. PENNEC, L. SOLER, N. AYACHE. *A complete Augmented Reality Guidance System for Liver Punctures: First Clinical Evaluation*, in "Proceedings of the 8th Int. Conf. on Medical Image Computing and Computer-Assisted Intervention - MICCAI 2005, Part I, Palm Springs, CA, USA, October 26-29", J. DUNCAN, G. GERIG (editors), LNCS, vol. 3749, Springer Verlag, 2005, p. 539–547, http://springerlink.metapress.com/openurl.asp?genre=article&issn=0302-9743&volume=3749&spage=539.

[127] D. NOBLE. *Modeling the Heart, from genes to cells to the whole organ*, in "Science", vol. 295, 2002, p. 1678–1682.

[128] J. OLIVO-MARIN. *Image Formation and Analysis in Microscopy*, june 2004, Invited Session at Int. Symp. on Biomedical Imaging (ISBI).

[129] S. OURSELIN, A. ROCHE, S. PRIMA, N. AYACHE. *Block Matching: A General Framework to Improve Robustness of Rigid Registration of Medical Images*, in "Third International Conference on Medical Robotics, Imaging And Computer Assisted Surgery (MICCAI 2000), Pittsburgh, Pennsylvanie USA", A. DIGIOIA, S. DELP (editors), Lectures Notes in Computer Science, vol. 1935, Springer, octobre 11-14 2000, p. 557–566, ftp://ftp-sop.inria.fr/epidaure/Publications/Malandain/ourselin-miccai-2000.pdf.

[130] A. QUARTERONI, L. FORMAGGIA. *Mathematical Modeling and Numerical Simulation of the Cardiovascular System*, in "Computational Models for the Human Body", N. AYACHE (editor), Elsevier, 2004, p. 3–128.

[131] M. SERMESANT, H. DELINGETTE, N. AYACHE. *An Electromechanical Model of the Heart for Image Analysis and Simulation*, in "IEEE Transactions in Medical Imaging", vol. 25, n° 5, 2006, p. 612–625, http://www.inria.fr/sophia/asclepios/Publications/Maxime.Sermesant/TMI2006Sermesant.pdf.

[132] M. SERMESANT, O. FARIS, F. EVANS, E. MCVEIGH, Y. COUDIÈRE, H. DELINGETTE, N. AYACHE. *Preliminary validation using in vivo measures of a macroscopic electrical model of the heart*, in "International Symposium on Surgery Simulation and Soft Tissue Modeling (IS4TM'03), Juan-les-Pins, France", N. AYACHE, H. DELINGETTE (editors), Lecture Notes in Computer Science, vol. 2673, Springer-Verlag, INRIA Sophia Antipolis, 2003, p. 230–243, ftp://ftp-sop.inria.fr/epidaure/Publications/Sermesant/IS4TM2003Sermesant.pdf.

[133] P. M. THOMPSON, K. HAYASHI, E. SOWELL, N. GOGTAY, J. GIEDD, J. RAPOPORT, G. I. DE ZUBICARAY, A. JANKE, S. ROSE, J. SEMPLE, D. DODDRELL, Y. WANG, T. VAN ERP, T. CANNON, A. W. TOGA. *Mapping Cortical Change in Alzheimer's Disease, Brain Development, and Schizophrenia*, in "NeuroImage", Special Issue : Mathematics in Brain Imaging, vol. 23, n° supplement 1, 2004, p. S2–S18.

[134] P. M. THOMPSON, M. I. MILLER, J. T. RATNANATHER, R. A. POLDRACK, T. E. NICHOLS. *Guest Editorial*, in "NeuroImage", Special Issue : Mathematics in Brain Imaging, vol. 23, n° Supplement 1, 2004, p. S1–S1.

[135] D. W. THOMPSON. *On Growth and Form*, Cambridge Univ. Pr., 1917.

[136] N. TOUSSAINT, M. SERMESANT, P. FILLARD. *vtkINRIA3D: A VTK Extension for Spatiotemporal Data Synchronization, Visualization and Management*, in "Proc. of Workshop on Open Source and Open Data for MICCAI, Brisbane, Australia", October 2007, http://www.inria.fr/sophia/asclepios/Publications/Pierre.Fillard/Fillard.MICCAI07.OpenWorkshop.pdf.

[137] N. TOUSSAINT, J.-C. SOUPLET, P. FILLARD. *MedINRIA: Medical Image Navigation and Research Tool by INRIA*, in "Proc. of MICCAI'07 Workshop on Interaction in medical image analysis and visualization, Brisbane, Australia", 2007, http://www.inria.fr/sophia/asclepios/Publications/Pierre.Fillard/Fillard.MICCAI07.InteractionWorkshop.pdf.

[138] K. VAN LEEMPUT, F. MAES, D. VANDERMEULEN, P. SUETENS. *A unifying framework for partial volume segmentation of brain MR images*, in "IEEE Trans Med Imaging", vol. 22, n° 1, January 2003, p. 105-19.

[139] S. K. WARFIELD, K. H. ZOU, W. M. WELLS. *Simultaneous truth and performance level estimation (STAPLE): an algorithm for the validation of image segmentation*, in "IEEE Transactions on Medical Imaging", vol. 23, n° 7, July 2004, p. 903-921.

[140] R. WEISSLEDER, U. MAHMOOD. *Molecular Imaging*, in "Radiology", Special Review, vol. 219, 2001, p. 316–333.