Activity Report 2017

Project-Team ATHENA

Computational Imaging of the Central Nervous System

RESEARCH CENTER
Sophia Antipolis - Méditerranée

THEME
Computational Neuroscience and Medicine

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Project-Team ATHENA

Creation of the Team: 2010 January 01, updated into Project-Team: 2010 July 01

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1. Personnel

Research Scientists

Rachid Deriche [Team leader, Inria, Senior Researcher, HDR]
Maureen Clerc Gallagher [Inria, Senior Researcher, HDR]
Samuel Deslauriers-Gauthier [Inria, Starting Research Position, from Feb 2017]
Théodore Papadopoulo [Inria, Senior Researcher, HDR]
Demian Wassermann [Inria, Researcher, until Sep 2017]

Post-Doctoral Fellows

Patryk Filipiak [Inria]
Lavinia Slabu [Université Côte d'Azur, from May 2017]

PhD Students

Abib Olushola Yessouffou Alimi [Inria]
Brahim Belaoucha [Université Côte d'Azur, until Aug 2017]
Isa Costantini [Université Côte d'Azur]
Kai Dang [Inria, until Mar 2017]
Rutger Fick [Inria, until Mar 2017]
Matteo Frigo [Inria, from Nov 2017]
Guillermo Gallardo Diez [Université Côte d'Azur]
Nathalie Gayraud [Inria]
Antonia Machlouzarides Shalit [Inria, from Jun 2017]
Kostiantyn Maksymenko [Inria]
Marco Pizzolato [Inria, until Mar 2017]
Federica Turi [Université Côte d'Azur]

Technical staff

Amandine Audino [Inria, until Sep 2017]
Romain Lacroix [Inria, from Nov 2017]
Emmanuel Olivi [Inria, from Feb 2017 until Jul 2017, granted by FP7 COBCOM project]

Intern

Gaston Zanitti [Inria, from Feb 2017 until Apr 2017]

Administrative Assistant

Claire Senica [Inria]

Visiting Scientists

Inaki Rabanillo Viloria [University of Valladolid, from Jun 2017 until Sep 2017]
Maxime Descoteaux [Sherbrooke University, from Feb 2017 until Mar 2017]

2. Overall Objectives

2.1. Presentation

The main objective of ATHENA is to develop rigorous mathematical models and computational tools for analyzing and modeling the complex Central Nervous System (brain and spinal cord) anatomy and function. These models and tools will help to better understand the architecture and the functioning of human Central Nervous System (CNS) and address pressing and challenging clinical and neuroscience questions. Exploring new directions to solve these challenging problems will push forward the state-of-the-art in Structural and Functional Computational Imaging of the CNS.

The relationship between CNS structure and function is fundamental in neuroscience. Developing computational models and techniques that recover the structural connectivity and the function of the CNS in vivo is thus of utmost importance: it will definitely improve the understanding of the CNS and its mechanisms. On the basis of our expertise and contributions to the field of Computational Imaging of the CNS and in order to have an impact on this field, our research focusses mainly on the Structural and Functional Imaging of the CNS with a particular emphasis on signal and image recording from Diffusion Magnetic Resonance Imaging (dMRI), Magneto-Encephalography (MEG) and Electro-Encephalography (EEG).

In order to further increase the impact of our research, we also aim to push our contributions towards some applications related to CNS diseases with characteristic abnormalities in the micro-structure of brain tissues that are not apparent and cannot be revealed reliably by standard imaging techniques. Diffusion MRI, a recent imaging modality based on the measurement of the random thermal movement (diffusion) of water molecules within samples can make visible these co-lateral damages to the fibers of the CNS white matter that connect different brain regions. This is why in our research, Diffusion MRI is the structural imaging modality that will be considered to recover the CNS connectivity.

Connectivity represents the network infrastructure of the CNS. Electric activity corresponds to communications over this network. MEG and EEG (jointly as M/EEG) reveal part of the cortical electric activity. M/EEG are also instrumental in diagnosing diseases linked to anomalous brain function - that in some cases structural or functional MR images do not reveal. In some CNS injuries (medullar injuries, strokes, AMS), the peripheral nervous system may not be able to execute commands that are issued by the brain.

Brain Computer Interfaces (BCI) use EEG, and translate in real-time the electrical activity of the brain in commands to control devices. While BCI is advocated as a means to communicate and help restore mobility or autonomy for very severe cases of disabled patients, it is also a new tool for interactively probing and training the human brain.

These considerations support the need to do research on new models and computational tools to analyse CNS signals and imaging data. Our main objective is to push forward the state-of-the-art in our research domain to better understand the architecture and function of the CNS and help address pressing and challenging clinical and neuroscience questions. This better understanding of the CNS will help the development of new biomarkers related to the progression of certain types of neurodegenerative diseases and will also help improving BCI systems with the goal of better interactive probing and training of the human brain. These long term and ambitious applications, if successful, will help us make true our dream to effectively contribute reducing the number of people suffering from CNS diseases.

In order to tackle these challenging objectives, our strategy is based on the following road map:

- Develop rigorous mathematical and computational tools for the analysis and interpretation of Diffusion MRI and M/EEG data.
- Improve acquisition and processing techniques and push forward the state-of-the-art in Computational CNS imaging.
- Use our expertise to address with collaborators clinical and neuroscience questions.

This is implemented through:

- Publications in international conferences and journals dedicated to promoting advances in computational methods for Diffusion MRI and M/EEG analysis and/or use of Diffusion MRI and M/EEG in clinical and neuroscience applications.
- A dense network of collaborations with national as well as international neuroimaging laboratories through which we have access equipment and data and with whom we will jointly contribute to solve common crucial problems of interest.
- Software packages developed to be used in a first stage by our national and international collaborators and then made available to other partners.

3. Research Program

3.1. Computational diffusion MRI

Diffusion MRI (dMRI) provides a non-invasive way of estimating in-vivo CNS fiber structures using the average random thermal movement (diffusion) of water molecules as a probe. It's a recent field of research with a history of roughly three decades. It was introduced in the mid 80's by Le Bihan et al [88], Merboldt et al [92] and Taylor et al [102]. As of today, it is the unique non-invasive technique capable of describing the neural connectivity in vivo by quantifying the anisotropic diffusion of water molecules in biological tissues.

3.1.1. Diffusion Tensor Imaging & High Angular Resolution Diffusion Imaging

In dMRI, the acquisition and reconstruction of the diffusion signal allows for the reconstruction of the water molecules displacement probability, known as the Ensemble Average Propagator (EAP) [101], [59]. Historically, the first model in dMRI is the 2nd order diffusion tensor (DTI) [54], [53] which assumes the EAP to be Gaussian centered at the origin. DTI has now proved to be extremely useful to study the normal and pathological human brain [89], [73]. It has led to many applications in clinical diagnosis of neurological diseases and disorder, neurosciences applications in assessing connectivity of different brain regions, and more recently, therapeutic applications, primarily in neurosurgical planning. An important and very successful application of diffusion MRI has been brain ischemia, following the discovery that water diffusion drops immediately after the onset of an ischemic event, when brain cells undergo swelling through cytotoxic edema.

The increasing clinical importance of diffusion imaging has drived our interest to develop new processing tools for Diffusion Tensor MRI. Because of the complexity of the data, this imaging modality raises a large amount of mathematical and computational challenges. We have therefore developed original and efficient algorithms relying on Riemannian geometry, differential geometry, partial differential equations and front propagation techniques to correctly and efficiently estimate, regularize, segment and process Diffusion Tensor MRI (DT-MRI) (see [91] and [90]).

In DTI, the Gaussian assumption over-simplifies the diffusion of water molecules. While it is adequate for voxels in which there is only a single fiber orientation (or none), it breaks for voxels in which there are more complex internal structures and limitates the ability of the DTI to describe complex, singular and intricate fiber configurations (U-shape, kissing or crossing fibers). To overcome this limitation, so-called Diffusion Spectrum Imaging (DSI) [107] and High Angular Resolution Diffusion Imaging (HARDI) methods such as Q-ball imaging [105] and other multi-tensors and compartment models [98], [100], [47], [46], [94] were developed to resolve the orientationnality of more complicated fiber bundle configurations.

Q-Ball imaging (QBI) has been proven very successful in resolving multiple intravoxel fiber orientations in MR images, thanks tO its ability to reconstruct the Orientation Distribution Function (ODF, the probability of diffusion in a given direction). These tools play a central role in our work related to the development of a robust and linear spherical harmonic estimation of the HARDI signal and to our development of a regularized, fast and robust analytical QBI solution that outperforms the state-of-the-art ODF numerical technique developed by Tuch. Those contributions are fundamental and have already started to impact on the Diffusion MRI, HARDI and Q-Ball Imaging community [72]. They are at the core of our probabilistic and deterministic tractography algorithms devised to best exploit the full distribution of the fiber ODF (see [69], [3] and [70], [4]).

3.1.2. Beyond DTI with high order tensors

High Order Tensors (HOT) models to estimate the diffusion function while overcoming the shortcomings of the 2nd order tensor model have also been recently proposed such as the Generalized Diffusion Tensor Imaging (G-DTI) model developed by Ozarslan et al [111], [112] or 4th order Tensor Model [52]. For more details, we refer the reader to our articles in [75], [98] where we review HOT models and to our articles in [90], co-authored with some of our close collaborators, where we review recent mathematical models and computational methods for the processing of Diffusion Magnetic Resonance Images, including state-of-the-art reconstruction of diffusion models, cerebral white matter connectivity analysis, and segmentation techniques. Recently, we started to work on Diffusion Kurtosis Imaging (DKI), of great interest for the company OLEA MEDICAL. Indeed, DKI is fast gaining popularity in the domain for characterizing the diffusion propagator or EAP by its deviation from Gaussianity. Hence it is an important tool in the clinic for characterizing the white-matter's integrity with biomarkers derived from the 3D 4th order kurtosis tensor (KT) [78].

All these powerful techniques are of utmost importance to acquire a better understanding of the CNS mechanisms and have helped to efficiently tackle and solve a number of important and challenging problems [46], [47]. They have also opened up a landscape of extremely exciting research fields for medicine and neuroscience. Hence, due to the complexity of the CNS data and as the magnetic field strength of scanners increase, as the strength and speed of gradients increase and as new acquisition techniques appear [2], these

imaging modalities raise a large amount of mathematical and computational challenges at the core of the research we develop at ATHENA [77], [98].

3.1.3. Improving dMRI acquisitions

One of the most important challenges in diffusion imaging is to improve acquisition schemes and analyse approaches to optimally acquire and accurately represent diffusion profiles in a clinically feasible scanning time. Indeed, a very important and open problem in Diffusion MRI is related to the fact that HARDI scans generally require many times more diffusion gradient than traditional diffusion MRI scan times. This comes at the price of longer scans, which can be problematic for children and people with certain diseases. Patients are usually unable to tolerate long scans and excessive motion of the patient during the acquisition process can force a scan to be aborted or produce useless diffusion MRI images. Recently, we have developed novel methods for the acquisition and the processing of diffusion magnetic resonance images, to efficiently provide, with just few measurements, new insights into the structure and anatomy of the brain white matter in vivo.

First, we contributed developing real-time reconstruction algorithm based on the Kalman filter [68]. Then, and more recently, we started to explore the utility of Compressive Sensing methods to enable faster acquisition of dMRI data by reducing the number of measurements, while maintaining a high quality for the results. Compressed Sensing (CS) is a recent technique which has been proved to accurately reconstruct sparse signals from undersampled measurements acquired below the Shannon-Nyquist rate [93].

We have contributed to the reconstruction of the diffusion signal and its important features as the orientation distribution function and the ensemble average propagator, with a special focus on clinical setting in particular for single and multiple Q-shell experiments [93], [60], [62]. Compressive sensing as well as the parametric reconstruction of the diffusion signal in a continuous basis of functions such as the Spherical Polar Fourier basis, have been proved through our recent contributions to be very useful for deriving simple and analytical closed formulae for many important dMRI features, which can be estimated via a reduced number of measurements [93], [60], [62].

We have also contributed to design optimal acquisition schemes for single and multiple q-shell experiments. In particular, the method proposed in [2] helps generate sampling schemes with optimal angular coverage for multi-shell acquisitions. The cost function we proposed is an extension of the electrostatic repulsion to multi-shell and can be used to create acquisition schemes with incremental angular distribution, compatible with prematurely stopped scans. Compared to more commonly used radial sampling, our method improves the angular resolution, as well as fiber crossing discrimination. The optimal sampling schemes, freely available for download [1], have been selected for use in the HCP (Human Connectome Project) [2].

We think that such kind of contributions open new perspectives for dMRI applications including, for example, tractography where the improved characterization of the fiber orientations is likely to greatly and quickly help tracking through regions with and/or without crossing fibers [76]

3.1.4. dMRI modelling, tissue microstructures features recovery & applications

The dMRI signal is highly complex, hence, the mathematical tools required for processing it have to be commensurate in their complexity. Overall, these last twenty years have seen an explosion of intensive scientific research which has vastly improved and literally changed the face of dMRI. In terms of dMRI models, two trends are clearly visible today: the parametric approaches which attempt to build models of the tissue to explain the signal based on model-parameters such as CHARMED [48], AxCaliber [49] and NODDI [108] to cite but a few, and the non-parametric approaches, which attempt to describe the signal in useful but generic functional bases such as the Spherical Polar Fourier (SPF) basis [51], [50], the Solid Harmonic (SoH) basis [71], the Simple Harmonic Oscillator based Reconstruction and Estimation (SHORE) basis [109] and more recent Mean Apparent Propagator or MAP-MRI basis [110].

[1] http://www.emmanuelcaruyer.com/
[2] http://humanconnectome.org/documentation/Q1/imaging-protocols.html

However, although great improvements have been made in the last twenty years, major improvements are still required primarily to optimally acquire dMRI data, better understand the biophysics of the signal formation, recover invariant and intrinsic microstructure features, identify bio-physically important bio-markers and improve tractography. For short, there is still considerable room for improvement to take dMRI from the benchside to the bedside.

Therefore, there is still considerable room for improvement when it comes to the concepts and tools able to efficiently acquire, process and analyze the complex structure of dMRI data. Develop ground-breaking tools and models for dMRI is one of the major objectives we would like to achieve in order to lead to a decisive advance and breakthrough in this field.

Then, we propose to investigate the feasibility of using our new models and methods to measure extremely important biological tissue microstructure quantities such as axonal radius and density in white matter. These parameters could indeed provide new insight to better understand the brain's architecture and more importantly could also provide new imaging bio-markers to characterize certain neurodegenerative diseases. This challenging scientific problem, when solved, will lead to direct measurements of important microstructural features that will be integrated in our analysis to provide much greater insight into disease mechanisms, recovery and development. These new microstructural parameters will open the road to go far beyond the limitations of the more simple bio-markers derived from DTI that are clinically used to this date – such as MD and FA which are known to be extremely sensitive to confounding factors such as partial volume and axonal dispersion, non-specific and not able to capture any subtle effects that might be early indicators of diseases [5].

3.1.5. Towards microstructural based tractography

In order to go far beyond traditional fiber-tracking techniques, we believe that first order information, i.e. fiber orientations, has to be superseeded by second and third order information, such as microstructure details, to improve tractography. However, many of these higher order information methods are relatively new or unexplored and tractography algorithms based on these high order based methods have to be conceived and designed. In this aim, we propose to work with multiple-shells to reconstruct the Ensemble Average Propagator (EAP), which represents the whole 3D diffusion process and use the possibility it offers to deduce valuable insights on the microstructural properties of the white matter. Indeed, from a reconstructed EAP one can compute the angular features of the diffusion in an diffusion Orientation Distribution Function (ODF), providing insight in axon orientation, calculate properties of the entire diffusion in a voxel such as the Mean Squared Diffusivity (MSD) and Return-To-Origin Probability (RTOP), or come forth with bio-markers detailing diffusion along a particular white matter bundle direction such as the Return-to-Axis or Return-to-Plane Probability (RTAP or RTPP). This opens the way to a ground-breaking computational and unified framework for tractography based on EAP and microstructure features [7]. Using additional a priori anatomical [10] and/or functional information, we could also constrain the tractography algorithm to start and terminate the streamlines only at valid processing areas of the brain.

This development of a computational and unified framework for tractography, based on EAP, microstructure and a priori anatomical and/or functional features, will open new perspectives in tractography, paving the way to a new generation of realistic and biologically plausible algorithms able to deal with intricate configurations of white matter fibers and to provide an exquisite and intrinsic brain connectivity quantification.

3.2. MEG and EEG

Electroencephalography (EEG) and Magnetoencephalography (MEG) are two non-invasive techniques for measuring (part of) the electrical activity of the brain. While EEG is an old technique (Hans Berger, a German neuropsychiatrist, measured the first human EEG in 1929), MEG is a rather new one: the first measurements of the magnetic field generated by the electrophysiological activity of the brain were made in 1968 at MIT by D. Cohen. Nowadays, EEG is relatively inexpensive and is routinely used to detect and qualify neural activities (epilepsy detection and characterisation, neural disorder qualification, BCI, ...). MEG is, comparatively, much more expensive as SQUIDS only operate under very challenging conditions (at liquid helium temperature) and as a specially shielded room must be used to separate the signal of interest from the ambient noise. However,

as it reveals a complementary vision to that of EEG and as it is less sensitive to the head structure, it also bears great hopes and an increasing number of MEG machines are being installed throughout the world. Inria and ODYSSÉE/ATHENA have participated in the acquisition of one such machine installed in the hospital "La Timone" in Marseille.

MEG and EEG can be measured simultaneously (M/EEG) and reveal complementary properties of the electrical fields. The two techniques have temporal resolutions of about the millisecond, which is the typical granularity of the measurable electrical phenomena that arise within the brain. This high temporal resolution makes MEG and EEG attractive for the functional study of the brain. The spatial resolution, on the contrary, is somewhat poor as only a few hundred data points can be acquired simultaneously (about 300-400 for MEG and up to 256 for EEG). MEG and EEG are somewhat complementary with fMRI and SPECT in that those provide a very good spatial resolution but a rather poor temporal resolution (of the order of a second for fMRI and a minute for SPECT). Also, contrarily to fMRI, which "only" measures an haemodynamic response linked to the metabolic demand, MEG and EEG measure a direct consequence of the electrical activity of the brain: it is acknowledged that the signals measured by MEG and EEG correspond to the variations of the post-synaptic potentials of the pyramidal cells in the cortex. Pyramidal neurons compose approximately 80% of the neurons of the cortex, and it requires at least about 50,000 active such neurons to generate some measurable signal.

While the few hundred temporal curves obtained using M/EEG have a clear clinical interest, they only provide partial information on the localisation of the sources of the activity (as the measurements are made on or outside of the head). Thus the practical use of M/EEG data raises various problems that are at the core of the ATHENA research in this topic:

- First, as acquisition is continuous and is run at a rate up to 1kHz, the amount of data generated by each experiment is huge. Data selection and reduction (finding relevant time blocks or frequency bands) and pre-processing (removing artifacts, enhancing the signal to noise ratio, ...) are largely done manually at present. Making a better and more systematic use of the measurements is an important step to optimally exploit the M/EEG data [1].
- With a proper model of the head and of the sources of brain electromagnetic activity, it is possible to simulate the electrical propagation and reconstruct sources that can explain the measured signal. Proposing better models [87], [9] and means to calibrate them [106] so as to have better reconstructions are other important aims of our work.
- Finally, we wish to exploit the temporal resolution of M/EEG and to apply the various methods we have developed to better understand some aspects of the brain functioning, and/or to extract more subtle information out of the measurements. This is of interest not only as a cognitive goal, but it also serves the purpose of validating our algorithms and can lead to the use of such methods in the field of Brain Computer Interfaces. To be able to conduct such kind of experiments, an EEG lab has been set up at ATHENA.

4. Application Domains

4.1. Applications of diffusion MRI

Clinical domain: Diagnosis of neurological disorder
Various examples of CNS diseases as Alzheimer's and Parkinson's diseases and others like multiple sclerosis, traumatic brain injury and schizophrenia have characteristic abnormalities in the micro-structure of brain tissues that are not apparent and cannot be revealed reliably by standard imaging techniques. Diffusion MRI can make visible these co-lateral damages to the fibers of the CNS white matter that connect different brain regions. This is why in our research, Diffusion MRI is the structural imaging modality that will be considered to recover the CNS connectivity.

4.2. Applications of M/EEG

Clinical domain: Diagnosis of neurological disorders

The dream of all M/EEG researchers is to alleviate the need for invasive recordings (electrocorticograms or intracerebral electrodes), which are often necessary prior to brain surgery, in order to precisely locate both pathological and vital functional areas. We are involved in this quest, particularly through our collaborations with the La Timone hospital in Marseille.
Subtopics include:

- Diagnosis of neurological disorders such as epilepsy, schizophrenia, tinnitus, ...
- Presurgical planning of brain surgery.

Cognitive research

- Aims at better understanding the brain spatio-temporal organisation.
- Collaboration with the *Laboratory for Neurobiology of Cognition* in order to develop methods that suit their needs for sophisticated data analysis.

Brain Computer Interfaces (BCI) aim to allow direct control of external devices using brain signals such as measured through EEG. In our project, BCI can be seen as an application of EEG processing techniques, but also as an object of fundamental and applied research as they open the way for more dynamical and active brain cognitive protocols.

We are developing research collaborations with the Neurelec company in Sophia Antipolis (subsidiary of Oticon Medical) and with the leading EEG software company BESA based in Munich. We collaborate with Nice University Hospital on the usage of BCI-based communication for ALS [3] patients.

5. Highlights of the Year

5.1. Highlights of the Year

5.1.1. Awards

- D. Wassermann has been awarded an ERC Starting Grant from the European Research Council. NEUROLANG is a 5-years project about *Accelerating Neuroscience Research by Unifying Knowledge Representation and Analysis Through a Domain Specific Language.*. Since October, Demian Wassermann moved to Inria Saclay where he joined the PARIETAL project-team.
- B. Belaoucha has received the Best Student Paper Award at PRNI'17 and Medal of excellence from UCA for the paper [28].

BEST PAPER AWARD:

[28]
B. BELAOUCHA, T. PAPADOPOULO. *Large brain effective network from EEG/MEG data and dMR information*, in "PRNI 2017 - 7th International Workshop on Pattern Recognition in NeuroImaging", Toronto, Canada, June 2017, https://hal.inria.fr/hal-01533445

6. New Software and Platforms

6.1. BCI-VIZAPP

BCI visual applications
KEYWORDS: Health - Brain-Computer Interface - GUI (Graphical User Interface)

[3] Nice University Hospital hosts a regional reference center for patients suffering from Amyotrophic Lateral Sclerosis

SCIENTIFIC DESCRIPTION: Bci-Vizapp is a library that allows (in interaction with OpenViBE) to build BCI (Brain Computer Interfaces) applications based on the P300 speller principle. Bci-Vizapp provides a library that allows you to create the BCI's stimulation part as part of the Qt toolkit. Being able to use a standard toolkit to make BCI applications is a strong Bci-Vizapp originality. Indeed, in general the use of such toolkits is prohibited by the need for a very precise control of the display timings, which generally eliminates high-level graphic toolkits such as Qt.
FUNCTIONAL DESCRIPTION: BCI-VIZAPP includes a virtual keyboard for typing text, a photodiode monitoring application for checking timing issues. It communicates with the OpenViBE acquisition server for signal acquisition and with the OpenViBE designer for signal processing. The configuration is performed through a wizard.

This software is a new version following the CoAdapt P300 stimulator software.
NEWS OF THE YEAR: Bci-Vizapp is undergoing a profound transmutation with the help of CRISAM's SED in ADT BciBrowser (part of the AMDT). This change aims at integrating the functionality of Bci-Vizapp in third-party applications such as a web browsers.

- Participants: Nathanaël Foy, Romain Lacroix, Maureen Clerc Gallagher and Théodore Papadopoulo
- Contact: Maureen Clerc Gallagher

6.2. DIPY

Diffusion Imaging in Python
KEYWORDS: MRI - Medical imaging
FUNCTIONAL DESCRIPTION: Diffusion Imaging in Python (Dipy) is a free and open source software project for computational neuroanatomy, focusing mainly on diffusion magnetic resonance imaging (dMRI) analysis. E. Garyfallidis (now Indiana University) is the founder and lead engineer of this open source project in the development of diffusion MRI methods. We continuously collaborate with this global effort and our effort is combined with Université de Sherbrooke, in Canada and Stanford University among others. See for example our registration, denoising, tractography and microstructures tutorials.

- Participants: Demian Wassermann and Rutger Fick
- Partner: Sherbrooke University
- Contact: Demian Wassermann
- URL: http://nipy.org/dipy/

6.3. High Performance Diffusion MRI

KEYWORDS: Health - Neuroimaging - Medical imaging
FUNCTIONAL DESCRIPTION: This library has been developed and transferred to the Cie Olea Medical currently in charge of its validation and inclusion in its Olea Sphere platform. We have been closely involved in pushing the frontiers of the diffusion MRI (dMRI) in the recent years, especially in the mathematical modelling and processing of the dMRI signal and have developed state-of-the-art software implementations in the form of a C++ library that can be effectively used to infer the complex microstructure of the cerebral white matter. The algorithms and software transfered to Olea Medical fall into four categories : (i) local tissue modelling, which includes both popular 2nd order models and advanced higher than 2nd order models such as DTI, higher order Cartesian tensors (HOTs), ODF, FOD, EAP, maxima extraction, regularization and segmentation, (ii) generation of scalar indices (or biomarkers), which include DTI biomarkers, Diffusion Kurtosis Imaging (DKI) and invariants of 4th order tensors, (iii) global structure estimation, which includes deterministic and probabilistic tractography, and (iv) data visualisation for scalar indices, local models and global structures.

- Participants: Aurobrata Ghosh, Rachid Deriche and Théodore Papadopoulo
- Partner: Olea Medical
- Contact: Rachid Deriche

6.4. OpenMEEG

KEYWORDS: Health - Neuroimaging - Medical imaging
SCIENTIFIC DESCRIPTION: OpenMEEG provides a symmetric boundary element method (BEM) implementation for solving the forward problem of electromagnetic propagation over heterogeneous media made of several domains of homogeneous and isotropic conductivities. OpenMEEG works for the quasistatic regime (frequencies < 100Hz and medium diameter < 1m).
FUNCTIONAL DESCRIPTION: OpenMEEG provides state-of-the art tools for modelling bio-electromagnetic propagation in the quasi-static regime. It is based on the symmetric BEM for the EEG/MEG forward problem, with a distributed source model. OpenMEEG has also been used to model the forward problem of ECoG, for modelling nerves or the cochlea. OpenMEEG is a free, open software written in C++ with python bindings. OpenMEEG is used through a command line interface, but is also interfaced in graphical interfaces such as BrainStorm, FieldTrip or SPM.
NEWS OF THE YEAR: OpenMEEG has had a large update including notably the parallelisation of some operators and bug corrections. The new version allows in addition the use of non-nested domains.

- Participants: Alexandre Gramfort, Emmanuel Olivi, Geoffray Adde, Jan Kybic, Kai Dang, Maureen Clerc Gallagher, Perrine Landreau, Renaud Keriven and Théodore Papadopoulo
- Contact: Théodore Papadopoulo
- Publications: OpenMEEG: opensource software for quasistatic bioelectromagnetics - Forward Field Computation with OpenMEEG. - Source modeling of ElectroCorticoGraphy (ECoG) data: Stability analysis and spatial filtering
- URL: http://openmeeg.github.io/

7. New Results

7.1. Computational Diffusion MRI

7.1.1. Spatio-Temporal dMRI Acquisition Design: Reducing the Number of qt Samples Through a Relaxed Probabilistic Model

Participants: Patryk Filipiak, Rutger Fick, Alexandra Petiet [ICM, CENIR, Paris], Mathieu Santin [ICM, CENIR, Paris], Anne-Charlotte Philippe [ICM, CENIR, Paris], Stephane Lehericy [ICM, CENIR, Paris], Demian Wassermann, Rachid Deriche.

Acquisition time is a major limitation in recovering brain microstructure with diffusion Magnetic Resonance Imaging. Finding a sampling scheme that maximizes signal quality and satisfies given time constraints is NP-hard. We alleviate that by introducing a relaxed probabilistic model of the problem, for which nearly-optimal solutions can be found effectively. Our model is defined in the qt-space, so that it captures both spacial and temporal phenomena. The experiments on in-vivo diffusion images of the C57Bl6 wild-type mice reveal superiority of our technique over random sampling and even distribution in the qt-space.

This work has been published in [33].

7.1.2. Diffusion MRI microstructure models with in vivo human brain Connectom data: results from a multi-group comparison

Participants: Uran Ferizi [CMIC, Dept. of Computer Science, UCL, UK], Rutger Fick, Rachid Deriche.

A large number of mathematical models have been proposed to describe the measured signal in diffusion-weighted (DW) magnetic resonance imaging (MRI) and infer properties about the white matter microstructure. However, a head-to-head comparison of DW-MRI models is critically missing in the field. To address this deficiency, we organized the "White Matter Modeling Challenge" during the International Symposium on Biomedical Imaging (ISBI) 2015 conference. This competition aimed at identifying the DW-MRI models that best predict unseen DW data. in vivo DW-MRI data was acquired on the Connectom scanner at the A.A.Martinos Center (Massachusetts General Hospital) using gradients strength of up to 300 mT/m and a broad set of diffusion times. We focused on assessing the DW signal prediction in two regions: the genu in the corpus callosum, where the fibres are relatively straight and parallel, and the fornix, where the configuration of fibres is more complex. The challenge participants had access to three-quarters of the whole dataset, and their models were ranked on their ability to predict the remaining unseen quarter of data. In this work, we provide both an overview and a more in-depth description of each evaluated model, report the challenge results, and infer trends about the model characteristics that were associated with high model ranking. This work provides a much needed benchmark for DW-MRI models. The acquired data and model details for signal prediction evaluation are provided online to encourage a larger scale assessment of diffusion models in the future.

This work has been published in [16].

7.1.3. Advanced dMRI signal modeling for tissue microstructure characterization

Participants: Rutger Fick, Demian Wassermann, Rachid Deriche.

Non-invasive estimation of brain white matter microstructure features using dMRI – otherwise known as Microstructure Imaging – has become an increasingly complex and difficult challenge over the last decade. Within the framework of Fick's PhD thesis [13], we contributed to the challenge to recover microstructure tissue parameters by studying the impact of using well-regularized functional basis together with multi-compartment approaches. We focused on the estimation and interpretation of microstructure-related markers, often referred to as *Microstructure Imaging* and we reviewed and compared most state-of-the-art microstructure models in PGSE-based Microstructure Imaging, emphasizing model assumptions and limitations, as well as validating them using spinal cord data with registered ground truth histology. We then presented contributions to 3D q-space imaging and microstructure recovery. We proposed closed-form Laplacian regularization for the recent MAP functional basis, allowing robust estimation of tissue-related q-space indices. We also applied this approach to Human Connectome Project data, where we used it as a preprocessing for other microstructure models. Finally, we compared tissue biomarkers in a ex-vivo study of Alzheimer rats at different ages. Last but not least, we contributed to representing the qt-space- varying over 3D q-space and diffusion time. Overall, we significantly contributed to the challenge of better understanding microstructure-related features of the brain's white matter.

This work has been published in [13].

7.1.4. White matter tractography guided by anatomical and microstructural priors

Participants: Gabriel Girard [SCIL, Sherbrooke University, CA], Maxime Descoteaux [SCIL, Sherbrooke University, CA], Demian Wassermann, Rachid Deriche.

In this work, performed within the framework of G. Girard's PhD thesis [81], we mainly focused in developing beyond the state-of-the-art and well grounded tractography solutions to recover the brain structural connectivity: We started reporting biases from tractography reconstruction and suggested to use anatomical priors, derived from a high resolution T1-weighted image to reduce these biases and to embed additional spatial information of the brain tissues in the tractography to guide tractography. We showed that optimizing tractography parameters, stopping and seeding strategies can reduce the biases in position, shape, size and length of the streamline distribution. Overall, we very nicely succeeded to show that this idea was able to significantly improve the tractography by reducing the rate of false positives produced and provides a more quantitative characterization of the WM structure. Going further, we then proposed to embed more intrinsic microstructural information in the reconstruction process and remarkably succeeded to show the great added value brought to tractography by the addition of intrinsic microstructural information such as the mean axonal

diameter information estimated from the orientation of maximal diffusion probability. This is an original and important step forward in microstructure informed tractography, paving the way to a new generation of algorithms able to deal with intricate configurations of white matter fibres and providing quantitative brain connectivity analysis.

This work has been published in [13] and its part related to AxTract, the micro-informed tractography algorithm, in [19].

7.1.5. Rational invariants of ternary forms under the orthogonal group

Participants: Paul Görlach, Evelyne Hubert, Théodore Papadopoulo, Rachid Deriche.

In [79], [80], [95] we started to explore the theory of tensor invariants as a mathematical framework for computing new biomarkers for HARDI. We pursued this work and, in collaboration with the project-team GALAAD/AROMATH, we succeeded to develop a complete set of rational invariants for ternary quartics [44]. Being rational, they are very close to the polynomial invariants developed in [80] but they constitute a complete set of invariants. They are also good tools to understand better the algebraic invariants of [95] and some others based on spherical harmonics decomposition [61]. We determined a generating set of rational invariants of minimal cardinality for the action of the orthogonal group O3 on the space $R[x,y,z]_{2d}$ of ternary forms of even degree 2d. The construction relies on two key ingredients: On one hand, the Slice Lemma allows us to reduce the problem to dermining the invariants for the action on a subspace of the finite subgroup B3 of signed permutations. On the other hand, our construction relies in a fundamental way on specific bases of harmonic polynomials. These bases provide maps with prescribed B3-equivariance properties. Our explicit construction of these bases should be relevant well beyond the scope of this work. The expression of the B3-invariants can then be given in a compact form as the composition of two equivariant maps. Instead of providing (cumbersome) explicit expressions for the O3-invariants, we provide efficient algorithms for their evaluation and rewriting. We also use the constructed B3-invariants to determine the O3-orbit locus and provide an algorithm for the inverse problem of finding an element in $R[x,y,z]_{2d}$ with prescribed values for its invariants. These are the computational issues relevant in brain imaging.

This work has been sumitted and is currently under review. A preprint is available in [44].

7.1.6. Non-parametric graphnet-regularized representation of dMRI in space and time

Participants: Rutger Fick, Alexandra Petiet [ICM, CENIR, Paris], Mathieu Santin [ICM, CENIR, Paris], Anne-Charlotte Philippe [ICM, CENIR, Paris], Stéphane Lehericy [ICM, CENIR, Paris], Demian Wassermann, Rachid Deriche.

Effective representation of the four-dimensional diffusion MRI signal – varying over three-dimensional q-space and diffusion time τ – is a sought-after and still unsolved challenge in diffusion MRI (dMRI). We propose a functional basis approach that is specifically designed to represent the dMRI signal in this qτ-space. Following recent terminology, we refer to our qτ-functional basis as "qτ-dMRI". qτ-dMRI can be seen as a time-dependent realization of q-space imaging by Paul Callaghan and colleagues. We use GraphNet regularization – imposing both signal smoothness and sparsity – to drastically reduce the number of diffusion-weighted images (DWIs) that is needed to represent the dMRI signal in the qτ-space. As the main contribution, qτ-dMRI provides the framework to – without making biophysical assumptions – represent the qτ-space signal and estimate time-dependent q-space indices (qτ-indices), providing a new means for studying diffusion in nervous tissue. We validate our method on both in-silico generated data using Monte–Carlo simulations and an in-vivo test-retest study of two C57Bl6 wild-type mice, where we found good reproducibility of estimated qτ-index values and trends. In the hopes of opening up new τ-dependent venues of studying nervous tissues, qτ-dMRI is the first of its kind in being specifically designed to provide open interpretation of the qτ-diffusion signal.

This work has been published in [17]

7.1.7. Computational diffusion & perfusion MRI in brain imaging

Participants: Marco Pizzolato, Rachid Deriche.

Diffusion and Perfusion Magnetic Resonance Imaging (dMRI & pMRI) represent two modalities that allow sensing important and different but complementary aspects of brain imaging. This work performed within the framework of M. Pizzolato's PhD thesis presents a theoretical and methodological investigation on the MRI modalities based on diffusion-weighted (DW) and dynamic susceptibility contrast (DSC) images. For both modalities, the contributions of the thesis are related to the development of new methods to improve quality, processing, and exploitation of the obtained signals. With respect to contributions in diffusion MRI, the nature of the complex DW signal is investigated to explore a new potential contrast related to tissue microstructure. In addition, the complex signal is exploited to correct a bias induced by acquisition noise of DW images, thus improving the estimation of structural scalar metrics. With respect to contributions in perfusion MRI, the DSC signal processing is revisited in order to account for the bias due to bolus dispersion. This phenomenon prevents the correct estimation of perfusion metrics but, at the same time, can give important insights about the pathological condition of the brain tissue. The contributions of the thesis are presented within a theoretical and methodological framework, validated on both synthetic and real images.

This work has been published in [15].

7.1.8. Solving the Inclination Sign Ambiguity in Three Dimensional Polarized Light Imaging with a PDE-Based Method

Participants: Abib Alimi, Marco Pizzolato, Rutger Fick, Rachid Deriche.

Three dimensional Polarized Light Imaging (3D-PLI) is a contrast-enhancing technique that measures the spatial fiber architecture in the human postmortem brain or heart at a submillimeter resolution. In a voxel, the 3D fiber orientation is defined by the direction angle and the inclination angle whose sign is unknown. To have an accurate explanation of fiber orientation, it is compulsory to clear up this sign ambiguity. A tilting process provides information about the true inclination sign, however the technique is highly sensitive to noise. In this work, a partial differential equations based method is proposed to reduce the noise: the total variation model of Rudin-Osher-Fatemi is extended to 3D orientation vector images to restore the sign. The proposed algorithm is evaluated on synthetic and human heart data and results show that the true sign of the inclination angle can be successfully extracted.

This work has been published in [27]

7.1.9. Brain correlates of apathy in Kleine Levin syndrome: a mean apparent propagator study

Participants: Anne-Charlotte Philippe [ICM, CENIR, Paris], Sophie Lavault [ICM, CENIR, Paris], Romain Valabregue [ICM, CENIR, Paris], Richard Levy [ICM, CENIR, Paris], Isabelle Arnulf [ICM, CENIR, Paris], Stéphane Lehericy [ICM, CENIR, Paris], Rutger Fick, Demian Wassermann, Rachid Deriche.

Kleine-Levin syndrome (KLS) is a rare neurological disorder characterized by episodes of severe hypersomnia, apathy, cognitive impairment, derealization and behavioral disturbances. Between episodes, patients have normal sleep, mood and behavior. Apathy is a prominent clinical feature of KLS but its pathophysiology is not known. Using new techniques to boost signal-to-noise ration and biomarker extraction in multi-shell dMRI [13], we have studied, in collaboration with the Brain and Spine Institute (ICM, Paris) the Klein-Levin syndrome (KLS) [45]. Our results highlight the presence of structural changes correlated to the apathy score i n the anterior portion of the CC during episodes, a region where fibers project onto the medial orbitofrontal cortex. As, these prefrontal regions are involved in motivation processes, this suggests that apathy in KLS could result from difficul ties to provide the affective/motivational value of a given behavioral context.

This work has been published in [45].

7.2. Unveiling brain activity using M/EEG

7.2.1. Dictionary learning for M/EEG processing

Participants: Maureen Clerc, Sebastian Hitziger, Théodore Papadopoulo.

Signals obtained from magneto- or electroencephalography (M/EEG) are very noisy and inherently multi-dimensional, i.e. provide a vector of measurements at each single time instant. To cope with noise, researchers traditionally acquire measurements over multiple repetitions (trials) and average them to classify various patterns of activity. This is not optimal because of trial-to-trial variability (waveform variations, jitters). The jitter-adaptive dictionary learning method (JADL) has been developed [82] to better handle for this variability, with a particular emphasis on jitters. It was generalized to handle variability both in jitter and in duration, in a method called Adaptive Waveform Learning [8]. These methods [83] are data-driven and learn a dictionary (prototype signals) from a set of signals, but are limited to a single channel, which restricts their capacity to work with very noisy multichannel data such as M/EEG. An extension to multidimensional signals has been developped in [96] and [41].

7.2.2. Accounting for conductivity in M/EEG leadfields

Participants: Maureen Clerc, Juliette Leblond [APICS project-team], Kostiantyn Maksymenko, Jean-Paul Marmorat [APICS project-team], Théodore Papadopoulo, Christos Papageorgakis [APICS project-team].

We aim at improving the EEG forward/inverse problem by better modelling the skull conductivity. Indeed, it has been shown that the complex conductivity profile of the skull has a major influence on the accuracy of the EEG forward/inverse problems.

- The skull conductivity is usually considered homogeneous, but the skull is actually made of several types of bone: hard (compacta) and soft (spongiosa) which may have different conductivity characteristics. By adapting a template to MR images of individual subjects, the influence of the spongiosa on source localization can be demonstrated [97]. Estimating the conductivity values of the skull compartments is an important problem, for which theoretical results on uniqueness and robustness have been obtained [64], [63], [26].
- Such studies show the need of easily obtaining EEG leadfields with various conductivity values. Recomputing a new leadfield for every different set of conductivities is expensive. We have thus developped a technique inspired by “reduced bases” which approximates the set of leadfields over a domain of conductivities using a low number of "base leadfields" [40]. The approach offers mathematical guarantees on the approximation level and provides an efficient methodological ground for attempting to compute both sources and conductivities in the EEG inverse problem.

7.2.3. Cochlear implant stimulation models

Participants: Maureen Clerc, Kai Dang, Dan Gnansia [Oticon Medical], Nicolas Guevara [CHU de Nice].

Our expertise on building forward models in bioelectromagnetism has led to a collaboration with Oticon Medical, a cochlear implant manufacturer. Through Dang’s PhD thesis [12], we developed computational models of cochlear implant stimulation, which can account for the anatomical shape of the inner ear, the shape of the implanted electrode, and the stimulation mode, for instance common ground or multi-mode grounding [67], [66]. The OpenMEEG software was extended to cope with zero-conductivity regions (e.g. the silicon electrode holder). The cochlear implant Boundary Element model was coupled with a lumped capacitor and constant phase element model, allowing time-domain simulation. Thorough validation campaigns were conducted, in vitro (notably using a 3D printer) and in situ (in human specimens).

7.3. Combining spatio-temporal CNS imaging modalities

7.3.1. Groupwise structural parcellation of the whole cortex: A logistic random effects model based approach

Participants: Guillermo Gallardo, William Wells [Harvard Medical School, Boston, MA, USA], Demian Wassermann, Rachid Deriche.

Current theories hold that brain function is highly related to long-range physical connections through axonal bundles, namely extrinsic connectivity. However, obtaining a groupwise cortical parcellation based on extrinsic connectivity remains challenging. Current parcellation methods are computationally expensive; need tuning of several parameters or rely on ad-hoc constraints. Furthermore, none of these methods present a model for the cortical extrinsic connectivity of the cortex. To tackle these problems, we propose a parsimonious model for the extrinsic connectivity and an efficient parceling technique based on clustering of tractograms. Our technique allows the creation of single subject and groupwise parcellations of the whole cortex. The parcellations obtained with our technique are in agreement with structural and functional parcellations in the literature. In particular, the motor and sensory cortex are subdivided in agreement with the human homunculus of Penfield. We illustrate this by comparing our resulting parcels with the motor strip mapping included in the Human Connectome Project data.

This work has been published in [6].

7.3.2. Spatial regularization based on dMRI to solve EEG/MEG inverse problem

Participants: Brahim Belaoucha, Théodore Papadopoulo.

In this work, we present a new approach to reconstruct dipole magnitudes of a distributed source model for magnetoencephalographic (MEG) and electroencephalographic (EEG). This approach is based on the structural homogeneity of the cortical regions which are obtained using diffusion MRI (dMRI). First, we parcellate the cortical surface into functional regions using structural information. Then, we use a weighting matrix that relates the dipoles' magnitudes of sources inside these functional regions. The weights are based on the region's structural homogeneity. Results of the simulated and real MEG measurement are presented and compared to classical source reconstruction methods.

This work has been published in [29], [11].

7.3.3. Large brain effective network from EEG/MEG data and dMR information

Participants: Brahim Belaoucha, Théodore Papadopoulo.

In this research, we aim at reconstructing the information flow in the brain for a given task. More than simple activations, we look at their relationship in time, so at networks constituted by nodes obtained from the parcellations of [55] and edges coming from tractographies obtained by dMRI. In [56] a multivariate auto-regressive model has been used to model the interactions between brain areas. Those areas are obtained using the methods depicted in paragraph 1. Then a putative network is built using connexions obtained by tractography augmented by cortico-cortical connexions (horizontal connexions between neighbor areas) which are not seen by dMRI. A two stage algorithm estimates the coefficients of the autoregressive matrices [57]. Those matrices are constrained to be sparse, so that the non-zero coefficients can be used to estimate the effective network that was activated during the task. The method was validated using simulated data and applied to real MEG and EEG datasets.

This work has been published in [28], [11].

7.3.4. Inference and Visualization of Information Flow in the Visual Pathway using dMRI and EEG

Participants: Samuel Deslauriers-Gauthier, Jean-Marc Lina [ETS - Ecole de Technologie Supérieure, Montréal, CA], Russel Buttler [SCIL, Sherbrooke University, CA], Pierre-Michel Bernier [SCIL, Sherbrooke University, CA], Kevin Whittingstall [SCIL, Sherbrooke University, CA], Maxime Descoteaux [SCIL, Sherbrooke University, CA], Rachid Deriche.

We propose a method to visualize information flow in the visual pathway following a visual stimulus. Our method estimates structural connections using diffusion magnetic resonance imaging and functional connections using electroencephalography. First, a Bayesian network which represents the cortical regions of the brain and their connections is built from the structural connections. Next, the functional information is added as evidence into the network and the posterior probability of activation is inferred using a maximum entropy on the mean approach. Finally, projecting these posterior probabilities back onto streamlines generates

a visual depiction of pathways used in the network. We first show the effect of noise in a simulated phantom dataset. We then present the results obtained from left and right visual stimuli which show expected information flow traveling from eyes to the lateral geniculate nucleus and to the visual cortex. Information flow visualiza-tion along white matter pathways has potential to explore the brain dynamics in novel ways.

This work has been published in [37].

7.3.5. Information Flow in the White Matter During a Motor Task: A Structural Connectivity Driven Approach

Participants: Guillermo Gallardo, Demian Wassermann, Maxine Descoteaux [SCIL, Sherbrooke University, CA], Samuel Deslauriers-Gauthier, Rachid Deriche.

Cognitive tasks emerge from the interaction of functionally specialized cortical regions . These interactions are supported by information flow through white matter fiber bundles connecting distant cortical regions. Estimating the information flow through white matter fiber bundles would therefore provide valuable information into the necessary cortical interactions to realize a task. In this work, we build a Bayesian network representing cortical regions and their connections using a structural connectivity driven parcellation derived from diffusion MRI (dMRI). We then introduce Magnetoencephalography (MEG) measurements as evidence into this network to infer the information flow between cortical regions. We show, for the first time, results on the interaction between the precentral, postcentral and occipital regions during a hand-movement task.

This work has been published in [39].

7.4. Brain Computer Interfaces

7.4.1. Multimodal BCI

Participants: Maureen Clerc, Lorraine Perronnet [Visages project-team], Saugat Bhattacharyya [Camin team].

We are conducting research in Multimodal BCI:

- In collaboration with Camin team in Montpellier, we are investigating the use of feedback using Functional electrical stimulation (FES) of limb muscles [58] for Motor Imagery and also studying the influence of the FES on brain signals.
- A study comparing unimodal and bimodal EEG-fMRI neurofeedback for 10 healthy volunteers showed that EEG-fMRI leads to stronger activations than EEG alone [24].

7.4.2. Automatizing calibration

Participants: Maureen Clerc, Nathalie Gayraud, Alain Rakotomamonjy [Université de Rouen].

One of the drawbacks of BCI is the time required for setup and calibration before its use. Instead of fine-tuning the BCI by collecting labeled data by asking the user to perform tasks without any purpose nor feedback, we propose to fine-tune the BCI after the user has started using it. This requires an initial - suboptimal - classifier, which we propose to build through "transfer learning" by re-using labeled data acquired from other subjects and other sessions. We have investigated two main directions for this:

- **Riemannian geometry of covariance matrices**. Covariance matrices of EEG signals are interesting features for BCI. Their information geometry has led to impressive transfer learning performance, as testified by their excellent ranking in several competitions. We are studying the advantages of these features and how they can be used to build separability markers within datasets [74].
- **Optimal transport theory**. A new strand of research is to use optimal transport methods for domain adaptation. The idea is to reuse the classifiers built from existing labeled datasets by transporting the new unlabeled data onto the domain of the existing data [34].

7.4.3. Translational research

Participants: Maureen Clerc, Claude Desnuelle [CHU de Nice], Violaine Guy [CHU de Nice], Théodore Papadopoulo, Marie-Hélène Soriani [CHU de Nice].

The P300-speller is a widespread BCI paradigm for communication, studied in many laboratories. Our involvement in this paradigm was triggered by the Nice University Hospital ALS reference center. Having evaluated with them existing P300-spellers, which were found difficult to get to work properly, we decided to develop our own P300-speller based on OpenViBE in collaboration with Inserm Lyon [65], [104]. Among its distinctive features: optimal stopping of flashes, principled choice of letter groups [103] and word completion and prediction. We demonstrated the feasibility of our "Coadapt P300 speller" in collaboration with Nice University Hospital during a clinical study with 20 ALS patients who participated in 3 sessions each [99], [20].

In order to bring this type of communication BCI closer to patients, we developed a user-friendly software, bci-vizapp, with far greater portability with respect to hardware (OS, screen and amplifier).

Our work aroused the interest of patient associations, in particular "Espoir Charcot" who helped a patient hospitalized in Chambéry acquire a consumer-grade (Emotiv-EPOC) EEG in order to use the P300-speller. He eventually succeeded in using the system, with the help of a local engineer, but notably without our physical presence at any stage. This represents an important first step for us in translational research.

8. Bilateral Contracts and Grants with Industry

8.1. Bilateral Contracts with Industry

- The Olea Medical company from La Ciotat (FR) funds 50% of the PhD of Marco Pizzolato, supervised by Rachid Deriche, which is funded by the PACA Region for the remaining 50%.
- The dMRI Library has been transfered to the Olea Medical company.
- The BESA company (Brain Electrical Source Analysis) from Germany funds 50% of the PhD of Christos Papageorgakis, co-supervised by Maureen Clerc (ATHENA) and Juliette Leblond (APICS), which is funded by the PACA Region for the remaining 50%.
- The Neurelec company (Cochlear Implants) supports a CIFRE PhD funding for Kai Dang, supervised by Maureen Clerc.

9. Partnerships and Cooperations

9.1. Regional Initiatives

9.1.1. Inria SAM Action Transverse

Participants: Paul Görlach, Evelyne Hubert [Aromath Project-Team], Théodore Papadopoulo, Rachid Deriche.

Finding biomarkers of abnormalities of the white matter is one important problem in dMRI processing. As these biomarkers need to be independent of the orientation of the head, they are functions of the rotational invariants of the shapes that characterize the diffusion probabilities in the white matter. While the situation is well understood for second order tensors, these are not powerful enough to represent crossings in the white matter. Acquisitions made with the HARDI scheme allow for a richer description of probabilities, which have been modelled in the literature team as (positive) ternary quartics (tensors of order 4). But invariants of these quartics are not well known. For a long period, only six (out of 12 in theory) were known. Previous work in the ATHENA team developed some new strategies to compute more invariants. But these were ever non-polynomial and had some stability problems [95]. Another strategy [80] was leading to polynomial and stable invariants, but the approach was generating a number of invariants (more than 12) for which it was impossible to extract an irreducible family.

The goal of this "Transverse action" was to join forces with the project-team GALAAD/AROMATH and leverage the methods they developed [85], [86], [84] to have a better insight in this problem of rotational invariants of ternary quartics.

In collaboration with GALAAD/AROMATH, we developped a complete set of rational invariants for ternary quartics [44]. Being rational, they are very close to the polynomial invariants developed in [80] but they constitute a complete set of invariants. They also are good tools to understand better the algebraic invariants of [95] and some others based on spherical harmonics decomposition [61].

9.1.2. Inria SAM Action Transverse

Participants: Yann Thanwerdas [Asclepios Project-Team], Xavier Pennec [Asclepios Project-Team], Maureen Clerc, Nathalie Gayraud.

The goal of the proposed internship will be to study and implement the barycentric subspace analysis procedure on SPD matrices endowed with the affine invariant metric and to test it with BCI datasets. In the context of BCI, the problem is not trivial. The cross-session and cross-subject variability must be taken into account during the process of selecting the optimal lower dimensional subspace. In a first step, algorithms will be developed to project points into a barycentric subspace, and then to optimize the location of the reference points themselves. In order to avoid an intensive optimization, one will usefully restrict reference points to belong to the original data points. In a second step, the barycentric coordinates will be used to describe the data in the hierarchy of embedded barycentric subspaces and one will study the power of this signature to classify / predict the correct brain state

9.1.3. Inria SAM Action Marquante

Participants: Demian Wassermann, Maureen Clerc, Théodore Papadopoulo, Amandine Audino.

Duration: *october 2016 to January 2018*

Elucidating the structure-function relationship of the brain is one of the main open question in neuroscience. The capabilities of diffusion MRI-based techniques to quantify the connectivity strength between brain areas, namely structural connectivity (SC), in combination with modalities such as electro encephalography (EEG) to quantify brain function have enabled advances in this field. However, the actual relationship between these SC measures and measures of information transport between neuronal patches is still far from being determined.

In this project, we will address this problem by establishing a relationship between diffusion MRI (dMRI) SC measures and electrical conductivity on the human brain cortex. We will exploit the ATHENA's competences in dMRI (Deriche-Wassermann) and EEG (Clerc-Papadopoulo) and our collaboration with the neurosurgical service at CHU Nice (Fontaine-Almairac). In successfully addressing this problem, we will set the bases to solve the current open problem of non-invasively measuring cortico-cortical (CC) connectivity in the human brain. This will boost the understanding of cognitive function as well as neurosurgical planning for the treatment of pathologies such as drug-resistant epilepsy and resection of glioblastomas.

9.2. National Initiatives

9.2.1. Inria Project Lab

9.2.1.1. IPL BCI-LIFT

Participants: Maureen Clerc, Théodore Papadopoulo, Nathanaël Foy, Nathalie Gayraud, Federica Turi.

Duration: *January 2015 to December 2018*

The Inria Project-Lab BCI-LIFT is an Inria-funded reasearch consortium to foster collaborative research on Brain-Computer Interfaces on the topic of Learning, Interaction, Feedback and Training. It is coordinated by Maureen Clerc. Its members are from 6 Inria teams: ATHENA, CAMIN, HYBRID, MJOLNIR, NEUROSYS, POTIOC, and from Dycog team from CRNL Lyon, and University of Rouen. The goal is to reach a next generation of non-invasive Brain-Computer Interfaces (BCI), more specifically BCI that are easier to appropriate, more efficient, and suit a larger number of people. For more information, refer to the BCI-LIFT website.

9.2.2. ANR

9.2.2.1. ANR MRSEI LEMONS

Participants: Maureen Clerc, Théodore Papadopoulo.

Duration: *October 2015 to April 2017*
Call: *ANR MRSEI Montage de réseaux scientifiques européens ou internationaux 2015*

LEMONS (Learning, Monitoring, Operating Neural Interface) aims to consolidate a European Network by organizing meetings and visits, in order to submit a proposal for a MSCA-ITN Training Network. The European consortium was led by ATHENA (coordinator Maureen Clerc). The European consortium was composed of 8 beneficiaries from 6 countries (Inria, EPFL, TU Graz, Fondazione Santa Lucia, Albert-Ludwigs Universität Freiburg, Universiteit Leiden, Université Lyon 1, eemagine GmbH) and 8 additional Partner Organizations from clinical and industrial sectors. The LEMONS project was submitted twice but was eventually not selected for EU funding.

9.2.2.2. ANR NeuroRef
Participants: Demian Wassermann, Antonia Machlouziredes, Guillermo Gallardo, Rachid Deriche.

Duration: *October 2016 to September 2019*
Call: *NSF-ANR Program Collaborative Research in Computational Neuroscience 2015*

This project is a collaboration with Pr.S.Bouix and his team at the Psychiatry NeuroImaging Lab, Dept of Radiology, Brigham and Women's Hospital, Harvard Medical School (USA) to build MRI reference atlases to analyze brain trauma and post-traumatic stress. The goal is to develop a robust framework to perform subject-specific neuroimaging analyses of Diffusion MRI (dMRI), as this modality has shown excellent sensitivity to brain injuries and can locate subtle brain abnormalities that are not detected using routine clinical neuroradiological readings.

9.2.2.3. ANR MOSIFAH
Participants: Rachid Deriche, Rutger Fick, Demian Wassermann, Maureen Clerc, Théodore Papadopoulo.

Duration: *October 2013 to September 2017*
Call: *ANR Numerical Models 2013*

This ANR project is about multimodal and multiscale modelling and simulation of the fiber architecture of the human heart. It started on October 2013 and involves three partners: Creatis Team, INSA, Lyon (I. Magnin, Y. Zhu); TIMC-IMAG, CNRS, Grenoble (Y. Uson) and the ATHENA project team.

It consists in modelling and simulating the ex vivo and in vivo 3D fiber architectures at various scales using multiphysical data from different imaging modalities working at different spatial resolutions. To this end, the myocardium of the human heart will be imaged using respectively Polarized Light Imaging (PLI) and dMRI.

9.2.2.4. ANR VIBRATIONS
Participants: Théodore Papadopoulo, Maureen Clerc, Rachid Deriche, Demian Wassermann.

Duration: *February 2014 to January 2018*
Call:ANR Programme de Recherche Translationnelle en Santé (PRTS) 2013

The VIBRATIONS project proposes to simulate in a biologically realistic way MEG and EEG fields produced by different configurations of brain sources, which will differ in terms of spatial and dynamic characteristics. The research hypothesis is that computational and biophysical models can bring crucial information to clinically interpret the signals measured by MEG and EEG. In particular, they can help to efficiently address some complementary questions faced by epileptologists when analyzing electrophysiological data.

9.2.3. ADT

9.2.3.1. AMDT BCI-Browser
Participants: Théodore Papadopoulo, Maureen Clerc.

Duration: 1 year

Most often, BCI techniques are demonstrated in simple toy applications made. The only "few" real BCI applications are specific developments and are not used much as they lack of functionality, maintenance, ... The goal of this development contract is to demonstrate a new approach to BCI, in which BCI interactions are integrated in existing applications. Ideally, the original software is not modified and not even recompiled. It is modified by providing either modified GUI libraries or providing extensions as plugins. As a proof of concept, we aim at modifying C++/Qt applications with a focus on web browsing, by redefining some of its basic interactions (mouse clicks, keyboard, ...) using some BCI components. In this manner, it might be possible to drive standard and state-of-the-art application using BCI and at a limited maintenance cost.

This contract is part of the AMDT initiative.

9.2.3.2. ADT BOLIS 2

Participants: Théodore Papadopoulo, Juliette Leblond [APICS project-team], Jean-Paul Marmorat [CMA Ecole des Mines Paritech].

Duration: *6 months.*

This contract is a follow-up of ADT BOLIS which aimed at building a sofware platform dedicated to inverse source localisation, building upon the elements of software found in FindSources3D. The platform is modular, ergonomic, accessible and interactive and offers a detailed visualisation of the processing steps and the results. Its goal is to provide a convenient graphical interface and a tool that can be easily distributed and used by professionals (target audience: clinicians and researchers). BOLIS 2 aims at simplifying some maintenance aspects of the software.

This contract is part of the AMDT initiative.

9.2.4. Other Funding Programs

9.2.4.1. Big Brain Theory ICM Program: MAXIM'S

Participants: Demian Wassermann, Alexandra Petiet [ICM, CENIR, Paris], Stéphane Lehericy [ICM, CENIR, Paris], Julien Valette [Institut d'Imagerie Biomédicale, CEA, France], Virginie Callot [Center for Magnetic Resonance in Biology and Medicine - UMR 7339, Center for Magnetic Resonance in Biology and Medicine - UMR 7339].

Shedding light on the specificity of microstructural MRI biomarkers of axonal and myelin integrity using multi-modal imaging in rodents and quantitative histological correlations.

Magnetic Resonance Imaging (MRI) biomarkers (BMs) of axonal and myelin integrity suffer from lack of specificity at the microstructural level, which hinders our understanding of disease mechanisms. A better knowledge of the role of the white matter (WM) microstructure in normal and abnormal function relies on the development of MRI metrics that can provide (i) increased specificity to distinct attributes of WM such as local fiber architecture, axon morphology, myelin content, and (ii) specific markers of axonal vs. myelin pathologies. Advanced diffusion-weighted (DW) imaging techniques based on biophysical models of cerebral tissues and cellular compartments can extract for example mean axonal diameters or cellular geometry. In addition, diffusion-weighted spectroscopy (DWS) offers new insights into the diffusion properties of intracellular metabolites. More specifically, probing metabolite diffusion at different time scales allows assessing fiber diameter and length, and the specific compartmentalization of different metabolites in different cell types allows differentiating between astrocytic and neuronal microstructural parameters. Although very promising, these novel techniques still need extensive histological validation.

We propose to develop these two cutting-edge MRI techniques – DW-MRI and DWS, at 11.7T to investigate axonopathy and myelinopathy in well-established mouse models with a single lesion type, and to validate these new microstructural BMs with multivariate quantitative histological analyses.

Duration: *March 2016 to March 2019*

9.3. European Initiatives

9.3.1. FP7 & H2020 Projects

9.3.1.1. ERC AdG CoBCoM

Program: H2020-EU.1.1. (ERC-ADG-2015 - ERC Advanced Grant)

Project acronym: CoBCoM - **ID:** 694665

Project title: *Computational Brain Connectivity Mapping*

Start date: 2016-09-01, End date: 2021-08-31

P.I : R. Deriche

Partners: ATHENA project-team

Abstract:

One third of the burden of all the diseases in Europe is due to problems caused by diseases affecting brain. Although exceptional progress has been obtained for exploring it during the past decades, **the brain is still terra-incognita** and calls for specific research efforts to better understand its architecture and functioning.

CoBCoM is our response to this great challenge of modern science with the overall goal to **develop a joint Dynamical Structural-Functional Brain Connectivity Network (**DSF-BCN**)** solidly grounded on advanced and integrated methods for diffusion Magnetic Resonance Imaging (dMRI) and Electro & Magneto-Encephalography (EEG & MEG).

To take up this grand challenge and achieve new frontiers for brain connectivity mapping, we will develop a new generation of computational models and methods for identifying and characterizing the structural and functional connectivities that will be at the heart of the DSF-BCN. Our strategy is to break with the tradition to incrementally and separately contributing to structure or function and develop **a global approach involving strong interactions between structural and functional connectivities.** To solve the limited view of the brain provided just by one imaging modality, our models will be developed under a rigorous computational framework integrating complementary non invasive imaging modalities: dMRI, EEG and MEG.

CoBCoM will push far forward the state-of-the-art in these modalities, developing **innovative models and ground-breaking processing tools** to provide in-fine a joint DSF-BCN solidly grounded on a detailed mapping of the brain connectivity, both in space and time.

Capitalizing on the strengths of dMRI, MEG & EEG methodologies and building on the **bio-physical and mathematical foundations** of our new generation of computational models, CoBCoM will be applied to high-impact diseases, and its **ground-breaking comput ational nature and added clinical value** will open new perspectives in neuroimaging.

9.3.1.2. ERC StG NeuroLang

Program: H2020-EU.1.1. (ERC-StG-2016 - ERC Starting Grant)

Project acronym: NEUROLANG

Project title: Accelerating Neuroscience Research by Unifying Knowledge Representation and Analysis Through a Domain Specific Language

Start date: March 2018, End date: Fe. 2023

P.I : D. Wassermann

Partners: ATHENA project-team (Till Oct. 2017). PARIETAL project-team (Since Nov. 2017)

Abstract: The grand challenge of NeuroLang is to unify neuroanatomical descriptions into a formal language embodied by a Domain Specific Language (DSL) which can be used to perform neuroimaging data analysis. NeuroLang will formalise neuroanatomical knowledge into a DSL, providing an individualized as well as a population-based methodology to represent the anatomy and function of the brain and facilitating the analysis of large neuroimaging datasets and ontologies. Besides formalizing and unifying neuroanatomy, there are four major challenges in NeuroLang: (i) Developing a Neuroanatomical DSL,(ii) Representation of Neuroanatomical Data, (iii) Enabling Large-Scale Inference in a Neuroanatomical DSL and (iv) Reproducible Research and Applicability in Clinical and Cognitive Research.

9.3.1.3. ChildBrain ETN

ATHENA is an Associated Partner in the ChildBrain European Training Network: the team participates in training workshops and receive PhD students in secondments.

Program: European Training Network

Project acronym: ChildBrain

Project title: Advancing brain research in children's developmental neurocognitive disorders

Duration: March 2015 to March 2019

Coordinator: Prof. Paavo Leppänen, University of Jyväskylä, Finland

Other partners: University of Leuven (Belgium), University of Münster (Germany), Rabboud University (The Netherlands), Aston University (United Kingdom), IcoMetrix (Belgium), Elekta (Finland), BESA (Germany)

Abstract: The purpose of the ChildBrain ETN is to train young scientists, i.e. Early Stage Researchers (ESRs), to utilise evidence-based neuroscientific knowledge for helping children, especially those at high risk for dropout due to neurocognitive disorders, to meet future educational and societal demands.

9.4. International Initiatives

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

9.4.1.1. LargeBrainNets

Title: Characterizing Large-scale Brain Networks Using Novel Computational Methods for dMRI and fMRI-based Connectivity

International Partner (Institution - Laboratory - Researcher):

Stanford (United States) - Stanford Cognitive and Systems Neuroscience Laboratory - Vinod Menon

Duration :Jan. 2016 – Dec. 2018

Partners: ATHENA project-team,

See also: http://www-sop.inria.fr/members/Demian.Wassermann/large-brain-nets.html

The first major goal of this project is to develop and validate appropriate sophisticated computational and mathematical tools for identifying functional nodes at the whole-brain level and measuring structural and functional connectivity between them, using state-of-the-art human brain imaging techniques and open-source HCP data. To this end, we will first develop and validate novel computational tools for (1) identifying stable functional nodes of the human brain using resting-state functional MRI and (2) measuring structural connectivity between functional nodes of the brain using multi-shell high-angular diffusion MRI. Due to the complementarity of the two imaging techniques fMRI and dMRI, our novel computational methods methods, the synergy between the two laboratories of this associate team will allow us to reveal in unprecedented detail the structural and functional connectivity of the human brain. The second major goal of this project is to use our newly developed computational tools to characterize normal structural and functional brain networks in neurotypical adults.

9.4.2. Inria International Partners

9.4.2.1. Declared Inria International Partners

- Sherbrooke University, CA (M. Descoteaux)
- Harvard Medical School, USA (S. Bouix)
- CMRR, University of Minnesota, USA (Christophe Lenglet)
- Verona University, It (Gloria Menegaz)
- Department of CISE, the University of Florida, Gainesville, USA (Baba C. Vemuri)
- Centre for Medical Image Computing (CMIC), Dept. Computer Science, UCL, UK (D. Alexander)
- SBIA, University of Pennsylvania Medical School, USA (R. Verma).
- BESA company on EEG/MEG modeling.

9.4.3. Participation in Other International Programs

- University Houari Boumedienne (USTHB, Algiers) (L. Boumghar) and University of Boumerdes, (D. Cherifi), Algeria.

9.5. International Research Visitors

9.5.1. Visits of International Scientists

- Dr. Lang Chen, Research Fellow, Stanford Medical School, USA (October 2017)

9.5.1.1. Internships

- Gaston Zanitti, Computer Science Department, School of Sciences, University of Buenos Aires, Argentina (Mars-June 2017)

10. Dissemination

10.1. Promoting Scientific Activities

10.1.1. Scientific Events Organisation

10.1.1.1. General Chair, Scientific Chair

R. Deriche and S. Deslauriers-Gauthier organized the CoBCoM Winter School Workshop in Juan Les Pins from November 20 to 24, 2017. Organized within the framework of the ERC CoBCoM and targeted at graduate students, early career and senior researchers interested in structural and functional brain connectivities via multi imaging modalities including diffusion MRI, functional MRI, MEG, and EEG, this Winter School Workshop offered several tutorials and advanced lectures from more than 20 leading researchers and experts on Computational Brain Connectivity Mapping. In addition, it included 3 sessions dedicated to 27 posters presentations from participants.

10.1.2. Scientific Events Selection

10.1.2.1. Member of the Conference Program Committees

- T. Papadopoulo is member of the Program Commitee of GRETSI 2017.
- D. Wassermann serves as part of the Conference Program of MICCAI 2017; IPMI 2017; and ISMRM 2017.

10.1.2.2. Reviewer

- M. Clerc serves several international institutions in reviewing applications : ERC, FET-Open, ANR-NSF.
- M. Clerc serves several international conferences (Graz International BCI Conference, BaCI, IEEE EMBC Neural Eneering).
- R. Deriche serves several international institutions in reviewing applications : ERC Grants, Swiss National Science Foundation, the Netherlands Organisation for Scientific Research (NWO)...
- R. Deriche serves several international conferences (ISBI, MICCAI, ISMRM, ...) and international workshops (CD-MRI Miccai, MFCA Miccai...).
- T. Papadopoulo serves several international conferences as a reviewer (GRETSI, ICIP, ISBI).
- D. Wassermann serves several international conferences as a reviewer (MICCAI, ISMRM, HBM, CDMRI, etc)
- D. Wassermann serves several international institutions in reviewing applications: ANR, the Netherlands Organisation for Scientific Research (NWO), ERC FET program, Argentina MINCyT.

10.1.3. Journal

10.1.3.1. Member of Editorial Boards

- R. Deriche is member of the Editorial Board of the Journal of Neural Engineering, Associate Editor of SIAM Journal on Imaging Sciences (SIIMS), editorial board member at Springer for the book series entitled Computational Imaging and Vision and member of the Editorial Board of the Medical Image Analysis Journal
- M. Clerc is member of the Editorial Board of the Journal of Neural Engineering, and of the ISTE-Wiley book series.

10.1.3.2. Reviewer - Reviewing Activities

- M. Clerc serves several international journals (Brain Topography, Trends in Biotechnology, Journal of Neural Engineering, Biomedical Engineering OnLine).
- R. Deriche serves several international journals (NeuroImage, IEEE Transactions on Medical Imaging, Magnetic Resonance in Medicine, Journal of Mathematical Imaging and Vision, Medical Image Analysis Journal, ...).
- T. Papadopoulo serves several international journals (NeuroImage, Frontiers Neuroscience, IEEE PAMI, Pattern Recognition, ...).
- D. Wassermann serves several international journals (NeuroImage, IEEE Transactions on Medical Imaging, Human Brain Mapping, Medical Image Analysis Journal, ...).

10.1.4. Invited Talks

- M. Clerc gave several invited talks: MiniCours axe MTC-NSC in Sophia Antipolis, Journées des Jeunes Chercheurs en Interfaces Cerveau Ordinateurs in Bordeaux, CoBCoM in Antibes.
- R. Deriche gave an invited talk at Huawei Vision Forum, Le Phébus.
- T. Papadopoulo gave an invited talk at CoBCoM in Antibes.
- D. Wassermann gave several invited talks at international institutions including Stanford Medical School, USA; National University of the South, Argentina; Brain and Spine Institute, and NeuroSpin, France

10.1.5. Leadership within the Scientific Community

- M. Clerc is in charge of the BCI-LIFT Inria Project Lab. She is also a founding member and vice-president of the CORTICO association (Collectif pour la Recherche Transdisciplinaire sur les Interfaces Cerveau Ordinateur), the French association for BCI.
- R. Deriche is the P.I. of the ERC AdG CoBCoM.
- D. Wassermann is the P.I. of the ERC StG NeuroLang, ANR-NSF NeuroRef, and the Associated Team LargeBrainNets

10.1.6. Scientific Expertise

- M. Clerc is a member of the Inria Evaluation Committee since 2015.
- M. Clerc is a member of the Scientific Committee of Académie 4 of Université Côte d'Azur.
- M. Clerc is a member of the Steering Committee of the Magneto-Encephalography Platform of La Timone, Marseille.
- R. Deriche is a member of the Scientific Committee of Académie 2 of Université Côte d'Azur.
- R. Deriche serves several international institutions in reviewing applications : ERC Grants, Swiss National Science Foundation, the Netherlands Organisation for Scientific Research (NWO).
- D. Wassermann serves several international institutions in reviewing applications: ANR, the Netherlands Organisation for Scientific Research (NWO), ERC FET, Argentine MINCyT

10.1.7. Research Administration

- M. Clerc is Déléguée Scientifique Adjointe (vice-head of Science) of the Sophia Antipolis Inria Research Center since 2014.
- M. Clerc is member of the Commission Scientifique Interne (CoSI) of Inria since 2014.
- M. Clerc was vice-president of the hiring committee for CR2 at Inria Sophia Antipolis in 2017.
- M. Clerc was a member of the CR1 hiring committee at Inria in 2017.
- R. Deriche is member of the Academic Council of UCA (Université Côte d'Azur)
- R. Deriche is member of the Scientific Council of Académy 2 *Complex Systems*, Université Côte d'Azur and member of the Scientific Council of Olea Medical Company (http://www.olea-medical.com/
- T. Papadopoulo represents Inria at the Administration Council of the CIU Santé.
- T. Papadopoulo is member of the Software Development Committee at Inria.
- T. Papadopoulo is the head of the DTK platform committee of the Sophia Antipolis Inria Research Center since 2016.

10.2. Teaching - Supervision - Juries

10.2.1. Teaching

BS : M. Clerc made a presentation to medical school students enrolled in "Ecole de l'Inserm", in Sèvres.

Master: M. Clerc taught a course on "Brain Machine Interfaces" at Sciences Po, Paris, in a Master program on "Disruptive Technologies and Public Policies".

Master: R. Deriche, Variational approaches and Geometrical Flows for Computational Brain Imaging, 36 ETD, M2 "Computational Biology and Biomedicine", Université Côte d'Azur. France.

Master: R. Deriche, Advanced Image Processing Techniques, 12 ETD, M1 International CBB & Ubinet, Université Côte d'Azur, France.

Master: T. Papadopoulo, *3D Computer Vision*, 12 ETD, M1 International Ubinet, Université Côte d'Azur. France.

Master: T. Papadopoulo, *Inverse Problems in Brain Functional Imaging*, 36 ETD, M2 "Computational Biology and Biomedicine", Université Côte d'Azur. France.

Master: T. Papadopoulo, *Inverse problems for brain functional imaging*, 24 ETD, M2, Mathématiques, Vision et Apprentissage, ENS Cachan, France.

Master: D. Wassermann, *Fundamentals of Computer Science*, 36 ETD, M2 "Computational Biology and Biomedicine", Université Côte d'Azur. France.

Master: D. Wassermann, *Machine Learning in Neuroimaging*, 36 ETD, National University of the South, Argentina.

10.2.2. Supervision

PhD defended [13]: Rutger Fick, "Microstructure Recovery via dMRI", Université Côte d'Azur. Supervisor: Rachid Deriche.

PhD defended [12]: Kai Dang, "Modeling and characterizing electrical conductivity for cochlear implantation", started Dec. 2013, Université Université Côte d'Azur. Supervisor: Maureen Clerc.

PhD defended [15]: Marco Pizzolato, "Diffusion & Perfusion MRI: From bench to bedside" started Dec. 2013, Université Côte d'Azur. Supervisor: Rachid Deriche.

PhD defended [11]: Brahim Belaoucha, "Using diffusion MR information to reconstruct networks of brain activations from MEG and EEG measurements", Université Côte d'Azur, started Oct. 2013. Supervisor: Théodore Papadopoulo.

PhD defended [14]: Christos Papageorgakis, "Patient-specific conductivity models: characterization of the skull bones", Université Côte d'Azur. Supervisor: Juliette Leblond, Co-supervisor: Maureen Clerc

PhD defended: Lorraine Perronnet, "Combining EEG and FMRI for Neurofeedback", Université Rennes 1. Supervisors: Christian Barillot and Anatole Lécuyer, Co-supervisor: Maureen Clerc.

PhD in progress: Mouloud Kachouane, "Invariants and biomarqueurs in dMRI", started Oct. 2012. Supervisors: Rachid Deriche & L. Boumghar (USTHB, Algiers).

PhD in progress: Thinhinane Megherbi, "HARDI & High Order Tensors", started Sept. 2011. Supervisors: Rachid Deriche & L. Boumghar (USTHB, Algiers)

PhD in progress: Abib Alimi, "Diffusion & PLI" started Nov, 1st, 2016, Université Côte d'Azur. Supervisor: Rachid Deriche.

PhD in progress: Isa Costantini, "Brain Connectomics" started Oct. 1st, 2016, Université Côte d'Azur.. Supervisor: Rachid Deriche.

PhD in progress: Kostiantyn Maksymenko, "Inverse problem in EEG/MEG/SSEG: towards a better consideration of anatomo-functional constraints", Université Côte d'Azur,, started Oct. 2016. Supervisors: Théodore Papadopoulo and Maureen Clerc.

PhD in progress: Guillermo Gallardo Diez, "Connectivity-Based Brain Parcellation", started Nov. 2015, Université Côte d'Azur. Supervisors: D. Wassermann and R. Deriche

PhD in progress: Antonia Machlouzarides-Shalit, "Semantic Representations of Brain Anatomy", started Jun. 2017, Université Paris Sud. Supervisor: D. Wassermann

PhD in progress: Nathalie Gayraud, "Structured Dictionary Learning", Université Côte d'Azur, started November 2015. Supervisor: Maureen Clerc.

PhD in progress: Federica Turi, "User-adapted Brain Computer Interaction", Université Côte d'Azur, started October 2016. Supervisor: Maureen Clerc.

Master: Paul Görlach, "Rotational Invariants of Ternary Quartics", Supervised by E. Hubert and T. Papadopoulo.

Master: Gaston Zanitti, "An ADMM Algorithm for Regularised Random Effect Representations of Anatomo-Functional Connectivity", Supervised by D. Wassermann.

10.2.3. Juries

- R. Deriche chaired the HDR jury of P. Montesinos at LIRMM, UMR 5506 CNRS - Université Montpellier, June 9, 2017.
- R. Deriche chaired the PhD jury of B. Belaoucha at Université Côte d'Azur, May 29, 2017.
- R. Deriche participated as a reviewer in the PhD jury of T.C.J. Dela Haije at TU/e Eindhoven University of Technology, May 16, 2017.
- R. Deriche participated as a reviewer in the PhD Jury of R. Hedouin at Université de Rennes 1, June 12, 2017.
- R. Deriche participated in the PhD jury of C. Lian at Université de Technologie de Compiègne., Jan. 27, 2017.
- R. Deriche participated in the PhD jury of R. Fick at Université Côte d'Azur, March 10, 2017.
- R. Deriche participated in the PhD jury of M. Pizzolato at Université Côte d'Azur, Mars 31, 2017.
- M. Clerc chaired the PhD jury of Thomas Demarcy at Université Côte d'Azur in June 2017.
- M. Clerc participated as a reviewer in the PhD jury of Sara Sommariva at University of Genova, Italy, in February 2017.
- M. Clerc participated as a reviewer in the PhD jury of Emmanuelle Kristensen at Université Grenoble Alpes, in June 2017.
- M. Clerc participated as a reviewer in the PhD jury of Etienne Combrisson at Université de Lyon, in December 2017.
- M. Clerc participated in the PhD jury of Sara Rebagliati at University of Genova, Italy, in February 2017.
- M. Clerc participated in the PhD jury of L. Perronnet, at Rennes 1 University in September 2017.
- M. Clerc participated in the PhD jury of K. Dang, at Université Côte d'Azur in June 2017.
- M. Clerc participated in the PhD jury of C. Papageorgakis at Université Côte d'Azur in December 2017.
- M. Clerc participated in a BIM Masters 1 jury at Université Côte d'Azur.
- T. Papadopoulo participated in the PhD jury of B. Belaoucha at Université Côte d'Azur, May 29, 2017.
- T. Papadopoulo participated in a BIM Masters 1 jury at Université Côte d'Azur.
- D. Wassermann participated in the PhD jury of V. D. Nguyen, Paris Sud University, February 24, 2017

10.3. Popularization

- The P300 speller enjoyed a large publicity: on French TV *Le Magazine de la Santé* of France 5 in January 2017. It was featured in a newspaper article in La dépêche du midi in February 2017.
- M. Clerc gave interviews for Le Temps (Switzerland), Science et Vie Magazine on the topic of Brain-Computer Interfaces.

11. Bibliography

Major publications by the team in recent years

[1] C. BÉNAR, T. PAPADOPOULO, B. TORRÉSANI, M. CLERC. *Consensus Matching Pursuit for Multi-Trial EEG Signals*, in "Journal of Neuroscience Methods", 2009, vol. 180, pp. 161–170 [*DOI :* DOI: 10.1016/J.JNEUMETH.2009.03.005], http://www.sciencedirect.com/science/article/B6T04-4VWHVX5-2/2/e6ebdc581a60cde843503fe30f9940d1

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[8] S. HITZIGER, M. CLERC, S. SAILLET, C. BÉNAR, T. PAPADOPOULO. *Adaptive Waveform Learning: A Framework for Modeling Variability in Neurophysiological Signals*, in "IEEE Transactions on Signal Processing", April 2017, vol. 65, n° 16, pp. 4324–4338, http://dx.doi.org/10.1109/TSP.2017.2698415

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Doctoral Dissertations and Habilitation Theses

[11] B. BELAOUCHA. *Using diffusion MR information to reconstruct networks of brain activations from MEG and EEG measurements*, Université Côte d'Azur, May 2017, https://hal.inria.fr/tel-01534876

[12] K. DANG. *Electrical conduction models for cochlear implant stimulation*, Université Côte d'Azur, June 2017, https://hal.inria.fr/tel-01562277

[13] R. FICK. *Advanced dMRI signal modeling for tissue microstructure characterization*, Université Côte d'Azur, March 2017, https://tel.archives-ouvertes.fr/tel-01534104

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Articles in International Peer-Reviewed Journals

[16] U. FERIZI, B. SCHERRER, T. SCHNEIDER, M. ALIPOOR, O. EUFRACIO, R. H. FICK, R. DERICHE, M. NILSSON, A. K. LOYA-OLIVAS, M. RIVERA, D. H. POOT, A. RAMIREZ-MANZANARES, J. L. MARROQUIN, A. ROKEM, C. PÖTTER, R. F. DOUGHERTY, K. SAKAIE, C. WHEELER-KINGSHOTT, S. K. WARFIELD, T. WITZEL, L. L. WALD, J. G. RAYA, D. C. ALEXANDER. *Diffusion MRI microstructure models with in vivo human brain Connectom data: results from a multi-group comparison*, in "NMR in Biomedicine", September 2017, vol. 30, n^{o} 9 [*DOI :* 10.1002/NBM.3734], https://hal.archives-ouvertes.fr/hal-01500472

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