



Activity Report 2018

Project-Team ATHENA

Computational Imaging of the Central
Nervous System

RESEARCH CENTER
Sophia Antipolis - Méditerranée

THEME
**Computational Neuroscience and
Medicine**

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Project-Team ATHENA

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

Keywords:

Computer Science and Digital Science:

- A3. - Data and knowledge
- A3.1. - Data
- A3.3. - Data and knowledge analysis
- A3.4. - Machine learning and statistics
- A5. - Interaction, multimedia and robotics
- A5.1. - Human-Computer Interaction
- A5.2. - Data visualization
- A5.3. - Image processing and analysis
- A5.9. - Signal processing
- A6. - Modeling, simulation and control
- A6.1. - Methods in mathematical modeling
- A6.2. - Scientific computing, Numerical Analysis & Optimization
- A6.3. - Computation-data interaction
- A7. - Theory of computation
- A8.6. - Information theory
- A8.7. - Graph theory
- A8.8. - Network science
- A8.12. - Optimal transport
- A9. - Artificial intelligence
- A9.2. - Machine learning
- A9.3. - Signal analysis
- A9.7. - AI algorithmics

Other Research Topics and Application Domains:

- B1. - Life sciences
- B1.2. - Neuroscience and cognitive science
- B1.2.1. - Understanding and simulation of the brain and the nervous system
- B1.2.2. - Cognitive science
- B1.2.3. - Computational neurosciences
- B2.2.2. - Nervous system and endocrinology
- B2.2.6. - Neurodegenerative diseases
- B2.5. - Handicap and personal assistances
- B2.5.1. - Sensorimotor disabilities
- B2.5.2. - Cognitive disabilities
- B2.5.3. - Assistance for elderly
- B2.6.1. - Brain imaging
- B2.6.2. - Cardiac imaging
- B2.7. - Medical devices

- B2.7.1. - Surgical devices
- B2.7.2. - Health monitoring systems

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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 Structural and Functional Computational Imaging of the CNS.

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

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

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

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

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

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

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

This is implemented through:

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

3. Research Program

3.1. Computational diffusion MRI

Diffusion MRI (dMRI) provides a non-invasive way of estimating in-vivo CNS fiber structures using the average random thermal movement (diffusion) of water molecules as a probe. It's a recent field of research with a history of roughly three decades. It was introduced in the mid 80's by Le Bihan et al [71], Merboldt et al [77] and Taylor et al [88]. 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) [87], [53]. Historically, the first model in dMRI is the 2nd order diffusion tensor (DTI) [51], [50] which assumes the EAP to be Gaussian centered at the origin. DTI (Diffusion Tensor Imaging) has now proved to be extremely useful to study the normal and pathological human brain [72], [62]. 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 driven 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 [74] and [73]).

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) [91] and High Angular Resolution Diffusion Imaging (HARDI) methods such as Q-ball imaging [89] and other multi-tensors and compartment models [84], [86], [44], [43], [80] were developed to resolve the orientationality 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 [89]. Those contributions are fundamental and have already started to impact on the Diffusion MRI, HARDI and Q-Ball Imaging community [61]. They are at the core of our probabilistic and deterministic tractography algorithms devised to best exploit the full distribution of the fiber ODF (see [58], [3] and [59], [4]).

3.1.2. Beyond DTI with high order tensors

High Order Tensors (HOT) models to estimate the diffusion function while overcoming the shortcomings of the 2nd order tensor model have also been recently proposed such as the Generalized Diffusion Tensor Imaging (G-DTI) model developed by Ozarslan et al [95], [96] or 4th order Tensor Model [49]. For more details, we refer the reader to our articles in [64], [84] where we review HOT models and to our articles in [73], 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(<http://www.olea-medical.com/>). Indeed, DKI is fastly gaining popularity in the domain for characterizing the diffusion propagator or EAP by its deviation from Gaussianity. Hence it is an important clinical tool for characterizing the white-matter's integrity with biomarkers derived from the 3D 4th order kurtosis tensor (KT) [67].

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 [43], [44]. 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 increases, as the strength and speed of gradients increase and as new acquisition techniques appear [2], these imaging modalities raise a large amount of mathematical and computational challenges at the core of the research we develop at ATHENA [66], [84].

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 [57]. 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 [78].

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. 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 [78], [54], [56].

We have also contributed to design optimal acquisition schemes for single and multiple Q-shell experiments. In particular, the method proposed in [2] helps generate sampling schemes with optimal angular coverage for multi-shell acquisitions. The cost function we proposed is an extension of the electrostatic repulsion to multi-shell and can be used to create acquisition schemes with incremental angular distribution, compatible with prematurely stopped scans. Compared to more commonly used radial sampling, our method improves the angular resolution, as well as fiber crossing discrimination. The optimal sampling schemes, freely available for download¹, 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 [65].

¹<http://www.emmanuelcaruyer.com/>

²<http://humanconnectome.org/documentation/Q1/imaging-protocols.html>

3.1.4. *dMRI modelling, tissue microstructures features recovery & applications*

The dMRI signal is highly complex, hence, the mathematical tools required for processing it have to be commensurate in their complexity. Overall, these last twenty years have seen an explosion of intensive scientific research which has vastly improved and literally changed the face of dMRI. In terms of dMRI models, two trends are clearly visible today: the parametric approaches which attempt to build models of the tissue to explain the signal based on model-parameters such as CHARMED [45], AxCaliber [46] and NODDI [92] 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 [48], [47], the Solid Harmonic (SoH) basis [60], the Simple Harmonic Oscillator based Reconstruction and Estimation (SHORE) basis [93] and more recent Mean Apparent Propagator or MAP-MRI basis [94].

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 (Mean Diffusivity) and FA (Fractional Anisotropy) which are known to be extremely sensitive to confounding factors such as partial volume and axonal dispersion, non-specific and not able to capture any subtle effects that might be early indicators of diseases [5].

3.1.5. *Towards microstructural based tractography*

In order to go far beyond traditional fiber-tracking techniques, we believe that first order information, i.e. fiber orientations, has to be superseded 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 [6]. Using additional a priori anatomical 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.

3.1.6. *Going beyond the state-of-the-art dMRI*

Overall, these last twenty years have seen an explosion of intensive scientific research which has vastly improved and literally changed the face of dMRI.

However, although great improvements have been made, 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

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 objective we would like to achieve in order to take dMRI from the benchside to the bedside and lead to a decisive advance and breakthrough in this field.

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 (Superconducting QUantum Interference Device) 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 ODYSÉE/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 (Functional MRI) and SPECT (Single-Photon Emission Computed Tomography) in that those provide a very good spatial resolution but a rather poor temporal resolution (of the order of a second for fMRI and a minute for SPECT). Also, contrarily to fMRI, which "only" measures an haemodynamic response linked to the metabolic demand, MEG and EEG measure a direct consequence of the electrical activity of the brain: it is acknowledged that the signals measured by MEG and EEG correspond to the variations of the post-synaptic potentials of the pyramidal cells in the cortex. Pyramidal neurons compose approximately 80% of the neurons of the cortex, and it requires at least about 50,000 active such neurons to generate some measurable signal.

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

- First, as acquisition is continuous and is run at a rate up to 1kHz, the amount of data generated by each experiment is huge. Data selection and reduction (finding relevant time blocks or frequency bands) and pre-processing (removing artifacts, enhancing the signal to noise ratio, ...) are largely done manually at present. Making a better and more systematic use of the measurements is an important step to optimally exploit the M/EEG data [1].
- With a proper model of the head and of the sources of brain electromagnetic activity, it is possible to simulate the electrical propagation and reconstruct sources that can explain the measured signal. Proposing better models [70], [7] and means to calibrate them [90] 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.

3.3. Combined M/EEG and dMRI

dMRI provides a global and systematic view of the long-range structural connectivity within the whole brain. In particular, it allows the recovery of the fiber structure of the white matter which can be considered as the wiring connections between distant cortical areas. These white matter based tractograms are analyzed e.g. to explore the differences in structural connectivity between pathological and normal populations. Moreover, as a by-product, the tractograms can be processed to reveal the nodes of the brain networks, i.e. by segregating together gray matter that share similar connections to the rest of the white matter. But dMRI does not provide information on:

- the cortico-cortical pathways (not passing through white matter) and to some extent, on the short-range connections in the white matter,
- the actual use of connections over time during a given brain activity.

On the opposite, M/EEG measures brain activation over time and provides, after source reconstruction (solving the so-called inverse problem of source reconstruction), time courses of the activity of the cortical areas. Unfortunately, deep brain structures have very little contribution to M/EEG measurements and are thus difficult to analyze. Consequently, M/EEG reveals information about the nodes of the network, but in a more blurry (because of the inverse problem) and fragmented view than dMRI (since it can only reveal brain areas measurable in M/EEG whose activity varies during the experimental protocol). Given its very high temporal resolution, the signal of reconstructed sources can be processed to reveal the functional connectivity between the nodes [85].

While dMRI and M/EEG have been the object of considerable research separately, there have been very few studies on combining the information they provide. Some existing studies deal with the localization of abnormal MEG signals, particularly in the case of epilepsy, and on studying the white matter fibers near the detected abnormal source [76], [79], but to our knowledge there are very few studies merging data coming both from M/EEG and dMRI at the analysis level [82], [63], [52], [83].

Combining the structural and functional information provided by dMRI and M/EEG is a difficult problem as the spatial and temporal resolutions of the two types of measures are extremely different. Still, combining the measurements obtained by these two types of techniques has the great potential of providing a detailed view both in space and time of the functioning brain at a macroscopic level. Consequently, it is a timely and extremely important objective to develop innovative computational tools and models that advance the dMRI and M/EEG state-of-the-art and combine these imaging modalities to build a comprehensive dynamical structural-functional brain connectivity network to be exploited in brain connectivities diseases.

The CoBCOM ERC project aims to develop a joint dynamical structural-functional brain connectivity network built on advanced and integrated dMRI and M/EEG ground-breaking methods. To this end, CoBCOM will provide new generation of computational dMRI and M/EEG models and methods for identifying and characterizing the connectivities on which the joint network is built. Capitalizing on the strengths of dMRI & M/EEG and building on the bio-physical and mathematical foundations of our models, CoBCOM will contribute to create a joint and solid network which will be exploited to identify and characterize white matter abnormalities in some high-impact brain diseases such as Multiple Sclerosis (MS), Epilepsy and mild Traumatic Brain Injury (mTBI).

4. Application Domains

4.1. Applications of diffusion MRI

Clinical domain: Diagnosis of neurological disorder

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

4.2. Applications of M/EEG

Clinical domain: Diagnosis of neurological disorders

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

Subtopics include:

- Diagnosis of neurological disorders such as epilepsy, schizophrenia, tinnitus, ...
- Presurgical planning of brain surgery.
- Collaboration with the *Institut de Neurosciences des Systèmes* on these topics <http://ins.univ-amu.fr/fr/>.

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 develop a research collaboration with the eemagine/ANT-Neuro company. We collaborate with Nice University Hospital on the usage of BCI-based communication for ALS³ patients.

5. New Software and Platforms

5.1. BCI-VIZAPP

BCI visual applications

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

SCIENTIFIC DESCRIPTION: Bci-Vizapp is a library that allows (in interaction with OpenViBE) to build BCI (Brain Computer Interfaces) applications based on the P300 speller principle. Bci-Vizapp provides a library that allows you to create the BCI's stimulation part as part of the Qt toolkit. Being able to use a standard toolkit to make BCI applications is a strong Bci-Vizapp originality. Indeed, in general the use of such toolkits is prohibited by the need for a very precise control of the display timings, which generally eliminates high-level graphic toolkits such as Qt.

FUNCTIONAL DESCRIPTION: BCI-VIZAPP includes a virtual keyboard for typing text, a photodiode monitoring application for checking timing issues. It communicates with the OpenViBE acquisition server for signal acquisition and with the OpenViBE designer for signal processing. The configuration is performed through a wizard.

This software is a new version following the CoAdapt P300 stimulator software.

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

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

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

5.2. DIPY

Diffusion Imaging in Python

KEYWORDS: MRI - Medical imaging

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

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

5.3. High Performance Diffusion MRI

KEYWORDS: Health - Neuroimaging - Medical imaging

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

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

5.4. OpenMEEG

KEYWORDS: Health - Neuroimaging - Medical imaging

SCIENTIFIC DESCRIPTION: OpenMEEG provides a symmetric boundary element method (BEM) implementation for solving the forward problem of electromagnetic propagation over heterogeneous media made of several domains of homogeneous and isotropic conductivities. OpenMEEG works for the quasistatic regime (frequencies < 100Hz and medium diameter < 1m).

FUNCTIONAL DESCRIPTION: OpenMEEG provides state-of-the art tools for modelling bio-electromagnetic propagation in the quasi-static regime. It is based on the symmetric BEM for the EEG/MEG forward problem, with a distributed source model. OpenMEEG has also been used to model the forward problem of ECoG, for modelling nerves or the cochlea. OpenMEEG is a free, open software written in C++ with python bindings. OpenMEEG is used through a command line interface, but is also interfaced in graphical interfaces such as BrainStorm, FieldTrip or SPM.

RELEASE FUNCTIONAL DESCRIPTION: OpenMEEG has had a large update including notably the parallelisation of some operators and bug corrections. The new version allows in addition the use of non-nested domains. NEWS OF THE YEAR: OpenMEEG has had a large update including notably the parallelisation of some operators and bug corrections. The new version allows in addition the use of non-nested domains. These improvements have been distributed with the two new releases (2.4.0 and 2.4.1) made in 2018.

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

6. New Results

6.1. Computational Diffusion MRI

6.1.1. Reducing the Number of Samples in Spatio-Temporal dMRI Acquisition Design

Participants: Patryk Filipiak, Rutger Fick [TheraPanacea, Paris], Alexandra Petiet [ICM, CENIR, Paris], Mathieu Santin [ICM, CENIR, Paris], Anne-Charlotte Philippe [ICM, CENIR, Paris], Stéphane Lehericy [ICM, CENIR, Paris], Philippe Ciuciu [CEA, Université Paris-Saclay], Demian Wassermann [Inria Parietal], Rachid Deriche.

Acquisition time is a major limitation in recovering brain white matter microstructure with diffusion magnetic resonance imaging. The aim of this work is to bridge the gap between growing demands on spatiotemporal resolution of diffusion signal and the real-world time limitations. We introduce an acquisition scheme that reduces the number of samples under adjustable quality loss. Finding a sampling scheme that maximizes signal quality and satisfies given time constraints is NP-hard. Therefore, a heuristic method based on a genetic algorithm is proposed in order to find suboptimal solutions in acceptable time. The analyzed diffusion signal representation is defined in the $q\tau$ space, so that it captures both spatial and temporal phenomena. The experiments on synthetic data and in vivo diffusion images of the C57Bl6 wild-type mouse corpus callosum reveal superiority of the proposed approach over random sampling and even distribution in the $q\tau$ space.

This work has been published in [12].

6.1.2. Dmipy, a Diffusion Microstructure Imaging toolbox in Python to improve research reproducibility

Participants: Abib Olushola Yessouffou Alimi, Rutger Fick [TheraPanacea, Paris], Demian Wassermann [Inria Parietal], Rachid Deriche.

The recovery of microstructure-related features of the brain's white matter is a current challenge in diffusion MRI (dMRI). In particular, multi-compartment (MC)-based models have been a popular approach to estimate these features. However, the usage of MC-models is often limited to those hard-coded in publicly available toolboxes.

In this work, we present Diffusion Microstructure Imaging in Python (Dmipy), a diffusion MRI toolbox which allows accessing any multi-compartment-based model and robustly estimates these important features from single-shell, multi-shell, and multi-diffusion time, and multi-TE data. Dmipy follows a *building block*-based philosophy to microstructure imaging, meaning an MC-model can be constructed and fitted to dMRI data using any combination of underlying tissue models, axon dispersion or diameter distributions, and optimization algorithms.using less than 10 lines of code, thus helps improve research reproducibility. In describing the toolbox, we show how Dmipy enables to easily design microstructure models and offers to the users the freedom to choose among different optimization strategies. We finally present three advanced examples of highly complex modeling approaches which are made easy using Dmipy.

This work has been published in [21], [30].

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

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

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

This work has been published in [11].

6.1.4. *Resolving the crossing/kissing fiber ambiguity using functionallyCOMMIT (Convex Optimization Modeling for Microstructure Informed Tractography)*

Participants: Matteo Frigo, Isa Costantini, Samuel Deslauriers-Gauthier, Rachid Deriche.

The architecture of the white matter is endowed with kissing and crossing bundles configurations. When these white matter tracts are reconstructed using diffusion MRI tractography, this systematically induces the reconstruction of many fiber tracts that are not coherent with the structure of the brain. The question on how to discriminate between true positive connections and false positive connections is the one addressed in this work. State-of-the-art techniques provide a partial solution to this problem by considering anatomical priors in the false positives detection process. We propose a novel model that tackles the same issue but takes into account both structural and functional information by combining them in a convex optimization problem. We validate it on two toy phantoms that reproduce the kissing and the crossing bundles configurations, showing that, through this approach, we are able to correctly distinguish true positives and false positives.

This work has been published in [25].

6.1.5. *Reducing false positive connection in tractograms using joint structure-function filtering*

Participants: Matteo Frigo, Guillermo Gallardo Diez, Isa Costantini, Alessandro Daducci [EPFL, Lausanne], Demian Wassermann [Inria Parietal], Samuel Deslauriers-Gauthier, Rachid Deriche.

Due to its ill-posed nature, tractography generates a significant number of false positive connections between brain regions. To reduce the number of false positives, Daducci et al. proposed the COMMIT framework, which has the goal of re-establishing the link between tractography and tissue microstructure. In this framework, the diffusion MRI signal is modeled as a linear combination of local models associated with streamlines where the weights are identified by solving a convex optimization problem. Streamlines with a weight of zero do not contribute to the diffusion MRI data and are assumed to be false positives. Removing these false positives yields a subset of streamlines supporting the anatomical data. However, COMMIT does not make use of the link between structure and function and thus weights all bundles equally. In this work, we propose a new strategy that enhances the COMMIT framework by injecting the functional information provided by functional MRI. The result is an enhanced tractogram filtering strategy that considers both functional and structural data.

This work has been published in [31].

6.1.6. Combining Improved Euler and Runge-Kutta 4th order for Tractography in Diffusion-Weighted MRI

Participants: Cherifi Dalila [IEEE University of Boumerdes, Algeria], Boudjada Messaoud [IEEE University of Boumerdes, Algeria], Morsli Abdelatif [IEEE University of Boumerdes, Algeria], Girard Gabriel [EPFL, Lausanne], Rachid Deriche.

In this work, we develop a general, deterministic tractography algorithm (CIERTE), which is a combination of Improved Euler and Range-Kutta fourth-order algorithm and test it on synthetic and real data. The proposed tractography method is validated using seven metrics of the tractometer evaluation system and positively compared to state-of-the-art tractography algorithms.

This work has been published in [9].

6.1.7. Fiber orientation distribution function from non-negative sparse recovery with quantitative analysis of local fiber orientations and tractography using DW-MRI datasets

Participants: Thinhinane Megherbi [USTHB, Algiers], Gabriel Girard [EPFL, Lausanne], Ghosh Aurobrata [AI Innovation Lab, Verisk Analytics], Fatima Oulebsir-Boumghar [USTHB, Algiers], Rachid Deriche.

In this work, we propose, evaluate and validate a new Diffusion Weighted MRI method to model and recover high quality tractograms even with multiple fiber populations in a voxel and from a limited number of acquisitions.

Our method relies on the estimation of the Fiber Orientation Distribution (FOD) function, parameterized as a non-negative sum of rank-1 tensors and the use of a non-negative sparse recovery scheme to efficiently recover the tensors, and their number. Each fiber population of a voxel is characterized by the orientation and the weight of a rank-1 tensor.

Using both deterministic and probabilistic tractography algorithms, we show that our method is able to accurately reconstruct narrow crossing fibers and obtain a high quality connectivity reconstruction even from a limited number of acquisitions. To this end, a validation scheme based on the connectivity recovered from tractography is developed to quantitatively evaluate and analyze the performance of our method. The tractometer tool is used to quantify the tractography obtained from a simulated DW-MRI dataset including a high angular resolution dataset of 60 gradient directions and a dataset of 30 gradient directions, each of them corrupted with Rician noise of SNR 10 and 20. The performance of our FOD model and its impact on the tractography results are also demonstrated and illustrated on in vivo DW-MRI datasets with high and low angular resolutions.

This work has been published in [15].

6.1.8. Solving the Cross-Subject Parcel Matching Problem Using Optimal Transport

Participants: Guillermo Gallardo Diez, Nathalie Gayraud, Maureen Clerc, Demian Wassermann [Inria Parietal], Samuel Deslauriers-Gauthier, Rachid Deriche.

Matching structural parcels across different subjects is an open problem in neuroscience. Even when produced by the same technique, parcellations tend to differ in the number, shape, and spatial localization of parcels across subjects. In this work, we propose a parcel matching method based on Optimal Transport. We test its performance by matching parcels of the Desikan atlas, parcels based on a functional criteria and structural parcels. We compare our technique against three other ways to match parcels which are based on the Euclidean distance, the cosine similarity, and the Kullback-Leibler divergence. Our results show that our method achieves the highest number of correct matches.

This work has been published in [32], [26].

6.1.9. A Closed-Form Solution of Rotation Invariant Spherical Harmonic Features in Diffusion MRI

Participants: Mauro Zucchelli, Samuel Deslauriers-Gauthier, Rachid Deriche.

Rotation invariant features are an indispensable tool for characterizing diffusion Magnetic Resonance Imaging (MRI) and in particular for brain tissue microstructure estimation. In this work, we propose a new mathematical framework for efficiently calculating a complete set of such invariants from any spherical function. Specifically, our method is based on the spherical harmonics series expansion of a given function of any order and can be applied directly to the resulting coefficients by performing a simple integral operation analytically. This enable us to derive a general closed-form equation for the invariants. We test our invariants on the diffusion MRI fiber orientation distribution function obtained from the diffusion signal both in-vivo and in synthetic data. Results show how it is possible to use these invariants for characterizing the white matter using a small but complete set of features.

This work has been published in [29].

6.1.10. Rational invariants of ternary forms under the orthogonal group

Participants: Paul Görlach [MPI for Mathematics in the Sciences], Evelyne Hubert [Inria, AROMATH], Théodore Papadopoulo, Rachid Deriche.

In [68], [69], [81] we started to explore the theory of tensor invariants as a mathematical framework for computing new biomarkers for HARDI. We pursued this work and, in collaboration with the project-team GALAAD/AROMATH, we succeeded to develop a complete set of rational invariants for ternary quartics [39]. Being rational, they are very close to the polynomial invariants developed in [69] but they constitute a complete set of invariants. They are also good tools to understand better the algebraic invariants of [81] and some others based on spherical harmonics decomposition [55]. We determined a generating set of rational invariants of minimal cardinality for the action of the orthogonal group $O(3)$ on the space $R[x, y, z]_{2d}$ of ternary forms of even degree $2d$. The construction relies on two key ingredients. On one hand, the Slice Lemma allows us to reduce the problem to determining the invariants for the action on a subspace of the finite subgroup $B(3)$ of signed permutations. On the other hand, our construction relies in a fundamental way on specific bases of harmonic polynomials. These bases provide maps with prescribed $B(3)$ -equivariance properties. Our explicit construction of these bases should be relevant well beyond the scope of this work. The expression of the $B(3)$ -invariants can then be given in a compact form as the composition of two equivariant maps. Instead of providing (cumbersome) explicit expressions for the $O(3)$ -invariants, we provide efficient algorithms for their evaluation and rewriting. We also use the constructed $B(3)$ -invariants to determine the $O(3)$ -orbit locus and provide an algorithm for the inverse problem of finding an element in $R[x, y, z]_{2d}$ with prescribed values for its invariants. These are the computational issues relevant in brain imaging.

This work has been submitted and is currently under review. A preprint is available in [39].

6.1.11. Edema-informed anatomically constrained particle filter tractography

Participants: Samuel Deslauriers-Gauthier, Drew Parker [UPenn, USA], François Rheault [SCIL, Sherbrooke University, CA], Steven Brem [UPenn, USA], Maxime Descoteaux [SCIL, Sherbrooke University, CA], Ragini Verma [UPenn, USA], Rachid Deriche.

In this work, we propose an edema-informed anatomically constrained tractography paradigm that enables reconstructing larger spatial extent of white matter bundles as well as increased cortical coverage in the presence of edema. These improvements will help surgeons to maximize the extent of the resection while minimizing the risk of cognitive deficits. The new paradigm is based on a segmentation of the brain into gray matter, white matter, corticospinal fluid, edema and tumor regions which utilizes a tumor growth model. Using this segmentation, a valid tracking domain is generated and, in combination with anatomically constrained particle filter tractography, allows streamlines to cross the edema region and reach the cortex. Using subjects with brain tumors, we show that our edema-informed anatomically constrained tractography paradigm increases the cortico-cortical connections that cross edema-contaminated regions when compared to traditional fractional anisotropy thresholded tracking.

This work has been published in [24].

6.1.12. *Towards the assessment of myelination using time-dependent diffusion MRI indices*

Participants: Abib Olushola Yessouffou Alimi, Alexandra Petiet [ICM, CENIR, Paris], Mathieu Santin [ICM, CENIR, Paris], Anne-Charlotte Philippe [ICM, CENIR, Paris], Stéphane Lehericy [ICM, CENIR, Paris], Demian Wassermann [Inria Parietal], Rachid Deriche.

In this work, we study the sensitivity of time-dependent diffusion MRI indices or $q\tau$ -indices to demyelination in the mouse brain. For this, we acquire in vivo four-dimensional diffusion-weighted images-varying over gradient strength, direction and diffusion time-and estimate the $q\tau$ -indices from the corpus callosum. First order Taylor approximation of each index gives fitting coefficients α and β whose variance we investigate. Results indicate that, cuprizone intoxication affects mainly index coefficient β by introducing inequality of variances between the two mice groups, most significantly in the splenium and that MSD increases and RTOP decreases over diffusion time τ .

This work has been published in [35].

6.1.13. *An Analytical Fiber ODF Reconstruction in 3D Polarized Light Imaging*

Participants: Abib Olushola Yessouffou Alimi, Yves Usson [UMR5525 TIMC-IMAG CNRS], Pierre-Simon Jouk [CHU Grenoble-Alpes], Gabrielle Michalowicz [CHU Grenoble-Alpes], Rachid Deriche.

Three dimensional polarized light imaging (3D-PLI) utilizes the birefringence in postmortem tissue to map its spatial fiber structure at a submillimeter resolution. In this work, we propose an analytical method to compute the fiber orientation distribution function (ODF) from high-resolution vector data provided by 3D-PLI. This strategy enables the bridging of high resolution 3D-PLI to diffusion magnetic resonance imaging with relatively low spatial resolution. First, the fiber ODF is modeled as a sum of K orientations on the unit sphere and expanded with a high order spherical harmonics series. Then, the coefficients of the spherical harmonics are derived directly with the spherical Fourier transform. We quantitatively validate the accuracy of the reconstruction against synthetic data and show that we can recover complex fiber configurations in the human heart at different scales.

This work has been published in [22].

6.1.14. *fMRI Deconvolution via Temporal Regularization using a LASSO model and the LARS algorithm*

Participants: Isa Costantini, Patryk Filipiak, Kostiantyn Maksymenko, Samuel Deslauriers-Gauthier, Rachid Deriche.

In the context of functional MRI (fMRI), methods based on the deconvolution of the blood oxygenated level dependent (BOLD) signal have been developed to investigate the brain activity, without a need of a priori knowledge about activations occurrence. In this work, we propose a novel temporal regularized deconvolution of the BOLD signal using the Least Absolute Shrinkage and Selection Operator (LASSO) model, solved by means of the Least-Angle Regression (LARS) algorithm. In this way, we were able to recover the underlying neurons activations and their dynamics.

This work has been published in [23], [37].

6.1.15. *A Second Order Multi-Stencil Fast Marching Method with a Non-Constant Local Cost Model*

Participants: Susana Merino-Caviedes [Universidad de Valladolid], Lucilio Cordero-Grande [King's College London], Maria Tereza Perez [Universidad de Valladolid], Pablo Casaseca-de-La-Higuera [Universidad de Valladolid], Marcos Martín-Fernández [Universidad de Valladolid], Carlos Alberola-Lopez [Universidad de Valladolid], Rachid Deriche.

The Fast Marching method is widely employed in several fields of image processing. Some years ago a Multi-Stencil version (MSFM) was introduced to improve its accuracy by solving the Eikonal equation for a set of stencils and choosing the best solution at each considered node. The following work proposes a modified numerical scheme for MSFM to take into account the variation of the local cost, which has proven to be second order. The influence of the stencil set choice on the algorithm outcome with respect to stencil orthogonality and axis swapping is also explored, where stencils are taken from neighborhoods of varying radius. The experimental results show that the proposed schemes improve the accuracy of their original counterparts, and that the use of permutation-invariant stencil sets provides robustness against shifted vector coordinates in the stencil set.

This work has been published in [16].

6.2. Unveiling brain activity using M/EEG

6.2.1. *Data-driven cortical clustering to provide a family of plausible solutions to the M/EEG inverse problem*

Participants: Maureen Clerc, Kostiantyn Maksymenko, Théodore Papadopoulo.

The Magneto/Electroencephalography (M/EEG) inverse problem consists in reconstructing cortical activity from M/EEG measurements. It is an ill-posed problem. Hence prior hypotheses are needed to constrain the solution space. In this work, we consider that the brain activity which generates the M/EEG signals is supported by single or multiple connected cortical regions. As opposed to methods based on convex optimization, which are forced to select one possible solution, we propose a cortical clustering based approach, which is able to find several candidate regions. These regions are different in term of their sizes and/or positions but fit the data with similar accuracy. We first show that even under the hypothesis of a single active region, several source configurations can similarly explain the data. We then use a multiple signal classification (MUSIC) approach to recover multiple active regions with our method. We validate our method on simulated and measured MEG data. Our results show that our method provides a family of plausible solutions which both accord with the priors and similarly fit the measurements.

This work is published in [41].

6.2.2. *Fast approximation of EEG forward problem and application to tissue conductivity estimation*

Participants: Maureen Clerc, Kostiantyn Maksymenko, Théodore Papadopoulo.

Bioelectric source analysis in the human brain from scalp electroencephalography (EEG) signals is sensitive to the conductivity of the different head tissues. Conductivity values are subject dependent, so non-invasive methods for conductivity estimation are necessary to suitably tune the EEG models. To do so, the EEG forward problem solution (so-called lead field matrix) must be computed for a large number of conductivity configurations. Computing one lead field requires a matrix inversion which is computationally intensive for realistic head models. Thus, the required time for computing a large number of lead fields can become impractical. In this work, we propose to approximate the lead field matrix for a set of conductivity configurations, using the exact solution only for a small set of basis points in the conductivity space. Our approach accelerates the computing time, while controlling the approximation error. Our method is tested for brain and skull conductivity estimation, with simulated and measured EEG data, corresponding to evoked somato-sensory potentials. This test demonstrates that the used approximation does not introduce any bias and runs significantly faster than if exact lead field were to be computed.

This work has been submitted to a journal and is available as a preprint [40].

6.2.3. *Model based optimal multipolar stimulation without a priori knowledge of nerve structure*

Participants: Maureen Clerc, Mélissa Dali [Inria Camin], David Guiraud [Inria Camin], Jérémy Laforêt [Inria Camin], Olivier Rossel [Inria Camin].

Multipolar cuff electrode can selectively stimulate areas of peripheral nerves and therefore enable to control independent functions. However, the branching and fascicularization are known for a limited set of nerves and the specific organization remains subject-dependent. This work presents general modeling and optimization methods in the context of multipolar stimulation using a cuff electrode without a priori knowledge of the nerve structure. Vagus nerve stimulation experiments based on the optimization results were then investigated.

The model consisted of two independent components: a lead field matrix representing the transfer function from the applied current to the extracellular voltage present on the nodes of Ranvier along each axon, and a linear activation model. The optimization process consisted in finding the best current repartition (ratios) to reach activation of a targeted area depending on three criteria: selectivity, efficiency and robustness.

The results showed that state-of-the-art configurations (tripolar transverse, tripolar longitudinal) were part of the optimized solutions but new ones could emerge depending on the trade-off between the three criteria and the targeted area. Besides, the choice of appropriate current ratios was more important than the choice of the stimulation amplitude for a stimulation without a priori knowledge of the nerve structure. We successfully assessed the solutions in vivo to selectively induce a decrease in cardiac rhythm through vagus nerve stimulation while limiting side effects. Compared to the standard whole ring configuration, a selective solution found by simulation provided on average 2.6 less adverse effects.

The preliminary results showed the correctness of the simulation, using a generic nerve geometry. It suggested that this approach will have broader applications that would benefit from multicontact cuff electrodes to elicit selective responses. In the context of the vagus nerve stimulation for heart failure therapy, we show that the simulation results were confirmed and improved the therapy while decreasing the side effects.

This work has been published in [10].

6.3. Combined M/EEG and dMRI

6.3.1. *Linking resting-state functional connectivity and the structural connectome – investigation of an eigen-structure model*

Participants: Rebecca Bonham-Carter, Samuel Deslauriers-Gauthier, Rachid Deriche.

Resting-state functional connectivity (rs-FC) dynamics are not random but rather structured with common dominant patterns called resting-state networks (RSNs). These dynamics are influenced by the underlying network of white-matter connections. Specifically, temporal correlations in resting-state BOLD fMRI signals have been correlated with the structural network determined via diffusion weighted imaging (DWI). The literature on this structure-function relationship encompasses generative non-linear models and a variety of linear models. The objective of this study is to provide new validation and understanding of two linear models. Both models enforce that the structural network Laplacian and rs-FC share a common eigen-structure. In contrast to previous work, in this work two linear models of resting-state functional connectivity (rs-FC), developed by Abdelnour et al., are validated on simulated BOLD fMRI data generated using The Virtual Brain18 (TVB) and 49 HCP subjects real structural connectomes. Both consider rs-FC as a diffusion process on the structural network. The mean correlations between rs-FC matrices we obtain 0.699 ± 0.086 and 0.518 ± 0.095 , and between rs-FC eigenvalues 0.981 ± 0.013 , agree with the original model implementations on empirical data. Using The Virtual Brain simulator together with real structural data is shown to offer a new and efficient test and validation framework for approaches predicting rs-FC from structure.

This work is under review.

6.3.2. *White Matter Information Flow Mapping from Diffusion MRI and EEG*

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

The human brain can be described as a network of specialized and spatially distributed regions. The activity of individual regions can be estimated using electroencephalography and the structure of the network can be measured using diffusion magnetic resonance imaging. However, the communication between the different cortical regions occurring through the white matter, coined information flow, cannot be observed by either modalities independently. Here, we present a new method to infer information flow in the white matter of the brain from joint diffusion MRI and EEG measurements. This is made possible by the millisecond resolution of EEG which makes the transfer of information from one region to another observable. A subject specific Bayesian network is built which captures the possible interactions between brain regions at different times. This network encodes the connections between brain regions detected using diffusion MRI tractography derived white matter bundles and their associated delays. By injecting the EEG measurements as evidence into this model, we are able to estimate the directed dynamical functional connectivity whose delays are supported by the diffusion MRI derived structural connectivity. We present our results in the form of information flow diagrams that trace transient communication between cortical regions over a functional data window. The performance of our algorithm under different noise levels is assessed using receiver operating characteristic curves on simulated data. In addition, using the well-characterized visual motor network as grounds to test our model, we present the information flow obtained during a reaching task following left or right visual stimuli. These promising results present the transfer of information from the eyes to the primary motor cortex. The information flow obtained using our technique can also be projected back to the anatomy and animated to produce videos of the information path through the white matter, opening a new window into multi-modal dynamic brain connectivity.

This work is under review.

6.3.3. *Bridging Brain Structure and Function by Correlating Structural Connectivity and Cortico-Cortical Transmission*

Participants: Fabien Almairac [CHU Nice], Patryk Filipiak, Lavinia Slabu, Maureen Clerc, Théodore Papadopoulo, Denys Fontaine [CHU Nice], Lydiane Mondot [CHU Nice], Stéphan Chanalet [CHU Nice], Demian Wassermann [Inria Parietal], Rachid Deriche.

Elucidating the structure-function relationship of the brain is one of the main open questions in neuroscience. The capabilities of diffusion MRI-based (dMRI) techniques to quantify the connectivity strength between brain areas, namely structural connectivity, in combination with modalities such as electrocorticography (ECoG) to quantify brain function have enabled advances in this field. In this work, we aim to establish a relationship between: i) dMRI structural connectivity measures, ii) direct measures of electrical properties of the human brain cortex obtained with ECoG, iii) response elicited by direct electrostimulation of the brain (DES).

The results of this multi-modal approach combining structure and function explorations of the brain should: i) help to elucidate the relationship between non-invasive (dMRI) structural connectivity measures and cortico-cortical transmission properties (delays, transfer functions), ii) help in understanding the organization of the brain for cognitive functions as well as neurosurgical planning for resection of brain tumors and drug-resistant epilepsy

This work has been presented in [36].

6.4. Brain Computer Interfaces

6.4.1. *Online enhancement of visuospatial attention performance*

Participants: Maureen Clerc, Thomas Brochier [Institut des Neurosciences de la Timone], Romain Trachel.

This study on real-time decoding of visuospatial attention has two objectives: first, to reliably decode self-directed shifts of attention from electroencephalography (EEG) data, and second, to analyze whether this information can be used to enhance visuospatial performance. Visuospatial performance was measured in a target orientation discrimination task, in terms of reaction time, and error rate. Our experiment extends the Posner paradigm by introducing a new type of ambiguous cues to indicate upcoming target location. The cues are designed so that their ambiguity is imperceptible to the user. This entails endogenous shifts of attention

which are truly self-directed. Two protocols were implemented to exploit the decoding of attention shifts. The first 'adaptive' protocol uses the decoded locus to display the target. In the second 'warning' protocol, the target position is defined in advance, but a warning is flashed when the target mismatches the decoded locus. Both protocols were tested in an online experiment involving ten subjects. The reaction time improved in both the adaptive and the warning protocol. The error rate was improved in the adaptive protocol only. This proof of concept study brings evidence that visuospatial brain-computer interfaces (BCIs) can be used to enhance improving human-machine interaction in situations where humans must react to off-center events in the visual field.

This work has been published in [8].

6.4.2. Review of classification methods for EEG-based Brain-Computer Interfaces: A 10-year update

Participants: Maureen Clerc, Laurent Bougrain [Neurosys, Inria Nancy], Fabien Lotte [Potioc, Inria Bordeaux], Alain Rakotomamonjy [Université de Rouen].

Most current Electroencephalography (EEG)-based Brain-Computer Interfaces (BCIs) are based on machine learning algorithms. There is a large diversity of classifier types that are used in this field, as described in the 2007 review paper [75]. Now, approximately 10 years after this review publication, many new algorithms have been developed and tested to classify EEG signals in BCIs. The time is therefore ripe for an updated review of EEG classification algorithms for BCIs. We surveyed the BCI and machine learning literature from 2007 to 2017 to identify the new classification approaches that have been investigated to design BCIs. We synthesize these studies in order to present such algorithms, to report how they were used for BCIs, what were the outcomes, and to identify their pros and cons. We found that the recently designed classification algorithms for EEG-based BCIs can be divided into four main categories: adaptive classifiers, matrix and tensor classifiers, transfer learning and deep learning, plus a few other miscellaneous classifiers. Among these, adaptive classifiers were demonstrated to be generally superior to static ones, even with unsupervised adaptation. Transfer learning can also prove useful although the benefits of transfer learning remain unpredictable. Riemannian geometry-based methods have reached state-of-the-art performances on multiple BCI problems and deserve to be explored more thoroughly, along with tensor-based methods. Shrinkage linear discriminant analysis and random forests also appear particularly useful for small training samples settings. On the other hand, deep learning methods have not yet shown convincing improvement over state-of-the-art BCI methods. This paper provides a comprehensive overview of the modern classification algorithms used in EEG-based BCIs, presents the principles of these Review of Classification Algorithms for EEG-based BCI 2 methods and guidelines on when and how to use them. It also identifies a number of challenges to further advance EEG classification in BCI.

This work has been published in [14].

6.4.3. Automating calibration

Participants: Maureen Clerc, Federica Turi, Nathalie Gayraud.

Brain Computer Interfaces (BCIs) based on visual evoked potentials (VEP) allow for spelling from a keyboard of flashing characters. Among VEP BCIs, code-modulated visual evoked potentials (c-VEPs) are designed for high-speed communication. In c-VEPs, all characters flash simultaneously. In particular, each character flashes according to a predefined 63-bit binary sequence (m-sequence), circular-shifted by a different time lag. For a given character, the m-sequence evokes a VEP in the electroencephalogram (EEG) of the subject, which can be used as a template. This template is obtained during a calibration phase at the beginning of each session. Then, the system outputs the desired character after a predefined number of repetitions by estimating its time lag with respect to the template. Our work avoids the calibration phase, by extracting from the VEP relative lags between successive characters, and predicting the full word using a dictionary.

This work has been published in [28].

7. Partnerships and Cooperations

7.1. Regional Initiatives

7.1.1. Université Côte d'Azur projects

7.1.1.1. Tech-ICOPA

Participants: Maureen Clerc, Théodore Papadopoulo, Sofiane Guebba, Marie-Hélène Soriani [CHU Nice], Mariane Bruno [CHU Nice], Violaine Guy [CHU Nice].

Duration: 24 months

Improving autonomy is a main priority for people with disabilities. The goal of this project is to create a version usable by patients at their home of a brain-computer interface (BCI) research prototype system developed in our project-team. Making this technology actually usable in the context of pathology inducing severe disabilities such as ALS (Amyotrophic Lateral Sclerosis) is a challenge. Tackling this challenge would allow both to meet the expectations of dependent people and to envision a more widespread use of this technology. To reach this goal, several technological advances and industrial developments are needed : (i) developing a suitable ergonomic headset, wireless, functional, comfortable, incorporating a miniaturized amplifier (Nice University Hospital Center - ALS Center), (ii) reducing the number of electrodes while maintaining signal quality (Inria - UCA) and (iii) testing the prolonged use of dry electrodes. In addition to these technological advances, the Tech-ICOPA translational project aims at (1) improving the use of BCI in communication, in accessing the digital world, home automation and robotics and (2) enhancing the use of BCI in commercial applications.

7.1.1.2. EPI-ANALYSE

Participants: Fabrice Duprat [IPMC], Théodore Papadopoulo, Massimo Mantegazza [IPMC], Maureen Clerc.

Duration: 12 months

This project aims at developing two complementary analysis softwares dedicated to the detection of epileptic seizures in mice in order to study epileptogenesis and the consequences of spontaneous seizures. The first software will be the adaptation to the mouse EEG of a powerful algorithm based on a dictionary learning method developed by our project-team. We will use video-EEG recordings already made and analyzed at the IPMC to optimize and validate the new software. This will allow a detailed analysis of seizures and events occurring between seizures (e.g., interictal spikes). The second software deals with the analysis of video recordings of 3 models of mice not recordable until now with EEG. The implementation, recordings and the analysis of the 3 models will be carried out during this project. A prototype of this software already exists at IPMC (in Python, with OpenCV) but the analysis algorithm must be optimized. Semi-automatic video analysis will allow an easy identification of temporal segments corresponding to epileptic seizures. This will help the experimenter to classify the behavioral severity of seizures.

7.1.1.3. MICADome

Participants: Maureen Clerc, Michel Pascal [CNR Nice].

Duration: 24 months

The MICA-Dome project (MICA : Musique Interactive Côte d'Azur) initiates collaborative research between arts, science and humanities within a laboratory for exploring the sound spatialization in 3D, and its usage for an immersive music composition. For this MICADome will be equipped with a "Dome" of loudspeakers for 3D spatialization. Our team collaborates in MICADome in order to develop and analyze EEG experiments to analyze the neural correlates of spatial auditory attention.

7.2. National Initiatives

7.2.1. Inria Project Lab

7.2.1.1. IPL BCI-LIFT

Participants: Maureen Clerc, Théodore Papadopoulo, Nathalie Gayraud, Federica Turi, Romain Lacroix.

Duration: January 2015 to December 2018

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

7.2.2. ANR

7.2.2.1. ANR NeuroRef

Participants: Demian Wassermann [Inria Parietal], Antonia Machlouziredes, Guillermo Gallardo Diez, Rachid Deriche.

Duration: October 2016 to September 2019

Call: NSF-ANR Program Collaborative Research in Computational Neuroscience 2015

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

7.2.2.2. ANR MOSIFAH

Participants: Rachid Deriche, Abib Olushola Yessouffou Alimi, Rutger Fick [TheraPanacea, Paris], Demian Wassermann [Inria Parietal], Théodore Papadopoulo.

Duration: October 2013 to September 2018

Call: ANR Numerical Models 2013

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

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

7.2.2.3. ANR VIBRATIONS

Participants: Théodore Papadopoulo, Maureen Clerc, Rachid Deriche, Demian Wassermann [Inria Parietal].

Duration: February 2014 to February 2019

Call: ANR Programme de Recherche Translationnelle en Santé (PRTS) 2013

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

7.2.3. ADT

7.2.3.1. ADT BCI-Browser

Participants: Théodore Papadopoulo, Maureen Clerc.

Duration: 1 year

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

This contract is part of the AMDT initiative.

7.2.3.2. ADT BOLIS 2

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

Duration: 6 months.

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

This contract is part of the AMDT initiative.

7.2.3.3. ADT OpenMEEG

Participants: Théodore Papadopoulo, Maureen Clerc, Kostiantyn Maksymenko, Alexandre Gramfort [PARIETAL], Joan Massich [PARIETAL].

Duration: 24 months.

The OpenMEEG ADT aims at improving OpenMEEG along 3 main directions:

1. Offer a user interface for the creation and verification of head models most importantly for a simpler management of non-nested head models.
2. Improve the Python interface (extension and reliability). This will also be useful to develop new research axes (in connection with point 3).
3. Enrich the available operators and refactor the code to offer new possibilities in OpenMEEG and reduce the cost of maintenance.

In addition to the expected gains in code maintenance, these improvements will allow a number of new – more sophisticated – applications as well as open OpenMEEG to a larger audience with a simplified interface for classical use-cases.

This contract is part of the AMDT initiative.

7.3. European Initiatives

7.3.1. FP7 & H2020 Projects

7.3.1.1. 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 computational nature and added clinical value** will open new perspectives in neuroimaging.

7.3.1.2. ChildBrain ETN

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

Program: European Training Network

Project acronym: ChildBrain

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

Duration: March 2015 to March 2019

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

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

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

7.4. International Initiatives

7.4.1. Inria International Partners

7.4.1.1. Declared Inria International Partners

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

7.4.1.2. Informal International Partners

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

7.5. International Research Visitors

7.5.1. Visits of International Scientists

- Dr. Ragini Verma, Section of Biomedical Image Analysis, Center for Biomedical Image Computing and Analytics, Department of Radiology, University of Pennsylvania, USA (Oct 1st, 2018 - Dec 21st, 2018)
- Dr. Moo K. Chung, Waisman Laboratory for Brain Imaging and Behavior, University of Wisconsin-Madison, From Sept.10 to 14, 2018

7.5.1.1. Internships

- Rebecca Bonham-Carter - Queen's University, Kingston, Canada, From early May to late July, 2018.
- Max Amatsuji-Berry - Queen's University, Kingston, Canada, From early May to late July, 2018.
- Etienne Saint-Onge - Sherbrooke University, From Early Feb. to early June 2018.

8. Dissemination

8.1. Promoting Scientific Activities

8.1.1. Scientific Events Organisation

8.1.1.1. Member of Organizing Committees

- M. Clerc organized the "journées C@UCA" for Université Côte d'Azur in Fréjus, June 14-15, 2018.

8.1.2. Scientific Events Selection

8.1.2.1. Member of Conference Program Committees

- T. Papadopoulo is member of the Program Committee of GRETSI 2019.

8.1.2.2. Reviewer

- M. Clerc serves several international conferences (ISBI, ICASSP, IEEE EMBS, IEEE NER).
- R. Deriche serves several international conferences (ISBI, MICCAI, ISMRM, ...) and international workshops (CD-MRI Miccai, MFCA Miccai...).
- T. Papadopoulo serves several international conferences (ICIP, ISBI, ICASSP, VISAPP).

8.1.3. Journal

8.1.3.1. Member of Editorial Boards

- M. Clerc is member of the Editorial Boards of the Journal of Neural Engineering, and of the journal Neurons, Behavior, Data and Theory.

- R. Deriche is member of the Editorial Board of the Journal of Neural Engineering, 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

8.1.3.2. Reviewer - Reviewing Activities

- M. Clerc serves several international journals (Journal of Neural Engineering, NeuroImage, Physics in Medicine and Biology).
- 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 access, Transactions on Pattern Analysis and Machine Intelligence, Frontiers in Neuroscience, Brain Topography, Transactions on Biomedical Engineering).

8.1.4. Invited Talks

- M. Clerc gave an invited talk at the ICM Colloquium, Paris, January 15, 2018.
- M. Clerc gave an invited talk at the ENS Data Science Colloquium, Paris, February 6, 2018.
- M. Clerc gave an invited talk at the SIAM Symposium on Imaging Sciences, Bologna, June 6, 2018.
- M. Clerc gave an invited talk at the Journées Scientifiques Inria, Bordeaux, June 27, 2018.
- M. Clerc gave an invited talk at the Colloque “Physique et Interrogations Fondamentales”, Bibliothèque Nationale de France, Paris, Nov 10, 2018.
- M. Clerc gave an invited talk at the “Journées des Jeunes Mathématiciens et Jeunes Mathématiciennes”, Orléans, Nov 29, 2018.
- R. Deriche gave an invited keynote speech at SPIE Medical Imaging, Houston, Texas United States (Feb. 12th, 2018).
- R. Deriche gave an invited keynote speech at EDITE ParisTech-Sorbonne Université, Paris (Dec. 10th, 2018).
- T. Papadopoulo gave an invited talk at “Inverse Problems: Modelling and Simulation”, Malta (May, 2018) [20].

8.1.5. Leadership within the Scientific Community

- M. Clerc is the coordinator of the Inria Project-Lab BCI-LIFT.
- M. Clerc is on the board of the CORTICO association (Collectif pour la Recherche Transdisciplinaire sur les Interfaces Cerveau Ordinateur).
- R. Deriche is the P.I. of the ERC AdG CoBCoM.

8.1.6. Scientific Expertise

- M. Clerc served Cordis-H2020 for FET-OPEN prosals evaluations.
- M. Clerc participated in an HCERES visiting committee in November 2018 (CentraleSupélec).
- R. Deriche serves several international institutions in reviewing applications : ERC Grants, Swiss National Science Foundation, the Netherlands Organisation for Scientific Research (NWO).
- T. Papadopoulo served Cordis-H2020 for FET-OPEN prosals evaluations.

8.1.7. Research Administration

- M. Clerc was adjoint deputy director for Science of Inria Sophia Antipolis (until August 2018).
- M. Clerc was member of the Evaluation Committee of Inria (until August 2018).
- M. Clerc was member of the Commission Scientifique Interne of Inria (until August 2018).
- M. Clerc was vice-president of the CRCN Selection Committee in Inria Sophia Antipolis.

- M. Clerc was a member of the CRCN Selection Committee in Inria Grenoble.
- M. Clerc is member of the Scientific Council of Academy 4 of Université Côte d'Azur.
- M. Clerc is co-animator of a structuring program on Neurosciences at Université Côte d'Azur.
- R. Deriche is member of the Academic Council of UCA (Université Côte d'Azur).
- R. Deriche is member of the Scientific Council of Academy 2 *Complex Systems*, Université Côte d'Azur and member of the Scientific Council of Olea Medical Company (<http://www.olea-medical.com/>).
- T. Papadopoulo represents Inria at the Administration Council of the **CIU Santé** (till July 2018).
- T. Papadopoulo is member of the Software Development Committee at Inria.

8.2. Teaching - Supervision - Juries

8.2.1. Teaching

Master: M. Clerc, Functional neuroimaging and data analysis, 36 ETD, MSc "Mod4NeuCog", Université Côte d'Azur, France.

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

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

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

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

8.2.2. Supervision

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

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

PhD in progress: Matteo Frigo, "Structure & Function" started Nov, 1st, 2017, Université Côte d'Azur. Supervisor: Rachid Deriche.

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

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

PhD defended on Dec. 21st, 2018: Guillermo Gallardo Diez, "Connectivity-Based Brain Parcellation", started Nov. 2015, Université Côte d'Azur. Supervisors: D. Wassermann and R. Deriche

PhD defended on Dec. 11th, 2018: Nathalie Gayraud, "Structured Dictionary Learning", Université Côte d'Azur, started November 2015. Supervisor: Maureen Clerc.

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

PhD in progress: Sara Sedlar, "Reconstruction and analysis of dynamical functional networks from EEG, MEG and dMRI measurements", Université Côte d'Azur, started October 2018. Supervisors: Théodore Papadopoulo and Maureen Clerc.

PhD in progress: Ivana Kojcic, "Estimation of cortical activity and of the structure–function link using EEG and dMRI", Université Côte d'Azur, started October 2018. Supervisors: Théodore Papadopoulo and Samuel Deslauriers-Gauthier.

8.2.3. Juries

- M. Clerc participated as a reviewer in the HDR jury of Denis Schwartz at Sorbonne Université, Paris on November 7, 2018.
- M. Clerc participated as a reviewer in the PhD jury of Fardin Afdideh, Université Grenoble Alpes on October 12, 2018.
- M. Clerc participated as a reviewer in the PhD jury of Aldo Mora Sanchez at Sorbonne Université, Paris on November 19, 2018.
- M. Clerc participated in the PhD jury of Yousra Bekhti at Telecom ParisTech on March 22, 2018.
- M. Clerc participated in the PhD jury of Tom Dupré Latour at Telecom ParisTech on November 26, 2018.
- M. Clerc participated in the PhD jury of N. Gayraud at Université Côte d'Azur on December 11, 2018.
- R. Deriche participated as a reviewer in the HDR jury of G. Varoquaux at UPMC, Paris on May 23, 2018.
- R. Deriche participated in the HDR jury of D. Tschumperle at GREYC Ecole Nationale Supérieure d'Ingénieurs de Caen, Oct. 3, 2018.
- R. Deriche chaired the PhD jury of Lorenza Brusini at Università di Verona on April 19th, 2018.
- R. Deriche participated as a reviewer in the PhD jury of Chendi Wang at the University of British Columbia - Vancouver, CA on May 2018.
- R. Deriche participated in the PhD jury of G. Gallardo at Université Côte d'Azur on Dec. 21, 2018.

8.3. Popularization

8.3.1. Interventions

- M. Clerc participated in the Brain Awareness Week with a talk about Brain Computer Interfaces at CHU Nice Pasteur, March 16 2018.
- M. Clerc participated in the Brain Awareness Week with a talk about Music and the Brain at Villa Arson, Nice, March 17 2018.
- M. Clerc, T. Papadopoulo, F. Turi and R. Lacroix participated in the Fête de la Science with a BCI demo where the general public could test a P300 speller system.

9. Bibliography

Major publications by the team in recent years

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