Activity Report 2016

Project-Team ATHENA

Computational Imaging of the Central Nervous System

RESEARCH CENTER
Sophia Antipolis - Méditerranée

THEME
Computational Neuroscience and Medecine

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

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1. Members

Research Scientists

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Demian Wassermann [Inria, Researcher]

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Jeremy Frey [Inria, from Aug 2016 to Sept 2016]
Amandine Audino [Inria, from Oct 2016]

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Others

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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 Anatomical 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 anatomical 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 Anatomical 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 major anatomical 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 anatomical 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 [90], Merboldt et al [94] and Taylor et al [103]. 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) [102], [72]. Historically, the first model in dMRI is the 2nd order diffusion tensor (DTI) [70], [69] 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 [91], [80]. 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 [93] and [92]).

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 [100], [101], [63], [62], [98] 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 [79]. They are at the core of our probabilistic and deterministic tractography algorithms devised to best exploit the full distribution of the fiber ODF (see [76], [5] and [77],[6]).

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 [109], [110] or 4th order Tensor Model [68]. For more details, we refer the reader to our articles in [81], [100] where we review HOT models and to our articles in [92], 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) [84].

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 [62], [63]. 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 [4], these imaging modalities raise a large amount of mathematical and computational challenges at the core of the research we develop at ATHENA [83], [100].

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 [75]. 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 [95].

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 [95], [73], [74]. 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 [95], [73], [74].

We have also contributed to design optimal acquisition schemes for single and multiple q-shell experiments. In particular, the method proposed in [4] 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 [82]

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

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

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 [64], AxCaliber [65] 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 [67], [66], the Solid Harmonic (SoH) basis [78], the Simple Harmonic Oscillator based Reconstruction and Estimation (SHORE) basis [96] and more recent Mean Apparent Propagator or MAP-MRI basis [97].

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 [7].

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 [8]. Using additional a priori anatomical [11] 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 [3].
- 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 [89], [10] 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 major anatomical imaging modality that will be considered to recover the CNS connectivity.

4.2. Applications of M/EEG

Applications of EEG and MEG:
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

R. Deriche and the ATHENA team has been awarded by an ERC Advanced Grant from the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation program (ERC AdG agreement No 694665 "Computational Brain Connectivity Mapping" started on Sept. 1st, 2016.)

Guillermo Guallardo, PhD has been awarded by a Merit Abstract Award by the 2016 OHBM Annual Meeting in Geneva, Switzerland for his work entitled *Efficient Population-Representative Whole-Cortex Parcellation Based on Tractography* [34].

5.1.2. Press coverage

Brain-Computer Interfaces developped in Athena attracted attention of the media, at regional and national levels: Nice Matin, Le Dauphiné Libéré and Le Figaro Santé have published articles about our translational research on the P300 speller. This system enables severely disabled patients, who are deprived of voluntary motor control, to communicate by using only their visual attention.

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

6. New Software and Platforms

6.1. Coadapt P300 Stimulator

KEYWORDS: Health - Brain-Computer Interface
FUNCTIONAL DESCRIPTION

In the domain of Brain Computer Interfaces, extracting relevant features requires a precise timing of all events occurring in the system. In particular, when dealing with evoked responses as in the P300 speller, the timing of the visual stimulations must be well controlled. To alleviate some timing issues with the P300 speller initially provided with OpenViBE, we have implemented an external visual stimulator that allows to flash the visual targets, in a time-robust manner. In 2016 a new generation of this software has been coded, which will be released publicly in 2017. It is being tested outside of Inria by a few beta-testers.

- Participants: Nathanaël Foy, Dieter Devlaminck, Loic Mahe, Maureen Clerc, Théodore Papadopoulo, Emmanuel Maby and Jérémie Mattout
- Partner: INSERM
- Contact: Maureen Clerc
- http://openvibe.inria.fr/coadapt-p300-stimulator-tutorial/

6.2. DIPY

Diffusion Imaging in Python
KEYWORDS: MRI - Medical imaging
FUNCTIONAL DESCRIPTION

Dipy is a free and open source software project focusing mainly on diffusion magnetic resonance imaging (dMRI) analysis. Nonetheless, as we solve problems in dMRI some of the solutions are applicable to the greater medical imaging and image processing communities. See for example our registration and denoising tutorials.

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

6.3. The White Matter Query Language

KEYWORDS: Neuroanatomy - Diffusion MRI - Automatic Segmentation - DSL
FUNCTIONAL DESCRIPTION The White Matter Query Language (WMQL) is a technique to formally describe white matter tracts and to automatically extract them from diffusion MRI volumes. This query language allows us to construct a dictionary of anatomical definitions describing white matter tracts. The definitions include adjacent gray and white matter regions, and rules for spatial relations. This enables the encoding of anatomical knowledge of the human brain white matter as well as the automated coherent labeling of white matter anatomy across subjects.

- Participants: Demian Wassermann
- Contact: Demian Wassermann
- URL:http://tract-querier.readthedocs.org/en/latest/

6.4. FindSources3D

KEYWORDS: Health - Neuroimaging - Visualization - Medical - Image - Processing
FUNCTIONAL DESCRIPTION

FindSources3D is a Matlab software program dedicated to the resolution of inverse source problems in electroencephalogrphy (EEG). From pointwise measurements of the electric potential, numerically obtained or taken by electrodes on the scalp, FindSources3D estimates pointwise dipolar current sources within the brain.

- Participants: Juliette Leblond, Maureen Clerc, Théodore Papadopoulo and Jean Paul Marmorat
- Contact: Juliette Leblond
- URL: http://www-sop.inria.fr/apics/FindSources3D/en/index.html

6.5. High Performance Diffusion MRI

KEYWORDS: Health - Neuroimaging - Medical imaging
FUNCTIONAL DESCRIPTION

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. These algorithms and software 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. This library has been transfered to the Company *Olea Medical*, where it will be at the heart of the new dMRI module to be included in the *Olea Sphere* platform.

- Participants: Aurobrata Ghosh, Théodore Papadopoulo, Rachid Deriche and Demian Wassermann
- Contact: Rachid Deriche

6.6. MedInria

KEYWORDS: Segmentation - Health - DWI - Visualization - Medical imaging
SCIENTIFIC DESCRIPTION

It aims at creating an easily extensible platform for the distribution of research algorithms developed at Inria for medical image processing. This project has been funded by the D2T (ADT MedInria-NT) in 2010 and renewed in 2012. The Visages team leads this Inria national project and participates in the development of the common core architecture and features of the software as well as in the development of specific plugins for the team's algorithm.
FUNCTIONAL DESCRIPTION

MedInria is a free software platform dedicated to medical data visualization and processing.

- Participants: Jaime Garcia Guevara, Théodore Papadopoulo, Olivier Commowick, Rene-Paul Debroize, Guillaume Pasquier, Laurence Catanese, Olivier Commowick, Alexandre Abadie, Benoit Bleuze, Clement Philipot, Fatih Arslan, Florian Vichot, John Stark, Julien Wintz, Loïc Cadour, Maxime Sermesant, Michael Knopke, Nicolas Toussaint, Olivier Clatz, Pierre Fillard, Sergio Medina, Stephan Schmitt and Hakim Fadil
- Partners: HARVARD Medical School - IHU - LIRYC - IHU - Strasbourg - NIH
- Contact: Olivier Commowick
- URL: http://med.inria.fr

6.7. OpenMEEG

KEYWORDS: Health - Neuroimaging - Medical imaging
FUNCTIONAL DESCRIPTION

OpenMEEG provides state-of-the art tools for processing EEG and MEG data. It incorporates a newly proposed, symmetric BEM for the forward problem, and a distributed source inverse problem, with three different types of regularizations, two of which are original, based on norms of the surface gradient of the source distribution. OpenMEEG is a free, open software written in C++, and can be accessed either through a command line interface or through a user-friendly interface. OpenMEEG is being used for functional neuroimaging, through third-party software (Brainstorm and Fieldtrip), as can be noticed by the citations to our articles [9] and [89].

- Participants: Théodore Papadopoulo, Maureen Clerc, Alexandre Gramfort, Emmanuel Olivi, Kai Dang, Geoffroy Adde, Perrine Landreau, Renaud Keriven and Jan Kybic
- Contact: Théodore Papadopoulo
- URL: http://openmeeg.github.io/

6.8. OpenVIBE

KEYWORDS: Neurosciences - Interaction - Virtual reality - Health - Real time - Neurofeedback - Brain-Computer Interface - EEG - 3D interaction
FUNCTIONAL DESCRIPTION

OpenViBE is a software platform for real-time neurosciences (that is, for real-time processing of brain signals). It can be used to acquire, filter, process, classify and visualize brain signals in real time from various signal sources. OpenViBE is free and open source software. It works on Windows and Linux operating systems.

- Participants: Yann Renard, Anatole Lécuyer, Fabien Lotte, Bruno Renier, Vincent Delannoy, Laurent Bonnet, Baptiste Payan, Jozef Legeny, Jussi Tapio Lindgren, Alison Cellard, Loic Mahe, Guillaume Serriere, Marsel Mano, Maureen Clerc, Théodore Papadopoulo, Laurent Bougrain, Jeremy Frey and Nathanaël Foy
- Partners: CEA-List - GIPSA-Lab - INSERM
- Contact: Anatole Lécuyer
- URL: http://openvibe.inria.fr

7. New Results

7.1. Modeling in Diffusion MRI

7.1.1. Computational brain connectivity mapping: A core health and scientific challenge

Participant: Rachid Deriche.

One third of the burden of all the diseases in Europe is due to problems caused by diseases affecting brain. Although exceptional progress have been obtained for exploring the brain during the past decades, it is still terra-incognita and calls for specific efforts in research to better understand its architecture and functioning. To take up this great challenge of modern science and to solve the limited view of the brain provided just by one imaging modality, this article advocates the idea developed we develop in my research group of a global approach involving new generation of models for brain connectivity mapping and strong interactions between structural and functional connectivities. Capitalizing on the strengths of integrated and complementary non invasive imaging modalities such as diffusion Magnetic Resonance Imaging (dMRI) and Electro and Magneto-Encephalography (EEG & MEG) will contribute to achieve new frontiers for identifying and characterizing structural and functional brain connectivities and to provide a detailed mapping of the brain connectivity, both in space and time. Thus leading to an added clinical value for high impact diseases with new perspectives in computational neuro-imaging and cognitive neuroscience.

The work leading to the objectives listed in this article has received funding from the European Research Council (ERC) under the European Union's Horizon 2020 research and innovation program (ERC Advanced Grant agreement No 694665 started on Sept. 1st, 2016).

This article has been published in [15].

7.1.2. A survey of current trends in diffusion MRI for structural brain connectivity

Participants: Aurobrata Ghosh [University College London, UK], Rachid Deriche.

In this work, we review the state of the art in diffusion magnetic resonance imaging (dMRI) and we present current trends in modelling the brain's tissue microstructure and the human connectome. dMRI is today the only tool that can probe the brain's axonal architecture in vivo and non-invasively, and has grown in leaps and bounds in the last two decades since its conception. A plethora of models with increasing complexity and better accuracy have been proposed to characterise the integrity of the cerebral tissue, to understand its microstructure and to infer its connectivity. Here, we discuss a wide range of the most popular, important and well-established local microstructure models and biomarkers that have been proposed from these models. Finally, we briefly present the state of the art in tractography techniques that allow us to understand the architecture of the brain's connectivity.

This work has been published in [17].

7.1.3. Multi-Spherical Diffusion MRI: Exploring Diffusion Time Using Signal Sparsity

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 t - 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 qt-space, which we call qt-dMRI. To drastically reduce the number of diffusionweighted images (DWIs) we need to represent the qt-space, we regularize the fitting of qt-dMRI by imposing both signal smoothness and sparsity. As the main contribution, qt-dMRI provides the framework for estimating time-dependent q-space indices (qt-indices), providing new means for studying subdiffusion 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 excellent reproducibility of estimated qt-index values and trends. In the hopes of opening up new t-dependent venues of studying nervous tissues, qt-dMRI is the first of its kind in being specifically designed to provide open interpretation of the qt-diffusion signal.

This work has been partly published in [31]. The test-retest study has been submitted to ISMRM'17 and an extended version has been submitted to Neuroimage.

7.1.4. Noise Floor Removal via Phase Correction of Complex Diffusion-Weighted Images: Influence on DTI and q-space Metrics

Participants: Marco Pizzolato, Rutger Fick, Timothé Boutelier [Olea Medical, La Ciotat], Rachid Deriche.

The non-Gaussian noise distribution in magnitude Diffusion-Weighted Images (DWIs) can severely affect the estimation and reconstruction of the true diffusion signal. As a consequence, also the estimated diffusion metrics can be biased. In this work, we study the effect of phase correction, a procedure that re-establishes the Gaussianity of the noise distribution in DWIs by taking into account the corresponding phase images. We quantify the debiasing effects of phase correction in terms of diffusion signal estimation and calculated metrics. We perform in silico experiments based on a MGH Human Connectome Project dataset and on a digital phantom, accounting for different acquisition schemes, diffusion-weightings, signal to noise ratios, and for metrics based on Diffusion Tensor Imaging and on Mean Apparent Propagator Magnetic Resonance Imaging, i.e. q-space metrics. We show that phase correction is still a challenge, but also an effective tool to debias the estimation of diffusion signal and metrics from DWIs, especially at high b-values.

This work has been published in [39] and [60].

7.2. Tissue Microstructures features recovery & applications

7.2.1. MAPL: Tissue microstructure estimation using Laplacian-regularized MAP-MRI and its application to HCP data

Participants: Rutger Fick, Demian Wassermann, Emanuel Caruyer, Rachid Deriche.

The recovery of microstructure-related features of the brain's white matter is a current challenge in diffusion MRI. To robustly estimate these important features from diffusion MRI data, we propose to analytically regularize MAP-MRI's coefficient estimation using the norm of the Laplacian of the reconstructed signal. We first compare our approach, which we call MAPL, with competing state-of-the-art functional basis approaches. We show that it outperforms the original MAP-MRI implementation and the recently proposed modified Spherical Polar Fourier (mSPF) basis with respect to signal fitting, EAP and ODF reconstruction in noisy, sparsely sampled data of a physical phantom with reference gold standard data. Then, to reduce the variance of parameter estimation using multi-compartment tissue models, we propose to use MAPL's signal fitting and extrapolation as a preprocessing step. We study the effect of MAPL on the estimation of axon diameter using a simplified Axcaliber model and axonal dispersion using the Neurite Orientation Dispersion and Density Imaging (NODDI) model. We show the positive effect of using it as a preprocessing step in estimating and reducing the variances of these parameters in the Corpus Callosum of six different subjects of the MGH Human Connectome Project. Finally we correlate the estimated axon diameter, dispersion and restricted volume fractions with Fractional Anisotropy (FA) and clearly show that changes in FA significantly correlate with changes with all estimated parameters. Overall, we illustrate the potential of using a well-regularized functional basis together with multi-compartment approaches to recover important microstructure tissue parameters with much less variability, thus contributing to the challenge of better understanding microstructure-related features of the brain's white matter.

This work has been published in [16]

7.2.2. Quantifying White Matter Microstructure with a Unified Spatio-Temporal Diffusion Weighted MRI Continuous Representation

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

A current problem Diffusion MRI (dMRI) based microscopy under the narrow pulse approximation is how to best exploit the 4D (q-space + diffusion time) nature of the signal. Assaf et al. showed that exploring the dMRI attenuation at different diffusion times provides information on the distribution of axonal diameters within a voxel in their seminal work: AxCaliber. However, AxCaliber requires knowing beforehand the predominant orientation of the axons within the analyzed volume to adjust the q-space sampling accordingly. In this work, we show that our novel sparse representation of the 3D+t dMRI signal, enables the recovery of axonal diameter distribution parameters without the need to know the axonal direction at acquisition time.

This work has been published in [61]

7.2.3. A sensitivity analysis of Q-space Indices with respect to changes in axonal diameter, dispersion and tissue composition

Participants: Rutger Fick, Marco Pizzolato, Demian Wassermann, Mario Zuccheli [Dpt of Computer Science, University of Verona], Gloria Menegaz [Dpt of Computer Science, University of Verona], Rachid Deriche.

In Diffusion MRI, q-space indices are scalar quantities that describe properties of the ensemble average propagator (EAP). Their values are often linked to the axonal diameter – assuming that the diffusion signal originates from inside an ensemble of parallel cylinders. However, histological studies show that these assumptions are incorrect, and axonal tissue is often dispersed with various tissue compositions. Direct interpretation of these q-space indices in terms of tissue change is therefore impossible, and we must treat them as as scalars that only give non-specific contrast – just as DTI indices. In this work, we analyze the sensitivity of q-space indices to tissue structure changes by simulating axonal tissue with changing axonal diameter, dispersion and tissue compositions. Using human connectome project data we then predict which indices are most sensitive to tissue changes in the brain. We show that, in both multi-shell and single-shell (DTI) data, q-space indices have higher sensitivity to tissue changes than DTI indices in large parts of the brain. Based on these results, it may be interesting to revisit older DTI studies using q-space indices as a marker for pathology.

This work has been published in [32]

7.2.4. Assessing the feasibility of estimating axon diameter using diffusion models and machine learning

Participants: Rutger Fick, Neda Sepasian [Eindhoven University of Technology, The Netherlands], Marco Pizzolato, Andrada Ianus [Centre for Medical Image Computing, Dept. of Computer Science, UCL, London, UK], Rachid Deriche.

Axon diameter estimation has been a focus of the diffusion MRI community for the past decade. The main argument has been that while diffusion models always overestimate the true axon diameter, their estimation still correlates with changes in true value. Until now, this remains more as a discussion point. The aim of this paper is to clarify this hypothesis using a recently acquired cat spinal cord data set, where the diffusion MRI signal of both a multi-shell and Ax- Caliber acquisition have been registered with the underlying histology values. We find that the axon diameter as estimated by signal models and AxCaliber does not correlate with their true sizes for axon diameters smaller than 3 microns. On the other hand, we also train a random forest machine learning algorithm to map signal-based features to histology values of axon diameter and volume fraction. The results show that, in this dataset, this approach leads to a more reliable estimation of physically relevant axon diameters than using sophisticated diffusion models.

This work has been submitted to ISBI'2017.

7.2.5. Rotational Invariants of Ternary Quartics

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

This work has been developed in the framework of an "Action Transverse" with the AROMATH team (see section 9.1.1). It aims at creating building blocks for biomarkers for the case of a representation of the diffusion information (acquired using HARDI sequences) as a ternary quartic. Previous work in the team had some drawbacks such as instabilities in the non-polynomial formulae [99] or missing guarantees of the polynomial results [85] (e.g. unknown completeness or impossibility to establish the redundancy of the obtained expressions). This work proposes an alternative construction based on rational expressions and shares some of the best characteristics of the two previous approaches: the set is complete and generative – and thus also generates polynomial invariants –, the number of generators is close to minimal (13 instead of 12 and the expression relating these 13 formulae is known), and has an improved stability compared to the non-polynomial approach. The obtained formulae are furthermore nested making their computation much more effective than previous approaches. Furthermore, the method is generic and can in theory be expanded to higher polynomial degrees.

7.3. Towards microstructural based tractography

7.3.1. White matter tractography guided by anatomical and microstructural priors

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

Diffusion-weighted magnetic resonance imaging is a unique imaging modality sensitive to the microscopic movement of water molecules in biological tissues. By characterizing the movement of water molecules, it is possible to infer the macroscopic neuronal pathways of the brain. The technique, so-called tractography, had become the tool of choice to study non-invasively the human brain's white matter in vivo. For instance, it has been used in neurosurgical intervention planning and in neurodegenerative diseases monitoring. In this thesis, we report biases from current tractography reconstruction and suggest methods to reduce them. We first use anatomical priors, derived from a high resolution T1-weighted image, to guide tractography. We show that knowledge of the nature of biological tissue helps tractography to reconstruct anatomically valid neuronal pathways, and reduces biases in the estimation of complex white matter regions. We then use microstructural priors, derived from the state-of-the-art diffusionweighted magnetic resonance imaging protocol, in the tractography reconstruction process. This allows tractography to follow the movement of water molecules not only along neuronal pathways, but also in a microstructurally specific environment. Thus, the tractography distinguishes more accurately neuronal pathways and reduces reconstruction errors. Moreover, it provides the mean to study white matter microstructure characteristics along neuronal pathways. Altogether, we show that anatomical and microstructural priors used during the tractography process improve brain's white matter reconstruction

This work has been published in [12].

7.3.2. Microstructure driven tractography in the human brain

Participants: Gabriel Girard [SCIL, Sherbrooke University, CA], Alessandro Daducci [SP Lab - Laboratoire de Traitement du signal, EPFL], Kevin Whittingstall [SCIL, Sherbrooke University, CA], Rachid Deriche, Maxime Descoteaux [SCIL, Sherbrooke University, CA], Demian Wassermann.

Diffusion-weighted (DW) magnetic resonance imaging (MRI) tractography has become the tool of choice to probe the human brain's white matter (WM) in vivo. However, the relationship between the resulting streamlines and underlying WM microstructure characteristics, such as axon diameter, remains poorly understood. In this work, we reconstruct human brain fascicles using a new approach to trace WM fascicles while simultaneously characterizing the apparent distribution of axon diameters within the fascicle. This provides the mean to estimate the microstructure characteristics of fascicles while improving their reconstruction in complex tissue configurations.

This work has been published in [24].

7.3.3. Reducing Invalid Connections with Microstructure Driven Tractography

Participants: Gabriel Girard [SCIL, Sherbrooke University, CA], Kevin Whittingstall [SCIL, Sherbrooke University, CA], Alessandro Daducci [SP Lab - Laboratoire de Traitement du signal, EPFL], Jean-Philippe Thiran [SP Lab - Laboratoire de Traitement du signal, EPFL], Laurent Petit [GIN - IMN UMR 5293 CNRS CEA Université de Bordeaux], Rachid Deriche, Demian Wassermann, Maxime Descoteaux [SCIL, Sherbrooke University, CA].

Diffusion-weighted imaging (DWI) tractography has become the tool of choice to probe the human brain's white matter (WM) in vivo. However, tractography algorithms produce a large number erroneous/invalid streamlines largely due to complex ambiguous local fiber configurations (e.g. crossing, kissing or fanning). Moreover, the relationship between the resulting streamlines and the underlying WM microstructure characteristics, such as axon diameter, remains poorly understood. The distinctive aspect of our tractography algorithm from previous methods is the active use of microstructure information about fascicles during the tracking. This enables us to solve areas of complex tissue configuration and separate parallel fascicles with different microstructure characteristics, hence improving the overall tractography process.

This work has been published in [35]

7.3.4. Quantitative evaluation of Fiber Orientations Extractions

Participants: Thinhinane Megherbi [LRPE, USTHB, Alger], Gabriel Girard [SCIL, Sherbrooke University, CA], Maxime Descoteaux [SCIL, Sherbrooke University, CA], Fatima Oulebsir Boumghar [LRPE, USTHB, Alger], Rachid Deriche.

Recovering the fiber orientations in each voxel constitutes an important step for the fiber tracking algorithms. In fact, the reliability of the resulted connectivity depends on how well the local fiber orientations were extracted. Based on the tractography results we evaluated and compared different methods of fiber orientations extraction. Thus, we analyzed quantitatively the resulted connectivity by using the Tractometer tool. This later allows by measuring a number of metrics to quantify the connections reliability and the tractography performance. All the methods of fiber orientations extraction were evaluated on two types of tractography algorithms, deterministic and probabilistic algorithms. Furthermore, all of these methods have been executed on two types of data, high angular resolution data acquired with 60 gradient directions and low angular resolution data, acquired with 30 gradient directions. These two types of data were corrupted with a Ricien noise of ratio SNR=20, 10. In this work, we present the results obtained by our validation and comparison work.

This work has been published in [37]

7.4. Perfusion MRI & PLI

7.4.1. Unveiling the dispersion kernel in DSC-MRI by means of dispersion-compliant bases and control point interpolation techniques

Participants: Marco Pizzolato, Rutger Fick, Timothé Boutelier [Olea Medical, La Ciotat], Rachid Deriche.

In DSC-MRI the presence of dispersion affects the estimation, via deconvolution, of the residue function that characterizes the perfusion in each voxel. Dispersion is descibed by a Vascular Transport Function (VTF) which knolewdge is essential to recover a dispersion-free residue function. State-of-the-art techniques aim at characterizing the VTF but assume a specific shape for it, which in reality is unknown. We propose to estimate the residue function without assumptions by means of Dispersion-Compliant Bases (DCB). We use these results to find which VTF model better describes the in-vivo data for each tissue type by means of control point interpolation approaches.

This work has been published in [57].

7.4.2. Elucidating dispersion effects in perfusion MRI by means of dispersion-compliant bases

Participants: Marco Pizzolato, Rutger Fick, Timothé Boutelier [Olea Medical, La Ciotat], Rachid Deriche.

Dispersion effects in perfusion MRI data have a relevant influence on the residue function computed from deconvolution of the measured arterial and tissular concentration time-curves. Their characterization allows reliable estimation of hemodynamic parameters and can reveal pathological tissue conditions. However the time-delay between the measured concentration time-curves is a confounding factor. We perform deconvolution by means of dispersion-compliant bases, separating dispersion from delay effects. In order to characterize dispersion we introduce shape parameters, such as the dispersion time and index. We propose a new formulation for the dispersed residue function and perform in-silico experiments that validate the reliability of our approach against the block-circulant Singular Value Decomposition. We successfully apply the approach to stroke MRI data and show that the calculated parameters are coherent with physiological considerations, highlighting the importance of dispersion as an effect to be measured rather than discarded.

This work has been published in [38].

7.4.3. Improved vascular transport function characterization in DSC-MRI via deconvolution with dispersion-compliant bases

Participants: Marco Pizzolato, Rutger Fick, Timothé Boutelier [Olea Medical, La Ciotat], Rachid Deriche.

Bolus dispersion phenomena affect the residue function computed via deconvolution of DSC-MRI data. Indeed the obtained effective residue function can be expressed as the convolution of the true one with a Vascular Transport Function (VTF) that characterizes the dispersion. The state-of-the-art technique CPI+VTF allows to estimate the actual residue function by assuming a model for the VTF. We propose to perform deconvolution representing the effective residue function with Dispersion-Compliant Bases (DCB) without assumptions on the VTF, and then apply the CPI+VTF on DCB results. We show that DCB improve robustness to noise and allow to better characterize the VTF.

This work has been published in [60].

7.4.4. Perfusion Deconvolution in DSC-MRI with Dispersion-Compliant Bases

Participants: Marco Pizzolato, Timothé Boutelier [Olea Medical, La Ciotat], Rachid Deriche.

Perfusion imaging of the brain via Dynamic Susceptibility Contrast MRI (DSC-MRI) allows characterization of tissue perfusion by recovering the tissue impulse response function and scalar parameters such as the cerebral blood flow (CBF), blood volume (CBV) and mean transit time (MTT). However, the presence of bolus dispersion causes the data to reflect macrovascular properties, in addition to tissue perfusion. In this case, when performing deconvolution of the measured arterial and tissue concentration time-curves it is only possible to recover the effective, i.e. dispersed, response function and parameters. We introduce Dispersion-Compliant Bases (DCB) to represent the response function in the presence and absence of dispersion. We perform in silico and in vivo experiments, and show that DCB deconvolution outperforms oSVD and the state-of-the-art CPI+VTF techniques in the estimation of effective perfusion parameters, regardless of the presence and amount of dispersion. We also show that DCB deconvolution can be used as a pre-processing step to improve the estimation of dispersion-free parameters computed with CPI+VTF, which employs a model of the vascular transport function to characterize dispersion. Indeed, in silico results show a reduction of relative errors up to 50% for dispersion-free CBF and MTT. Moreover, the DCB method recovers effective response functions that comply with healthy and pathological scenarios, and offers the advantage of making no assumptions about the presence, amount, and nature of dispersion.

This work has been submitted for publication in Medical Image Analysis.

7.4.5. Solving the inclination sign ambiguity in three dimensional polarized light imaging with a PDE-based method

Participants: Abib Olushola Yessouffou 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 postmortem human brain or heart at a sub-millimeter 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 submitted to ISBI'2017.

7.5. Structural Connectivity Network

7.5.1. Extracting the Core Structural Connectivity Network: Guaranteeing Network Connectedness Through a Graph-Theoretical Approach

Participants: Demian Wassermann, Dorian Mazauric [ABS Project Team], Guillermo Gallardo Diez, Rachid Deriche.

In this work, we present a graph-theoretical algorithm to extract the connected core structural connectivity network of a subject population. Extracting this core common network across subjects is a main problem in current neuroscience. Such network facilitates cognitive and clinical analyses by reducing the number of connections that need to be explored. Furthermore, insights into the human brain structure can be gained by comparing core networks of different populations. We show that our novel algorithm has theoretical and practical advantages. First, contrary to the current approach our algorithm guarantees that the extracted core subnetwork is connected Girardagreeing with current evidence that the core structural network is tightly connected. Second, our algorithm shows enhanced performance when used as feature selection approach for connectivity analysis on populations.

This work has been published in [26].

7.5.2. Groupwise Structural Parcellation of the Cortex: A Sound Approach Based on Logistic Models

Participants: Guillermo Gallardo Diez, Rutger Fick, William Wells, Rachid Deriche, Demian Wassermann.

Current theories hold that brain function is highly related with 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. 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 [33] and an extended version has been submitted to Neuroimage.

7.5.3. Efficient Population-Representative Whole-Cortex Parcellation Based on Tractography

Participants: Guillermo Gallardo Diez, Rachid Deriche, Demian Wassermann.

The human brain is arranged in areas based on criteria such as cytoarchitecture or extrinsic connectivity. Current hypotheses attribute specialized functions to several areas of this patchwork. Hence, parcellating the cortex into such areas and characterizing their interaction is key to understanding brain function. Diffusion MRI enables the exploration of physical connections through axonal bundles, namely extrinsic connectivity. Current theories hold that brain function is determined by extrinsic connectivity. However, obtaining a population-representative parcellation based on extrinsic connectivity remains challenging (Jbabdi 2013). Particularly, whole-cortex parcellation methods (Moreno-Dominguez 2014; Parisot 2015) are computationally expensive and need tuning of several parameters. Our main contribution is an efficient technique to create single-subject and population-representative parcellations based on tractography. Our method creates a dendrogram using only one parameter: the minimum size of each parcel. Then, by choosing cutting criteria, we can explore different parcellation granularities without recomputing the dendrogram. Experiments show that our parcellations are consistent within subjects with anatomical (Desikan 2006) and functional (Barch 2013) parcellations existent in the literature.

This work has been published in [34].

7.6. Clinical and Neurocognitive Applications of Diffusion MRI

7.6.1. 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], Rutger Fick, Demian Wassermann, Romain Valabregue [ICM, CENIR, Paris], Richard Levy [ICM, CENIR, Paris], Isabelle Arnulf [ICM, CENIR, Paris], Stéphane Lehericy [ICM, CENIR, Paris], 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. Here we used mean apparent propagator to investigate white matter changes in KLS and correlated diffusion changes with apathy scores. Results showed that the corpus callosum was involved in KLS during episodes and mean RTAP measures in the corpus callosum correlated with apathy scores. Results were in accordance with known motivation-based circuits involving the orbitomedial frontal cortex.

This work has been submitted to ISMRM'2017.

7.6.2. Comparison of Biomarkers in Transgenic Alzheimer Rats Using Multi-shell Diffusion MRI

Participants: Rutger Fick, Madelaine Daianu [Imaging Genetics Center, Mark & Mary Stevens Neuroimaging & Informatics Institute, USC, USA], Marco Pizzolato, Demian Wassermann, Russel Jacobs [Imaging Genetics Center, Mark & Mary Stevens Neuroimaging & Informatics Institute, USC, USA], Paul Thompson [Imaging Genetics Center, Mark & Mary Stevens Neuroimaging & Informatics Institute, USC, USA], Terrence Town [Imaging Genetics Center, Mark & Mary Stevens Neuroimaging & Informatics Institute, USC, USA], Rachid Deriche.

In this study, we assessed the evolution of diffusion MRI (dMRI) derived markers from different white matter models as progressive neurodegeneration occurs in transgenic Alzheimer rats (TgF344-AD) at 10, 15 and 24 months. We compared biomarkers reconstructed from Diffusion Tensor Imaging (DTI), Neurite Orientation Dispersion and Density Imaging (NODDI) and Mean Apparent Propagator (MAP)-MRI in the hippocampus, cingulate cortex and corpus callosum using multi-shell dMRI. We found that NODDI's dispersion and MAP-MRI's anisotropy markers consistently changed over time, possibly indicating that these measures are sensitive to age-dependent neuronal demise due to amyloid accumulation. Conversely, we found that DTI's mean diffusivity, NODDI's isotropic volume fraction and MAP-MRI's restriction-related metrics all followed a two-step progression from 10 to 15 months, and from 15 to 24 months. This two-step pattern might be linked with a neuroinflammatory response that may be occuring prior to, or during microstructural breakdown. Using our approach, we are able to provide for the first time-preliminary and valuable insight on relevant biomarkers that may directly describe the underlying pathophysiology in Alzheimer's disease.

This work has been published in [30].

7.7. MEEG and Diffusion MRI

7.7.1. Cortical surface parcellation via dMRI using mutual nearest neighbor condition

Participants: Brahim Belaoucha, Maureen Clerc, Théodore Papadopoulo.

This work aims at parcellating the cortical surface from individual anatomy. With respact to previous works, it works for the whole brain and produces connected patches. The parcellation is obtained using the Mutual Nearest Neighbor (MNN) criterion to obtain regions with similar structural connectivity. The structural connectivity is obtained by applying a probabilistic tractography on the diffusion MRI (dMRI). Several similarity measures of connectivity are compared. The results of our method are compared to some of the atlases that can be found in the literature. We show that these atlases have lower similarity of structural connectivity than the proposed algorithm implying that the regions of the atlases may have lower functional homogeneity.

This work has been published in [27].

7.7.2. Iterative estimation of focal sources and their interactions constrained by dMRI

Participants: Brahim Belaoucha, Mouloud Kachouane, Théodore Papadopoulo.

This work aims at further exploiting the dMRI constraints: not only sources are constrained anatomically by patches (extracted by the method of the previous paragraph) but their dynamical behaviour is constrained by a brain network extracted from an individual dMRI. The framework reconstructs spatially localized sources from Magnetoencephalogra-phy (MEG)/Electroencephalography (EEG) using spatiotemporal constraints extracted from dMRI. The spatial reconstruction is based on our previous work on patch reconstruction [71]. The source dynamics are represented by a Multivariate Autoregressive (MAR) model whose matrix elements are constrained by the anatomical connectivity obtained from dMRI. The framework assumes that the whole brain dynamic follows a constant MAR model in a time window of interest. The source activations and the MAR model parameters are estimated iteratively. The proposed framework outperforms the two-stage approaches which have traditionally been used to estimate source interactions. Such approaches first reconstruct sources and then compute the MAR model for the localized sources. They showed good results when working in high

signal-to-noise ratio (SNR) settings, but fail in detecting the true interactions when working in low SNR. Our framework iteratively refines both the reconstruction and the MAR model in two steps: sources activations are first estimated for a given MAR model and then, the MAR model is estimated for a given source reconstruction. These two steps are repeated until a stopping criterion is achieved. The work is exploratory in nature and for now focuses on simulations made with real MR data. We could confirm that accurate reconstructions and MAR models can be obtained with our method in both high and low noise levels.

This work has been published in [28], [21].

7.8. MEG, EEG

7.8.1. ECoG

Participants: Maureen Clerc, Analisa Pascarella [CNR-IAC Roma], Michele Piana [University of Genova].

Electrocorticography (ECoG) measures the distribution of the electrical potentials on the cortex produced by the neural currents. A full interpretation of ECoG data requires solving the ill-posed inverse problem of reconstructing the spatio-temporal distribution of the neural currents. This study addresses the ECoG source modeling developing a beamformer method. New method: We computed the lead-field matrix by using a novel routine provided by the OpenMEEG software. We performed an analysis of the numerical stability of the ECoG inverse problem by computing the condition number of the lead-field matrix for different configurations of the electrodes grid. We applied a Linear Constraint Minimum Variance (LCMV) beamformer to both synthetic data and a set of real measurements recorded during a rapid visual categorization task. For all considered grids the condition number indicates that the ECoG inverse problem is mildly ill-conditioned. For realistic SNR we found a good performance of the LCMV algorithm for both localization and waveforms reconstruction. Comparison with existing method: The flow of information reconstructed by analyzing real data seems consistent with both invasive monkey electrophysiology studies and non-invasive (MEG and fMRI) human studies. Despite a growing interest from the neuroscientific community, solving the ECoG inverse problem has not quite yet reached the level of systematicity found for EEG and MEG. Starting from an analysis of the numerical stability of the problem we considered the most widely utilized method for modeling neurophysiological data based on the beamformer method in the hope to establish benchmarks for future studies.

This work has been published in [18].

7.8.2. Conductivity estimation

Participants: Maureen Clerc, Christos Papageorgakis, Juliette Leblond [APICS project-team], Jean-Paul Marmorat [CMA Ecole des Mines Paritech].

Considering a geometry made of three concentric spherical nested layers, each with constant homogeneous conductivity, we establish a uniqueness result in inverse conductivity estimation, from partial boundary data in presence of a known source term. We make use of spherical harmonics and linear algebra computations, that also provide us with stability results and a robust reconstruction algorithm. As an application to electroencephalography (EEG), in a spherical 3-layer head model (brain, skull, scalp), we numerically estimate the skull conductivity from available data (electrical potential at electrodes locations on the scalp, vanishing current flux) and given pointwise dipolar sources in the brain. This work was supported by the Région Provence-Alpes-Côte d'Azur, France, and BESA GmbH, Germany.

This work has been published in [14] and [29].

7.8.3. Efficient lead field computation a la Reduced Basis Methods

Participants: Kostiantyn Maksymenko, Maureen Clerc, Théodore Papadopoulo.

Bioelectric source analysis in the human brain from scalp electroencephalography (EEG) signals is sensitive to geometry and conductivity properties of the different head tissues. These conductivities can vary a lot across subjects so non-invasive methods of conductivity estimation are required. To achieve this, we should have a possibility to compute a forward EEG problem solution for a large number of conductivity configurations. We propose a method of approximation of these solutions using a relatively small number of basis points, which will allow us to dramatically decrease required computing time.

7.9. Modeling electrical stimulation

7.9.1. Cochlear implants

Participants: Kai Dang, Maureen Clerc, Pierre Stahl [Oticon Medical], Dan Gnansia [Oticon Medical], Clair Vandersteen [Nice University Hospital], Nicolas Guevara [Nice University Hospital].

In cochlear implants, the hybrid common ground is a combination of a classic monopolar stimulation with a standard common ground. This new stimulation montage allows the current to return from both the non-stimulating electrodes on the electrode array and the reference electrode placed between the skull and scalp. In theory, this lead to reach a compromise between the current focality and the efficiency of the stimulation. Even if this stimulation type has already been adopted by some implant manufacturers, the 3D geometry of its current pathways remains to be studied. The study is two-fold. First, an in-vitro experiment aimed to measure the electrical field produced by the hybrid common ground stimulation. An electrode array of an XP implant (Oticon Medical, Neurelec) was placed in saline solution and the electrical field was recorded by a probe that moves along the programmed grid. During the stimulation, the current waveforms on all the grounding electrodes were also recorded. Second, an in-situ measurement was conducted. Another XP device was implanted into a human specimen. The same procedure as in the in-vitro measurement was performed to record, this time, the current waveforms only. The recorded two groups of current data were compared with each other to investigate how the current path is modified by the geometry of a human cochlea. The potential distribution measured during the in-vitro experiment was also compared with other stimulation types such as monopolar. The energy consumption of the stimulation was also computed from the collected data.

This work has been published in [58]. We thank the GRAPHDECO project-team for lending us THE 3D printer which was used in the in-vitro experiment.

7.10. Brain-Computer Interfaces

7.10.1. A new reference book in Brain-Computer Interfaces

Participants: Maureen Clerc, Laurent Bougrain [Neurosys project-team], Fabien Lotte [POTIOC project-team], All Ipl Bci-Lif Members.

Most of the results in Brain-Computer Interfaces are conducted in the context of the Inria Project-Lab BCI-LIFT (see contracts section). Researchers of this Inria Project-Lab (Maureen Clerc, Laurent Bougrain and Fabien Lotte) have edited a reference book in 2016 on the topic of Brain-Computer Intefaces. It consists of two volumes, “Foundations and Methods” (in French [54] and in English [1]) and “Technology and Applications” (in French [55] and in English [53]).

7.10.2. A Separability Marker Based on High-Dimensional Statistics for Classification Confidence Assessment

Participants: Nathalie Gayraud, Maureen Clerc, Nathanaël Foy, Alain Rakotomamonjy [University of Rouen].

This work provides a theoretical analysis framework for features that belong to the high dimensional Riemannian manifold of symmetric positive definite matrices. In non-invasive EEG-based Brain Computer Interfaces, such as the P300 speller, these are sample covariance matrices of the epoched EEG signal that are classified into two classes. An analysis of the class shape on the manifold is performed, and the separability level of the two classes is evaluated. The main contribution is the Separability Marker (SM)-confidence method, a method that appends a confidence marker to the prediction of a binary classifier whose decision function is based on the comparison of Riemannian distances.

This work has been published in [23].

7.10.3. Comparison of Hierarchical and Non-Hierarchical Classification for Motor Imagery Based BCI Systems

Participants: Nathalie Gayraud, Maureen Clerc, Cecilia Lindig-León [Neurosys project-team], Laurent Bougrain [Neurosys project-team].

Motor imagery (MI) based BCI systems record and analyze the brain activity to determine users' intentions while imagining moving some parts of their body. In order to build systems that are able to detect several commands, multiclass schemes need to be applied. Hierarchical methods allow solving multiclass problems by using a tree of binary classifiers, whose root discriminates between two groups, each one containing a half of the classes. Each succeeding node includes again only one half of the classes from the selected group, and the process is recursively repeated until each node contains a single class, from which the final decision can be inferred. In this study we compare a series of multiclass approaches to assert the benefits of hierarchical classification. The compared methods are based on two effective techniques for MI-discrimination, namely, Common Spatial Patterns (CSP) and Riemannian geometry, for which the hierarchical and non-hierarchical approaches have been considered. We include the CSP by Joint Diagonalization method (CSP by JAD), which corresponds with a non-hierarchical approach; and its hierarchical counterpart, namely, Binary CSP. In addition, the non-hierarchical Minimum Distance to Riemannian Mean method (MDRM) [4] is also evaluated, together with its analogous hierarchical approach; a contribution of the present work called Hierarchical MDRM algorithm (HMDRM). All these methods have been applied on dataset 2a of the BCI competition IV to facilitate their comparison. The highest accuracies were reached by the BCSP and HMDRM methods, confirming the effectiveness of hierarchical algorithms.

This work has been published in [36].

7.10.4. Motor imagery learning using Functional Electrical Stimulation

Participants: Maureen Clerc, Saugat Bhattacharyya [CAMIN project-team], Mitsuhiro Hayashibe [CAMIN project-team].

Functional Electrical Stimulation (FES) stimulates the affected region of the human body thus providing a neuroprosthetic interface to non-recovered muscle groups. FES in combination with Brain-computer interfacing (BCI) has a wide scope in rehabilitation because this system can directly link the cerebral motor intention of the users with its corresponding peripheral mucle activations. Such a rehabilitative system would contribute to improve the cortical and peripheral learning and thus, improve the recovery time of the patients. In this paper, we examine the effect of electrical stimulation by FES on the electroencephalography (EEG) during learning of a motor imagery task. The subjects are asked to perform four motor imagery tasks over six sessions and the features from the EEG are extracted using common spatial algorithm and decoded using linear discriminant analysis classifier. Feedback is provided in form of a visual medium and electrical stimulation representing the distance of the features from the hyperplane. Results suggest a significant improvement in the classification accuracy when the subject was induced with electrical stimulation along with visual feedback as compared to the standard visual one.

This work has been published in [13] and [22].

7.10.5. Brain training with neurofeedback

Participants: Maureen Clerc, Lorraine Perronnet [Hybrid project-team], Anatole Lécuyer [Hybrid project-team], Fabien Lotte [Potioc project-team], Christian Barillot [Visages project-team].

Neurofeedback is a promising tool for brain rehabilitation and peak performance training. Neurofeedback approaches usually rely on a single brain imaging modality such as EEG or fMRI. Combining these modalities for neurofeedback training could allow to provide richer information to the subject and could thus enable him/her to achieve faster or more specific self-regulation. Yet unimodal and multimodal neurofeedback have never been compared before. In the present work, we introduce a simultaneous EEG-fMRI experimental protocol in which participants performed a motor-imagery task in unimodal and bimodal NF conditions.

With this protocol we were able to compare for the first time the effects of unimodal EEG-neurofeedback and fMRI-neurofeedback versus bimodal EEG-fMRI-neurofeedback by looking both at EEG and fMRI activations. We also propose a new feedback metaphor for bimodal EEG- fMRI-neurofeedback that integrates both EEG and fMRI signal in a single bi-dimensional feedback (a ball moving in 2D). Such a feedback is intended to relieve the cognitive load of the subject by presenting the bimodal neurofeedback task as a single regulation task instead of two. Additionally, this integrated feedback metaphor gives flexibility on defining a bimodal neurofeedback target. Participants were able to regulate activity in their motor regions in all NF conditions. Moreover, motor activations as revealed by offline fMRI analysis were stronger during EEG-fMRI-neurofeedback than during EEG-neurofeedback. This result suggests that EEG-fMRI-neurofeedback could be more specific or more engaging than EEG-neurofeedback. Our results also suggest that during EEG-fMRI-neurofeedback, participants tended to regulate more the modality that was harder to control. Taken together our results shed light on the specific mechanisms of bimodal EEG-fMRI-neurofeedback and on its added-value as compared to unimodal EEG-neurofeedback and fMRI-neurofeedback.

This work has been published in [51] and [50].

7.10.6. Out-of-the-lab P300 speller

Participants: Maureen Clerc, Théodore Papadopoulo, Nathanaël Foy, Federica Turi, Étienne Guerlais.

New developments have been performed in the context of ADT OpenViBE-X to robustify the P300 speller system, correcting some timing issues (in OpenViBE), and making the system easier to use and install. This has been validated by the use of our system out-of-the-lab, by a patient in Chambéry (see article [104]).

This work has been published in [48]and [49].

7.10.7. Clinical study with the CoAdapt P300 speller

Participants: Maureen Clerc, Théodore Papadopoulo, Marie-Hélène Soriani [Nice University Hospital], Claude Desnuelle [Nice University Hospital], Violaine Guy [Nice University Hospital], Mariane Bruno [Nice University Hospital].

Amyotrophic Lateral Sclerosis (ALS) is a progressive neurodegenerative disease which, a few years after onset, restricts patients' communication capacity. In this study, the usability by disabled patients with ALS of a visual Brain-Computer Interface (BCI), the P300-speller, is evaluated as a viable alternative to existing assistive communication tools. After clinical evaluation of their physical, cognitive and language capacities, 20 patients with ALS were included. The study consisted of two 3-block sessions, at 2 to 4-week interval, using a P300-speller BCI in several modes of operation in view of evaluating its usability in its 3 components: effectiveness, efficiency and satisfaction. Over all participants, the system is effective (100% of participants successfully achieved copy spelling and free spelling tasks). It is also efficient (over 95% of correct symbols were selected by 65% of participants). The average number of correct symbols/min ranged from 3.6 (without word prediction) to 5.04 (with word prediction). Participants expressed satisfaction through an average of 8.7/10 measuring comfort, ease of use and utility. Patients quickly learned how to operate this system and were able to use it with good performance without much learning effort. Word prediction and other algorithmic optimizations improve the information transfer rate and make such systems competitive with existing solutions of alternative communication such as eye trackers.

This work was published in [25].

8. Bilateral Contracts and Grants with Industry

8.1. Bilateral Grants 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) has obtained 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 [99]. Another strategy [85] 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 team AROMATH and leverage the methods they developed [87], [88], [86] to have a better insight in this problem of rotational invariants of ternary quartics.

9.1.2. 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. 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* The ANR MRSEI LEMONS aims to consolidate a European Network by organizing meetings and visits, in order to submit a proposal for a MSCA-ITN. The European consortium is led by Inria (coordinator Maureen Clerc).

9.2.2.2. ANR MOSIFAH

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

Duration: *October 2013 to September 2017*

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.

Appropriate diffusion models will be explored including second and fourth order DTI models as well as HARDI models such as the single shell Q-Ball Imaging (QBI). These various types of images will be processed within the right Riemannian mathematical framework to provide tensor as well as Ensemble Average Propagator (EAP) and Orientation Distribution Function (ODF) fields. Virtual cardiac fiber structure (VCFS) will then be modelled using myocardial fiber information derived from each of these imaging modalities. Finally, diffusion behavior of water molecules in these VCFSs will be simulated by means of quantum spin theory, which allows computing ex vivo and in vivo virtual diffusion magnetic resonance (MR) images at various scales ranging from a few microns to a few millimeters. From the obtained virtual diffusion MR images, multiscale and probabilistic atlas describing the 3D fiber architecture of the heart ex vivo and in vivo will be constructed. Meanwhile, the simulation involving a large number of water molecules, grid computing will be used to cope with huge computation resource requirement.

We expect to construct a complete database containing a very wide range of simulated (noise and artifact-free) diffusion images that can be used as benchmarks or ground-truth for evaluating or validating diffusion image processing algorithms and create new virtual fiber models allowing mimicking and better understanding the heart muscle structures. Ultimately, the proposed research can open a completely novel way to approach the whole field of heart diseases including the fundamental understanding of heart physiology and pathology, and new diagnosis, monitoring and treatment of patients.

9.2.2.3. ANR VIBRATIONS

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

Duration: *February 2014 to January 2018*

Computational modeling, under the form of a “virtual brain” is a powerful tool to investigate the impact of different configurations of the sources on the measures, in a well-controlled environment.

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.

The project follows a three-fold strategy:

- construct virtual brain models with both dynamic aspects (reproducing both hyperexcitability and hypersynchronisation alterations observed in the epileptic brain) and a realistic geometry based on actual tractography measures performed in patients
- explore the parameter space though large-scale simulations of source configurations, using parallel computing implemented on a computer cluster.
- confront the results of these simulations to simultaneous recordings of EEG, MEG and intracerebral EEG (stereotactic EEG, SEEG). The models will be tuned on SEEG signals, and tested versus the surface signals in order to validate the ability of the models to represent real MEG and EEG signals.

The project constitutes a translational effort from theoretical neuroscience and mathematics towards clinical investigation. A first output of the project will be a database of simulations, which will permit in a given situation to assess the number of configurations that could have given rise to the observed signals in EEG, MEG and SEEG. A second – and major - output of the project will be to give the clinician access to a software platform which will allow for testing possible configurations of hyperexcitable regions in a user-friendly way. Moreover, representative examples will be made available to the community through a website, which will permit its use in future studies aimed at confronting the results of different signal processing methods on the same 'ground truth' data.

9.2.3. ADT

9.2.3.1. ADT BOLIS

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

Duration: *December 2014 to December 2016*

ADT BOLIS aims to:

- build a sofware platform dedicated to inverse source localisation, building upon the elements of software found in FindSources3D. The platform will be modular, ergonomic, accessible and interactive. It will offer a detailed visualisation of the processing steps and the results. The 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).
- Upgrade medInria to use the latest libraries versions involved (this most notably encompasses VTK 6, Qt 5, and DTK 1.0). Then, these new versions will be used to implement a composer (a graphical tool to chain various actions in medInria) and to develop python scripting (for chaining actions and for adding non-regression testing).

9.2.3.2. ADT OpenViBE-X

Participants: Théodore Papadopoulo, Maureen Clerc, Nathanaël Foy.

Duration: *October 2014 to October 2016*

The OpenViBE-X ADT addresses the OpenViBE Brain Computer Interfaces (BCI) platform, in order to:

1. make BCI easier to apprehend by end-users
2. enrich the interaction with multimodal biosignals (eye gaze, heart-rate)
3. implement methods for auto-calibration and online adaptation of the classification
4. provide support, maintenance and dissemination for this software.

The OpenViBE platform is a central element to BCI research at Inria, and in the international community.

9.2.4. Other Funding Programs

9.2.4.1. Big Brain Theory: 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 clini cal value** will open new perspectives in neuroimaging.

9.3.1.2. ChildBrain ETN

ATHENA is an Associated Partner in this European Training Network: the team will participate 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

Start year: Jan. 2016

Partners: ATHENA project-team,

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

In the past two decades, brain imaging of neurotypical individuals and clinical populations has primarily focused on localization of function and structures in the brain, revealing activation in specific brain regions during performance of cognitive tasks through modalities such as functional MRI. In parallel, technologies to identify white matter structures have been developed using diffusion MRI. More recently, interest has shifted towards developing a deeper understanding of the brain's intrinsic architecture and its influence on cognitive and affective information processing. Using for this resting state fMRI and diffusion MRI to build the functional and structural networks of the human brain.

The human brain is a complex patchwork of interconnected regions, and graph-theoretical approaches have become increasingly useful for understanding how functionally connected systems engender, and constrain, cognitive functions. The functional nodes of the human brain and their

structural inter-connectivity, collectively the "connectome", are, however, poorly understood. Critically, there is a dearth of computational methods for reliably identifying functional nodes of the brain and their structural inter-connectivity in vivo, despite an abundance of high-quality data from the Human Connectome Project (HCP). Devising and validating methods for investigating the human connectome has therefore taken added significance.

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. Informal International Partners

- SCIL Laboratory, Sherbrooke University, CA (Maxime Descoteaux)
- 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).
- University Houari Boumedienne (USTHB, Algiers) (L. Boumghar) and University of Boumerdes, (D. Cherifi), Algeria.
- BESA company on EEG/MEG modeling.
- CRM, Centre de Recherche Mathématiques, Montréal, Canada.

9.4.3. Participation in Other International Programs

9.4.3.1. Program: Collaborative Research in Computational Neuroscience (NSF – ANR)

Project acronym: NEUROREF

Project title: *Building MRI Reference Atlases to Analyze Brain Trauma and Post- Traumatic Stress*

Start date: 2016-10-01, End date: 2019-12-31

P.I : D. Wassermann (Athena) – S. Bouix (Harvard Medcical School)

Partners: ATHENA project-team,

International Partner (Institution - Laboratory - Researcher):

Harvard Medical School (United States) - Psychiatry and Neuroimaging Lab - Sylvain Bouix

Abstract:

While mild traumatic brain injury (mTBI) has become the focus of many neuroimaging studies, the understanding of mTBI, particularly in patients who evince no radiological evidence of injury and yet experience clinical and cognitive symptoms, has remained a complex challenge. Sophisticated imaging tools are needed to delineate the kind of subtle brain injury that is extant in these patients, as existing tools are often ill-suited for the diagnosis of mTBI. For example, conventional magnetic resonance imaging (MRI) studies have focused on seeking a spatially consistent pattern of abnormal signal using statistical analyses that compare average differences between groups, i.e., separating mTBI from healthy controls. While these methods are successful in many diseases, they are not as useful in mTBI, where brain injuries are spatially heterogeneous. The goal of this proposal 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. New algorithms will be developed to create Individualized Brain Abnormality (IBA) maps that will have a number of clinical and research applications. In this proposal, this technology will be used to analyze a previously acquired dataset from the INTRuST Clinical Consortium, a multi-center effort to study subjects with Post- Traumatic Stress Disorder (PTSD) and mTBI. Neuroimaging abnormality measures will be linked to clinical and neuropsychological assessments. This technique will allow us to tease apart neuroimaging differences between PTSD and mTBI and to establish baseline relationships between neuroimaging markers, and clinical and cognitive measures. Upon completion of this project, a set of tools, which have the potential to establish radiological evidence of brain injury in mTBI, will have been designed and evaluated, thereby enhancing both the diagnosis and monitoring of progression/recovery of injury, as well assessing the efficacy of therapies on the injured brain.

9.5. International Research Visitors

9.5.1. Visits of International Scientists

- Sadegh Masjoodi (PhD Student, Tehran University of Medical Sciences, Iran) visited ATHENA from April 2nd, 2016 to Sept, 10, 2016
- Lorenza Brusini (PhD Student, Univ. of Verona, Italy), visited ATHENA from Jan. 2016 until Apr 2016.
- Maria Carla Piastra (PhD Student, Univ. Clinic of Münster, Germany), visited ATHENA from Jul 2016 until Aug 2016.
- Mouloud Kachouane (PhD Student, Univ. USTHB, Alger) visited ATHENA from Nov. 2015 until Aug 2016.
- Thinhinane Megherbi (PhD Student, Univ. USTHB, Alger) visited ATHENA from Jan. 2016 until Feb. 2016.
- Vinod Menon (Stanford Medical School) visited ATHENA during June 2016
- John Kolchaka (Stanford Medical School) visited ATHENA during June 2016

9.5.1.1. Internships

Graeme Baker

Date: May 2016 – Sept 2016

Queen's University,

Supervisor: Rachid Deriche

Nahuel Lascano

Date: Jun 2016 – Sept 2016

University of Buenos Aires,

Supervisor: Demian Wassermann

Leonel Exequiel Gomez

Date: Jun 2016 – Sept 2016

University of Buenos Aires,

Supervisor: Demian Wassermann

Paul Gorlach

Date: Jul 2016 – Dec. 2016

University of Buenos Aires,

Supervisor: Theo Papadopoulo and Evelyne Hubert

10. Dissemination

10.1. Promoting Scientific Activities

10.1.1. Scientific Events Organisation

10.1.1.1. General Chair, Scientific Chair

- R. Deriche is Adj. Director at the Doctoral School EDSTIC (Website: http://edstic.i3s.unice.fr/index.html)
- T. Papadopoulo (since september 2011) is a co-coordinator of the Master of Science in Computational Biology and Biomedicine from University of Nice Sophia Antipolis (Website: http://cbb.unice.fr). The scientific goal of this program is to focus on the human being from different perspectives (understanding and modeling functional aspects or interpreting biomedical signals from various devices) and at different scales (from molecules to organs and the whole organism).

10.1.1.2. Member of the Organizing Committees

- M. Clerc organized, with Bruno Cessac from Biovision team,the conference neurostim2016.inria.fr on neurostimulation of the sensory and central nervous systems.

10.1.2. Scientific Events Selection

10.1.2.1. Member of the Conference Program Committees

- R. Deriche is member of the conference Programme Committee (PC) of the International Symposium on Biomedical Imaging (ISBI), member of the PC of MICCAI 2016 Workshop on Computational Diffusion MRI and member of the PC of MFCA 2016 MICCAI workshop on Mathematical Foundations of Computational Anatomy.
- Demian Wassermann, member of the Program Committee of MICCAI 2016.
- Maureen Clerc was member of the BCI Meeting 2016 Program Committee.

10.1.2.2. Reviewer

- 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 (ICIP, EMBC, MICCAI, ISBI, CDMRI, HBM).
- D. Wassermann serves several international institutions in reviewing applications: ANR, the Netherlands Organisation for Scientific Research (NWO), ...

- D. Wassermann serves several international conferences as a reviewer (MICCAI, ISMRM, HBM, CDMRI, etc)

10.1.3. Journal

10.1.3.1. Member of the 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 Biomedical Engineering OnLine, and of the ISTE-Wiley book series.

10.1.3.2. Reviewer - Reviewing Activities

- 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 (IEEE Transactions on Biomedical Engineering, Frontiers Neuroscience, Journal of Physics A, International Journal on Computer Vision,...).
- 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 invited talks at: Seminar SIESTE (ENS Lyon, March 2016), Imaging Seminar in Paris (Institut Henri Poincaré, November 2016)
- R. Deriche gave two plenary talks at the *13th IEEE International Conference on Signal Processing, November 7, 2016* in Chengdu and at the *Big Data in Medical Imaging Forum, November 10th, 2016* in Guiyang, both in China.
- R. Deriche gave a plenary talk at the *Summer school on Brain Connectomics, September 20, 2016* in Verona, Italy.
- T. Papadopoulo gave an invited talk in the ChildBrain symposium at the *Biomag conference, October 6, 2016* in Seoul, Korea [20].
- D. Wassermann gave a invited talks at: Stanford Medical School and at the Brain and Spine Institute, Paris.

10.1.5. Leadership within the Scientific Community

- M. Clerc coordinates the Inria Project Lab BCI-LIFT.
- R. Deriche is the P.I of the ERC AdG CoBCoM.

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 University Côte d'Azur.
- R. Deriche is a member of the Scientific Committee of Académie 2 of University 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).

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.

- R. Deriche is Chair of the 2015 and 2016 Inria Sophia Antipolis recruitment commitees
- R. Deriche is member of 4 Scientific Councils: University of Nice Sophia Antipolis, ITMO ITS (Institut des Technologies pour la Santé), Olea Medical Company (http://www.olea-medical.com/ and the GIS UNS-ENSL-CNRS-Inria.
- R. Deriche is member of the Administration Council of AFRIF (Association Française pour la Reconnaissance et l'Interprétation des Formes) and member of the Academic Council of UCA (Nice Côte d'Azur University)
- 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

Tutorial course by M. Clerc at ChildBrain Winter School (Jyväskylä, Finland, January 2016) : "Advanced Signal Processing".

Tutorial course by M. Clerc at IEEE International Conference on Systems Man and Cybernetics (Budapest, Hungary, October 2016): "Why bother with avanced modeling in BCI ? Lessons from neuroimaging".

Master: R. Deriche, Variational approaches and Geometrical Flows for Computational Brain Imaging, 36 ETD, M2 "Computational Biology and Biomedicine", University of Nice Sophia Antipolis, France.

Master: R. Deriche, Advanced Image Processing Techniques, 12 ETD, M1 International CBB & Ubinet, University of Nice Sophia Antipolis, France.

Master: T. Papadopoulo, *3D Computer Vision*, 12 ETD, M1 International Ubinet, University of Nice Sophia Antipolis, France.

Master: T. Papadopoulo, *Inverse Problems in Brain Functional Imaging*, 36 ETD, M2 "Computational Biology and Biomedicine", University of Nice Sophia Antipolis, France.

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

Master: D. Wassermann, *Introduction to Computer Science*, 24 ETD, M2, "Computational Biology and Biomedicine", University of Nice Sophia Antipolis, France.

Master: D. Wassermann, *Machine Learning in Neuroimaging*, 36 ETD, University of Buenos Aires, Argentina

10.2.2. Supervision

PhD in progress: Rutger Fick, "Microstructure Recovery via dMRI", started Oct. 2013, Université Nice Sophia Antipolis. Supervisor: Rachid Deriche.

PhD in progress: Kai Dang, "Modeling and characterizing electrical conductivity for cochlear implantation", started Dec. 2013, Université Nice Sophia Antipolis. Supervisor: Maureen Clerc.

PhD defended in April 20, 2016: Gabriel Girard, "fMRI & dMRI", started Sept. 2012, Supervisors: Rachid Deriche & Maxime Descoteaux (University of Sherbrooke, CA).

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: Marco Pizzolato, "Diffusion & Perfusion MRI: From bench to bedside" started Dec. 2013, Université Nice Sophia Antipolis. Supervisor: Rachid Deriche.

PhD in progress: Abib Alimi, “Diffusion & PLI” started Nov, 1st, 2016, Université Nice Sophia Antipolis. Supervisor: Rachid Deriche.

PhD in progress: Isa Costantini, “Brain Connectomics” started Oct. 1st, 2016, Université Nice Sophia Antipolis. Supervisor: Rachid Deriche.

PhD in progress: Brahim Belaoucha, “Using diffusion MR information to reconstruct networks of brain activations from MEG and EEG measurements”, Université Nice Sophia Antipolis, started Oct. 2013, Supervisor: Theo Papadopoulo.

PhD in progress: Kostiantyn Maksymenko, “Inverse problem in EEG/MEG/SSEG: towards a better consideration of anatomo-functional constraints ”, Université Nice Sophia Antipolis, started Oct. 2016, Supervisor: Theo Papadopoulo and Maureen Clerc.

PhD in progress: Guillermo Gallardo Diez, “Connectivity-Based Brain Parcellation”, started Nov. 2015, Université Nice Sophia Antipolis. Supervisors: D. Wassermann/ R. Deriche

PhD in progress: Nathalie Gayraud, “Structured Dictionary Learning”, University Nice Sophia Antipolis, started November 2015, supervisor: Maureen Clerc.

PhD in progress: Federica Turi, “User-adapted Brain Computer Interaction”, University Nice Sophia-Antipolis, started October 2016, supervisor: Maureen Clerc.

Master: Kostiantyn Maksymenko, “Efficient lead field computation a la Reduced Basis Methods”, Supervised by T. Papadopoulo and M. Clerc.

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

Master: Nahuel Lascano, “Weigthed Newtwork Representations of Structural Connectivity”, Supervised by D. Wassermann.

Master: Leonel Exequiel Gomez, “Super-resolution approaches to Multi-Shell dMRI”, Supervised by D. Wassermann.

Internship: Federica Turi, “Novel flashing strategies for the P300-speller”, Supervised by M. Clerc.

10.2.3. Juries

- M. Clerc participated in PhD juries of: Michaël Acquadro (Grenoble, April 2016) as reviewer, Tafkarinas Medani (Paris 6, September 2016) as reviewer, Flavie Torrecillos (Marseille, October 2016) as examiner, Andéol Evain (Rennes, December 2016) as examiner.
- M. Clerc participated in HDR jury of Sophie Achard as reviewer (Grenoble, March 2016) and Fabien Lotte (Bordeaux, September 2016) as examiner.
- M. Clerc participated in the recruitment jury of Professor in section 26 in University Nice Sophia Antipolis.
- M. Clerc participated in the recruitment jury for CR2/CR1 in Inria Sophia Antipolis.
- R. Deriche chaired the recruitment jury for CR2/CR1 in Inria Sophia Antipolis.
- R. Deriche chaired the PhD jury of Simona Schiavi at Ecole Polytechnique, Paris Saclay, Dec. 1st, 2016.
- R. Deriche chaired the PhD jury of Mehdi Hadj-Hamou at Nice University, Dec. 14th, 2016.
- R. Deriche participated in the PhD Jury of P. Gori at ICM, Paris, Jan. 8th, 2016
- R. Deriche participated in the PhD Jury of G. Girard at Sherbrooke University, April, 20, 2016.
- T. Papadopoulo participated in the PhD Jury of G. Girard as reviewer at Sherbrooke University, April, 20, 2016.
- T. Papadopoulo participated in the PhD Jury of A. Pillain as reviewer at Telecom Bretagne, October, 12, 2016.

10.3. Popularization

During the “Semaine du Cerveau” (Brain Awareness week) in March 2016, Maureen Clerc organized a “Cafe Technologique” about Brain-Computer Interfaces, in which over 100 attendees could see a live demo of the P300 speller with both clinical-grade and consumer-grade devices.

Maureen Clerc participated in a “Gala for Amyotrophic Lateral Sclerosis” at the AXA Headquarters in Paris, a fundraising event, where she presented the P300 speller project.

11. Bibliography

Major publications by the team in recent years

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[2] M. CLERC, L. BOUGRAIN, F. LOTTE (editors). *Brain-Computer Interfaces 2*, Wiley-ISTE, July 2016, http://eu.wiley.com/WileyCDA/WileyTitle/productCd-1848219636.html

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Publications of the year

Doctoral Dissertations and Habilitation Theses

[12] G. GIRARD. *White matter tractography guided by anatomical and microstructural priors*, Université Nice Sophia Antipolis, April 2016, https://tel.archives-ouvertes.fr/tel-01369022

Articles in International Peer-Reviewed Journals

[13] S. BHATTACHARYYA, M. CLERC, M. HAYASHIBE. *A study on the effect of electrical stimulation as a user stimuli for motor imagery classification in Brain-Machine Interface*, in "European Journal of Translational Myology", June 2016, vol. 26, n° 2, pp. 165-168 [*DOI :* 10.4081/EJTM.2016.6041], https://hal-lirmm.ccsd.cnrs.fr/lirmm-01402537

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[20] T. PAPADOPOULO. *Modelling thin tissue compartiments using the immersed FEM (continuous Galerkin)*, in "Biomag 2016 - 20th International Conference on Biomagnetism", Seoul, South Korea, October 2016, https://hal.inria.fr/hal-01412820

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[21] B. BELAOUCHA, T. PAPADOPOULO. *Iterative two-stage approach to estimate sources and their interactions* , in "20th International Conference on Biomagnetism (BIOMAG2016)", Seoul, South Korea, October 2016, https://hal.inria.fr/hal-01377967

[22] S. BHATTACHARYYA, M. CLERC, M. HAYASHIBE. *A Study on the Effect of Electrical Stimulation During Motor Imagery Learning in Brain-Computer Interfacing*, in "SMC: Systems, Man, and Cybernetics", Budapest, Hungary, October 2016, https://hal.archives-ouvertes.fr/hal-01402794

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