

Inria

Activity Report 2019

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

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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 structure and function. These models and tools will help to better understand the structure and the functioning of the human brain 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 Brain Connectivity Mapping.

The relationship between brain structure and function is fundamental in neuroscience. Developing computational models and techniques that recover the structural and functional connectivities of the brain in vivo is thus of utmost importance: it will definitely improve the understanding of the brain and its mechanisms. On the basis of our expertise and contributions to the field of computational neuroimaging and in order to have an impact on this field, our research focusses mainly on the structural and functional Imaging of the brain 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 brain 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 non invasive 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 brain white matter and can also help in the development of new biomarkers related to the progression of certain types of neurodegenerative disease. Diffusion MRI is the imaging modality that we will primarily consider to recover the structural brain connectivity.

Connectivity represents the network infrastructure of the brain. Electric activity corresponds to communications over this network. MEG and EEG (jointly as M/EEG), two non-invasive techniques, reveal part of the cortical electric activity and are instrumental in better understanding the brain functional connectivity and in diagnosing diseases linked to anomalous brain function - that in some cases structural or other functional MR images do not reveal. MEG and EEG are the imaging modalities that we will primarily consider to recover the functional brain connectivity.

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 brain signals such as measured through EEG, and translate in real-time the electrical activity of the brain in commands to control external 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 brain signals and imaging data. Our main objective is to push forward the state-of-the-art in Structural and Functional Computational Brain Connectivity Mapping to better understand the structure and function of the brain.

In order to tackle these long term and 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 brain 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 relatively recent field of research with a history of roughly three decades. It was introduced in the mid 80's by Le Bihan et al [63], Merboldt et al [68] and Taylor et al [78]. 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) [77], [47]. Historically, the first model in dMRI is the 2nd order diffusion tensor (DTI) [45], [44] 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 [64], [55]. 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 [66] and [65]).

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) [81] and High Angular Resolution Diffusion Imaging (HARDI) methods such as Q-ball imaging [79] and other multi-tensors and compartment models [74], [76], [38], [37], [71] 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 [79]. Those contributions are fundamental and have already started to impact on the Diffusion MRI, HARDI and Q-Ball Imaging community [54]. They are at the core of our probabilistic and deterministic tractography algorithms devised to best exploit the full distribution of the fiber ODF (see [51], [3] and [52], [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 proposed such as the Generalized Diffusion Tensor Imaging (G-DTI) model developed by Ozarslan et al [85], [86] or 4th order Tensor Model [43]. For more details, we refer the reader to our articles in [57], [74] where we review HOT models and to our articles in [65], 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. We also worked on Diffusion Kurtosis Imaging (DKI), of great interest for the company OLEA MEDICAL (<https://www.olea-medical.com/en>). 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) [60].

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 [37], [38]. 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 [59], [74].

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. 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 [50]. Then, 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 relatively recent technique which has been proved to accurately reconstruct sparse signals from undersampled measurements acquired below the Shannon-Nyquist rate [69].

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 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 [69], [48], [49].

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 [58].

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 [39], AxCaliber [40] and NODDI [82] 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 [42], [41], the Solid Harmonic (SoH) basis [53], the Simple Harmonic Oscillator based Reconstruction and Estimation (SHORE) basis [83] and more recent Mean Apparent Propagator or MAP-MRI basis [84].

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.

¹<http://www.emmanuelcaruyer.com/>

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

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 high order invariant and intrinsic microstructure features, identify bio-physically important bio-markers and improve tractography.

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 dMRI tools and models for brain connectomics 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 ODYSSEE/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 [62], [7] and means to calibrate them [80] 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 [75].

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 [67], [70], but to our knowledge there are very few studies merging data coming both from M/EEG and dMRI at the analysis level [72], [56], [46], [73].

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/>

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.

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

5. Highlights of the Year

5.1. Highlights of the Year

Maureen Clerc left the group and took up her new position as new Director and Head of the Inria Sophia Antipolis - Méditerranée research centre on 8 November 2019.

5.1.1. Awards

The European Association for Signal Processing (EURASIP) elevated on Sept. 2019 Rachid DERICHE to EURASIP FELLOW, the Association's most prestigious honour in recognition of outstanding achievements in the broad field of Signal Processing and in particular in Computational Brain Imaging.

November 22nd 2019, Université Côte d'Azur officially launched its new Institute of artificial intelligence *3IA Côte d'Azur*. Rachid Deriche and Maureen Clerc are among the 27 awarded 3IA chairs.

6. New Software and Platforms

6.1. Dmipy

Diffusion MRI Multi-Compartment Modeling and Microstructure Recovery Made Easy

KEYWORDS: Diffusion MRI - Multi-Compartment Modeling - Microstructure Recovery

FUNCTIONAL DESCRIPTION: Non-invasive estimation of brain microstructure features using diffusion MRI (dMRI) – known as Microstructure Imaging – has become an increasingly diverse and complicated field over the last decades. Multi-compartment (MC)-models, representing the measured diffusion signal as a linear combination of signal models of distinct tissue types, have been developed in many forms to estimate these features. However, a generalized implementation of MC-modeling as a whole, providing deeper insights in its capabilities, remains missing. To address this fact, we present Diffusion Microstructure Imaging in Python (Dmipy), an open-source toolbox implementing PGSE-based MC-modeling in its most general form. Dmipy allows on-the-fly implementation, signal modeling, and optimization of any user-defined MC-model, for any PGSE acquisition scheme. Dmipy follows a “building block”-based philosophy to Microstructure Imaging, meaning MC-models are modularly constructed to include any number and type of tissue models, allowing simultaneous representation of a tissue's diffusivity, orientation, volume fractions, axon orientation dispersion, and axon diameter distribution. In particular, Dmipy is geared toward facilitating reproducible, reliable MC-modeling pipelines, often allowing the whole process from model construction to parameter map recovery in fewer than 10 lines of code. To demonstrate Dmipy's ease of use and potential, we implement a wide range of well-known MC-models, including IVIM, AxCaliber, NODDI(χ), Bingham-NODDI, the spherical mean-based SMT and MC-MDI, and spherical convolution-based single- and multi-tissue CSD. By allowing parameter cascading between MC-models, Dmipy also facilitates implementation of advanced approaches like CSD with voxel-varying kernels and single-shell 3-tissue CSD. By providing a well-tested, user-friendly toolbox that simplifies the interaction with the otherwise complicated field of dMRI-based Microstructure Imaging, Dmipy contributes to more reproducible, high-quality research.

- Authors: Rutger Fick, Demian Wassermann and Rachid Deriche
- Contact: Rachid Deriche

6.2. 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

6.3. 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: [inria-00467061v2](#) - [inria-00584205v1](#) - [hal-01278377v1](#)
- URL: <http://openmeeg.github.io/>

6.4. OpenVIBE

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

FUNCTIONAL DESCRIPTION: OpenViBE is a free and open-source software platform devoted to the design, test and use of Brain-Computer Interfaces (BCI). The platform consists of a set of software modules that can be integrated easily and efficiently to design BCI applications. The key features of OpenViBE software are its modularity, its high-performance, its portability, its multiple-users facilities and its connection with high-end/VR displays. The designer of the platform enables to build complete scenarios based on existing software modules using a dedicated graphical language and a simple Graphical User Interface (GUI). This software is available on the Inria Forge under the terms of the AGPL licence, and it was officially released in June 2009. Since then, the OpenViBE software has already been downloaded more than 60000 times, and it is used by numerous laboratories, projects, or individuals worldwide. More information, downloads, tutorials, videos, documentations are available on the OpenViBE website.

- Participants: Cedric Riou, Thierry Gaugry, Anatole Lécuyer, Fabien Lotte, Jussi Tapio Lindgren, Laurent Bougrain, Maureen Clerc and Théodore Papadopoulo
- Partners: INSERM - GIPSA-Lab
- Contact: Anatole Lécuyer
- URL: <http://openvibe.inria.fr>

6.5. 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.

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: Théodore Papadopoulo

7. New Results

7.1. Computational Diffusion MRI

7.1.1. Coarse-Grained Spatiotemporal Acquisition Design for Diffusion MRI

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], Demian Wassermann [Inria Parietal], Rachid Deriche.

Acquisition protocols that allow to capture time-dependent changes in diffusion signal require long imaging time. We address this issue through an optimized subsampling scheme that maximizes accuracy of the spatiotemporal diffusion signal representation, q_T -dMRI, for given time constraints. Our proposed coarse-grained variant of the problem reduces the space of feasible acquisition parameters compared to the fine-grained approach causing no significant deterioration of a reconstruction accuracy in most of the studied cases.

This work has been published in [25].

7.1.2. A Computational Framework For Generating Rotation Invariant Features And Its Application In Diffusion MRI

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

In this work, we present a novel computational framework for analytically generating a complete set of algebraically independent Rotation Invariant Features (RIF) given the Laplace-series expansion of a spherical function. Our computational framework provides a closed-form solution for these new invariants, which are the natural expansion of the well known spherical mean, power-spectrum and bispectrum invariants. We highlight the maximal number of algebraically independent invariants which can be obtained from a truncated Spherical Harmonic (SH) representation of a spherical function and show that most of these new invariants can be linked to statistical and geometrical measures of spherical functions, such as the mean, the variance and the volume of the spherical signal. Moreover, we demonstrate their application to dMRI signal modeling including the Apparent Diffusion Coefficient (ADC), the diffusion signal and the fiber Orientation Distribution Function (fODF). In addition, using both synthetic and real data, we test the ability of our invariants to estimate brain tissue microstructure in healthy subjects and show that our framework provides more flexibility and open up new opportunities for innovative development in the domain of microstructure recovery from diffusion MRI.

This work has been published in [20].

7.1.3. A Novel Characterization of Traumatic Brain Injury in White Matter with Diffusion MRI Spherical-Harmonics Rotation Invariants

Participants: Mauro Zucchelli, Samuel Deslauriers-Gauthier, Drew Parker [Penn Applied Connectomics and Imaging Group, Philadelphia], Junghoon John Kim [Department of Molecular, Cellular & Biomedical Sciences, New York], Ragini Verma [Penn Applied Connectomics and Imaging Group, Philadelphia], Rachid Deriche.

The current DTI-based markers of traumatic brain injury are able to capture affected WM in the brain, but miss the areas of crossing fibers and complex WM due to the simplicity of the model. In this work, we use a novel set of spherical-harmonics rotation invariant indices, recently proposed in the literature. We demonstrate that these 12 invariants capture all the information provided by DTI. But in addition, they capture differences in complex WM, beyond DTI measures. This combined with the clinical feasibility of the method, paves the way for them to be used as better markers of brain injury.

This work has been published in [31].

7.1.4. The Dmipy Toolbox: Diffusion MRI Multi-Compartment Modeling and Microstructure Recovery Made Easy

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

Non-invasive estimation of brain microstructure features using diffusion MRI (dMRI)—known as Microstructure Imaging—has become an increasingly diverse and complicated field over the last decades. Multi-compartment (MC)-models, representing the measured diffusion signal as a linear combination of signal models of distinct tissue types, have been developed in many forms to estimate these features. However, a generalized implementation of MC-modeling as a whole, providing deeper insights in its capabilities, remains missing. To address this fact, we present Diffusion Microstructure Imaging in Python (Dmipy), an open-source toolbox implementing PGSE-based MC-modeling in its most general form. Dmipy allows on-the-fly

implementation, signal modeling, and optimization of any user-defined MC-model, for any PGSE acquisition scheme. Dmipy follows a “building block”-based philosophy to Microstructure Imaging, meaning MC-models are modularly constructed to include any number and type of tissue models, allowing simultaneous representation of a tissue’s diffusivity, orientation, volume fractions, axon orientation dispersion, and axon diameter distribution. In particular, Dmipy is geared toward facilitating reproducible, reliable MC-modeling pipelines, often allowing the whole process from model construction to parameter map recovery in fewer than 10 lines of code. To demonstrate Dmipy’s ease of use and potential, we implement a wide range of well-known MC-models, including IVIM, AxCaliber, NODDI(x), Bingham-NODDI, the spherical mean-based SMT and MC-MDI, and spherical convolution-based single- and multi-tissue CSD. By allowing parameter cascading between MC-models, Dmipy also facilitates implementation of advanced approaches like CSD with voxel-varying kernels and single-shell 3-tissue CSD. By providing a well-tested, user-friendly toolbox that simplifies the interaction with the otherwise complicated field of dMRI-based Microstructure Imaging, Dmipy contributes to more reproducible, high-quality research.

This work has been published in [12].

7.1.5. *Effects of tractography filtering on the topology and interpretability of connectomes.*

Participants: Matteo Frigo, Samuel Deslauriers-Gauthier, Drew Parker [Penn Applied Connectomics and Imaging Group, Philadelphia], Abdol Aziz Ould Ismail [Penn Applied Connectomics and Imaging Group, Philadelphia], Junghoon John Kim [Department of Molecular, Cellular & Biomedical Sciences, New York], Ragini Verma [Penn Applied Connectomics and Imaging Group, Philadelphia], Rachid Deriche.

The analysis of connectomes and their associated network metrics forms an important part of clinical studies. These connectomes are based on tractography algorithms to estimate the structural connectivity between brain regions. However, tractography algorithms, are prone to false positive connections and this affects the quality of the connectomes. Several tractography filtering techniques (TFTs) have been proposed to alleviate this issue in studies, but their effect on connectomic analyses of pathology has not been investigated. The aim of this work is to investigate how TFTs affect network metrics and their interpretation in the context of clinical studies.

This work has been published in [29]

7.1.6. *Spherical convolutional neural network for fiber orientation distribution function and micro-structure parameter estimation from dMRI*

Participants: Sara Sedlar, Samuel Deslauriers-Gauthier, Théodore Papadopoulo, Rachid Deriche.

Convolutional neural networks (CNNs) are proven to be a powerful tool for many computer vision problems where the data is acquired on a regular grid in Euclidean space. As the dMRI signals used in our experiments are acquired on spheres, we have investigated spherical CNN model (S2-CNN). In regular CNNs, during convolution, kernels are translated over the input feature maps with equidistant steps. In S2-CNN, both kernels and feature maps are represented in the 3D rotation group - $SO(3)$ manifold. A rotation in $SO(3)$ is analogous to a translation in Euclidean space. However, there is no regular equidistant grid in $SO(3)$. As a consequence, the convolution is performed in the rotational harmonics (Fourier) domain. In this work, we investigate how the S2-CNN can be adapted to properties of dMRI data, such as antipodal symmetry, the presence of Rician noise, multiple sampling shells, etc.

This work currently in progress.

7.1.7. *Adaptive phase correction of diffusion-weighted images*

Participants: Marco Pizzolato [Signal Processing Lab (LTS5), EPFL, Lausanne], Guillaume Gilbertb [MR Clinical Science, Philips Healthcare Canada, Markham, ON], Jean-Philippe Thiran [Signal Processing Lab (LTS5), EPFL, Lausanne], Maxime Descoteaux [Université de Sherbrooke, Sherbrooke], Rachid Deriche.

Phase correction (PC) is a preprocessing technique that exploits the phase of images acquired in Magnetic Resonance Imaging (MRI) to obtain real-valued images containing tissue contrast with additive Gaussian noise, as opposed to magnitude images which follow a non-Gaussian distribution, e.g. Rician. PC finds its natural application to diffusion-weighted images (DWIs) due to their inherent low signal-to-noise ratio and consequent non-Gaussianity that induces a signal overestimation bias that propagates to the calculated diffusion indices. PC effectiveness depends upon the quality of the phase estimation, which is often performed via a regularization procedure. We show that a suboptimal regularization can produce alterations of the true image contrast in the real-valued phase-corrected images. We propose adaptive phase correction (APC), a method where the phase is estimated by using MRI noise information to perform a complex-valued image regularization that accounts for the local variance of the noise. We show, on synthetic and acquired data, that APC leads to phase-corrected real-valued DWIs that present a reduced number of alterations and a reduced bias. The substantial absence of parameters for which human input is required favors a straightforward integration of APC in MRI processing pipelines.

This work has been published in [17].

7.1.8. *Towards validation of diffusion MRI tractography: bridging the resolution gap with 3D Polarized Light Imaging*

Participants: Abib Olushola Yessouffou Alimi, Samuel Deslauriers-Gauthier, Rachid Deriche.

Three-dimensional Polarized Light Imaging (3D-PLI) is an optical approach presented as a good candidate for validation of diffusion Magnetic Resonance Imaging (dMRI) results such as orientation estimates (fiber Orientation Distribution Functions) and tractography. We developed an analytical approach to reconstruct fiber ODFs from 3D-PLI datasets. From these fODFs, here we compute brain fiber tracts via dMRI-based probabilistic tractography algorithm. Reconstructed fODFs at different scales proves the ability to bridge the resolution gap between 3D-PLI and dMRI, demonstrating, therefore, a great promise to validate diffusion MRI tractography thanks to multi-scale fiber tracking based on 3D-PLI.

This work has been published in [21].

7.1.9. *Analytical Fiber ODF Reconstruction in 3D Polarized Light Imaging: Performance Assessment*

Participants: Abib Olushola Yessouffou Alimi, Samuel Deslauriers-Gauthier, Felix Matuschke [INM-1 - Institute of Neuroscience and Medicine, Jülich], Daniel Schmitz [INM-1 - Institute of Neuroscience and Medicine, Jülich], Markus Axer [INM-1 - Institute of Neuroscience and Medicine, Jülich], Rachid Deriche.

Three dimensional Polarized Light Imaging (3D-PLI) allows to map the spatial fiber structure of postmortem tissue at a sub-millimeter resolution, thanks to its birefringence property. Different methods have been recently proposed to reconstruct the fiber orientation distribution function (fODF) from high-resolution vector data provided by 3D-PLI. Here, we focus on the analytical fODF computation approach, which uses the spherical harmonics to represent the fODF and analytically computes the spherical harmonics coefficients via the spherical Fourier transform. This work deals with the assessment of the performance of this approach on rich synthetic data which simulates the geometry of the neuronal fibers and on human brain dataset. A computational complexity and robustness to noise analysis demonstrate the interest and great potential of the approach.

This work has been published in [22].

7.2. Unveiling brain activity using M/EEG

7.2.1. *Fast Approximation of EEG Forward Problem and Application to Tissue Conductivity Estimation*

Participants: Kostiantyn Maksymenko, Maureen Clerc, 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 fine 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 published in [15].

7.2.2. *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 has been published in [8].

7.2.3. *Convolutional autoencoder for waveform learning*

Participants: Sara Sedlar, Maureen Clerc, Rachid Deriche, Théodore Papadopoulo.

Electro- or Magneto-encephalographic (M/EEG) signals measured on the scalp can be modeled as a linear combination of source signals occurring in different cortical regions. Analysis of specific recurrent waveforms from measurements can help in the evaluation of several neurological disorders such as epilepsy, Alzheimer's disease, and narcolepsy. In addition, detection of the neural events evoked by certain stimuli is crucial for brain-computer interfaces. Such M/EEG signals are quite faint and inherently affected by an important noise, generated by irrelevant brain activities, by other organs, by external ambient noise or imperfections of the measuring devices. In addition, there are intra- and inter-subject variabilities, meaning that the relevant waveforms vary in terms of amplitudes, shapes, and time delays. This makes waveform learning on such signals a quite complex task. In order to address these problems, a number of dictionary (here waveforms) learning based approaches has been proposed. The common framework behind those approaches is an alternative estimation of data-driven waveforms and their corresponding activations in terms of amplitudes and positions over time. Motivated by the success of these methods and the advances in deep learning, we propose a method based on a convolutional auto-encoder that aims at improving more traditional approaches. Auto-encoders are unsupervised neural network models that have been successfully used for data compression, feature learning, denoising and clustering. Auto-encoders are composed of an encoder which creates a code also known as bottle-neck and decoder that is supposed to reconstruct input signal given the code. By penalizing reconstruction loss function with certain constraints we can guide the auto-encoder to perform compression, denoising, clustering etc. For the moment, the properties of the model are investigated on

single-channel synthetic data imitating three types of neurological activities (spikes, short oscillatory and low frequency saw-tooth waveforms) mixed using a realistic leadfield matrix (source space to sensor space transform).

This work is in current progress.

7.2.4. Automatic detection of epileptic seizures by video-EEG

Participants: Mamoudou Sano, Hugo Cadis [IPMC], Fabrice Duprat [IPMC], Massimo Mantegazza [IPMC], Maureen Clerc, Théodore Papadopoulo.

Epilepsy is a serious condition that affects almost 50 million people worldwide. Despite several generations of antiepileptic treatments, the rate of drug-resistant patients remains around 30% and the discovery of new pharmacological targets is therefore a crucial issue.

In order to find pharmacological targets, several animal models make it possible to study the mechanisms of establishment of epileptic disease, or epileptogenesis, and the consequences of repeated spontaneous attacks which characterize epilepsy. Recording an electroencephalogram (EEG) remains the best way to understand these mechanisms. However, the placement of electrodes on small animals such as mice is difficult or even impossible depending on the age of the animal or other used protocols. The use of video recordings over several days, weeks or months makes it possible to observe the animals with a minimum of disturbances and to assess the severity of the crises on a behavioral scale. In both cases, the visual analysis of hundreds of hours of video and/or EEG recordings is very long and error-prone.

The goal of this joint IPMC, ATHENA work was to improve acquisition techniques and develop software tools to automate both EEG and video analysis. EEG analysis was based on the "Adaptive Waveform Learning" that was developed in the group a few years ago [61]. This is work in progress.

7.3. Combined fMRI, M/EEG and dMRI

7.3.1. White Matter Information Flow Mapping from Diffusion MRI and EEG.

Participants: Samuel Deslauriers-Gauthier, Jean-Marc Lina [ETS - Ecole de Technologie Supérieure, Montréal], Russel Butler [Université de Sherbrooke, Sherbrooke], Kevin Whittingstall [Université de Sherbrooke, Sherbrooke], Pierre-Michel Bernier [Université de Sherbrooke, Sherbrooke], Maxime Descoteaux [Université de Sherbrooke, Sherbrooke], 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 has been published in [11].

7.3.2. Structural connectivity to reconstruct brain activation and effective connectivity between brain regions

Participants: Brahim Belaoucha, Théodore Papadopoulo.

Understanding how brain regions interact to perform a specific task is very challenging. EEG and MEG are two non-invasive imaging modalities that allow the measurement of brain activation with high temporal resolution. Several works in EEG/MEG source reconstruction show that estimating brain activation can be improved by considering spatio-temporal constraints but only few of them use structural information to do so. In this work, we present a source reconstruction algorithm that uses brain structural connectivity, estimated from diffusion MRI (dMRI), to constrain the EEG/MEG source reconstruction. Contrarily to most source reconstruction methods which reconstruct activation for each time instant, the proposed method estimates an initial reconstruction for the first time instants and a multivariate autoregressive model that explains the data in further time instants. This autoregressive model can be thought as an estimation of the effective connectivity between brain regions. We called this algorithm iterative Source and Dynamics reconstruction (iSDR). This paper presents the overall iSDR approach and how the proposed model is optimized to obtain both brain activation and brain region interactions. The accuracy of our method is demonstrated using synthetic data in which it shows a good capability to reconstruct both activation and connectivity. iSDR is also tested with real data (face recognition task). The results are in phase with other works published with the same data and others that used different imaging modalities with the same task showing that the choice of using an autoregressive model gives relevant results.

This work has been submitted to the non-invasive brain imaging special issue of Journal of Neural Engineering.

7.3.3. Estimation of Axon Conduction Delay, Conduction Speed, and Diameter from Information Flow using Diffusion MRI and MEG.

Participants: Samuel Deslauriers-Gauthier, Rachid Deriche.

The different lengths and conduction velocities of axons connecting cortical regions of the brain yield information transmission delays which are believed to be fundamental to brain dynamics. While early work on axon conduction velocity was based on ex vivo measurements, more recent work makes use of a combination of diffusion Magnetic Resonance Imaging (MRI) tractography and electroencephalography (EEG) to estimate axon conduction velocity in vivo. An essential intermediary step in this later strategy is to estimate the inter hemispheric transfer time (IHTT) using EEG. The IHTT is estimated by measuring the latency between the peaks or by computing the lag to maximum correlation on contra lateral electrodes. These approaches do not take the subjects anatomy into account and, due to the limited number of electrodes used, only partially leverage the information provided by EEG. In our previous work, we proposed a method, named Connectivity Informed Maximum Entropy on the Mean (CIMEM), to estimate information flow in the white matter of the brain. CIMEM is built around a Bayesian network which represents the cortical regions of the brain and their connections, observed using diffusion MRI tractography. This Bayesian network is used to constrain the EEG inverse problem and estimate which white matter connections are used to transfer information between cortical regions. In our previous work, CIMEM was used to infer the information flow in the white matter by assuming a constant conduction velocity for all connections. In this context, the conduction speed, and thus the delays, were inputs used to help constrain the problem. Here, we instead assume that the connection used to transfer information across the hemispheres is known, due the design of the acquisition paradigm, but that its conduction velocity must be estimated.

This work has been published in [23].

7.3.4. Estimation of Axonal Conduction Speed and the Inter Hemispheric Transfer Time using Connectivity Informed Maximum Entropy on the Mean

Participants: Samuel Deslauriers-Gauthier, Rachid Deriche.

The different lengths and conduction velocities of axons connecting cortical regions of the brain yield information transmission delays which are believed to be fundamental to brain dynamics. A critical step in the estimation of axon conduction speed in vivo is the estimation of the inter hemispheric transfer time (IHTT). The IHTT is estimated using electroencephalography (EEG) by measuring the latency between the peaks of specific electrodes or by computing the lag to maximum correlation on contra lateral electrodes. These approaches do not take the subject's anatomy into account and, due to the limited number of electrodes used, only partially leverage the information provided by EEG. Using the previous published Connectivity Informed Maximum Entropy on the Mean (CIMEM) method, we propose a new approach to estimate the IHTT. In CIMEM, a Bayesian network is built using the structural connectivity information between cortical regions. EEG signals are then used as evidence into this network to compute the posterior probability of a connection being active at a particular time. Here, we propose a new quantity which measures how much of the EEG signals are supported by connections, which is maximized when the correct conduction delays are used. Using simulations, we show that CIMEM provides a more accurate estimation of the IHTT compared to the peak latency and lag to maximum correlation methods.

This work has been published in [24].

7.3.5. *A Unified Model for Structure–function Mapping Based on Eigenmodes*

Participants: Samuel Deslauriers-Gauthier, Rachid Deriche.

Characterizing the connection between brain structure and brain function is essential for understanding how behaviour emerges from the underlying anatomy. To this end, a common representation of the brain is that of a network, where nodes represent cortical and sub-cortical gray matter volumes and edges represent the strength of structural or functional connectivity. A convenient representation of this network is that of a matrix, where entries represent the strength of the structural connectivity (SC) or functional connectivity (FC) between nodes. A number of studies have shown that the network structure of the white matter shapes functional connectivity, leading to the idea that it should be possible to predict the function given the structure. A strategy is to learn a direct mapping from the SC matrix to the FC matrix. In this work, we show that the mappings currently proposed in the literature can be generalized to a single model and that this model can be used to generate new structure-function mappings. We tested our general model on 40 subjects of the Human Connectome Project and demonstrated that for specific choices of parameters, our model reduces to previously proposed models and yields comparable results. However, by allowing to choose the eigenvalue and eigenvector mapping independently, our models can also produce novel mapping that improve the prediction of FC from SC.

This work is currently under submission to OHBM.

7.3.6. *Connectivity-informed spatio-temporal MEG source reconstruction: Simulation results using a MAR model*

Participants: Ivana Kojcic, Théodore Papadopoulo, Samuel Deslauriers-Gauthier, Rachid Deriche.

Recovering brain activity from M/EEG measurements is an ill-posed problem and prior constraints need to be introduced in order to obtain unique solution. The majority of the methods use spatial and/or temporal constraints, without taking account of long-range connectivity. In this work, we propose a new connectivity-informed spatio-temporal approach to constrain the inverse problem using supplementary information coming from diffusion MRI. We present results based on simulated brain activity using a Multivariate Autoregressive Model, with realistic subject anatomy obtained from Human Connectome Project dataset.

This work has been published in [35].

7.3.7. *Connectivity-informed solution for spatio-temporal M/EEG source reconstruction*

Participants: Ivana Kojcic, Théodore Papadopoulo, Samuel Deslauriers-Gauthier, Rachid Deriche.

Recovering brain activity from M/EEG measurements is an ill-posed problem and prior constraints need to be introduced in order to obtain unique solution. The majority of the methods use spatial and/or temporal constraints, without taking account of long-range connectivity. In this work, we propose a new connectivity-informed spatio-temporal approach to constrain the inverse problem using supplementary information coming from diffusion MRI. We present results based on simulated brain activity obtained with realistic subject anatomy from Human Connectome Project dataset.

This work has been published in [34].

7.3.8. Deconvolution of fMRI Data using a Paradigm Free Iterative Approach based on Partial Differential Equations

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

Functional magnetic resonance imaging (fMRI) is a technique which indirectly measures neural activations via the blood oxygenated level dependent (BOLD) signal. So far, few approaches have been proposed to regularize the fMRI data, while recovering the underlying activations at the voxel level. In particular, for task fMRI, voxels time courses are fitted on a given experimental paradigm. To avoid the necessity of a priori information on the pattern, supposing the brain works with blocks of constant activation, Farouj et al. has developed a deconvolution approach which solves the optimizations problem by splitting it into two regularization problems, i.e. spatial and temporal. Starting from this idea, we propose a paradigm-free iterative algorithm based on partial differential equations (PDEs) which minimizes the image variations, while preserving sharp transitions (i.e. brain activations), in the space and the time dimensions at once.

This work has been published in [27].

7.3.9. Novel 4-D Algorithm for Functional MRI Image Regularization using Partial Differential Equations

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

State-of-the-art techniques for denoising functional MRI (fMRI) images consider the problems of spatial and temporal regularization as decoupled tasks. In this work we propose a partial differential equations (PDEs)-based algorithm that acts directly on the 4-D fMRI image. Our approach is based on the idea that large image variations should be preserved as they occur during brain activation, but small variations should be smoothed to remove noise. Starting from this principle, by means of PDEs we were able to smooth the fMRI image with an anisotropic regularization, thus recovering the location of the brain activations in space and their timing and duration.

This work has been published in [28].

7.3.10. Spatially Varying Monte Carlo Sure for the Regularization of Biomedical Images

Participants: Marco Pizzolato [Signal Processing Lab (LTS5), EPFL, Lausanne], Erick Jorge Canales-Rodríguez [Radiology Department CHUV, Lausanne], Jean-Philippe Thiran [Signal Processing Lab (LTS5), EPFL, Lausanne], Rachid Deriche.

Regularization, filtering, and denoising of biomedical images requires the use of appropriate filters and the adoption of efficient regularization criteria. It has been shown that the Stein's Unbiased Risk Estimate (SURE) can be used as a proxy for the mean squared error (MSE), thus giving an effective criterion for choosing the regularization amount as to that minimizing SURE. Often, due to the complexity of the adopted filters and solvers, this proxy must be calculated with a Monte Carlo method. In practical biomedical applications, however, images are affected by spatially-varying noise distributions, which must be taken into account. We propose a modification to the Monte Carlo method, called svSURE, that accounts for the spatial variability of the noise variance, and show that it correctly estimates the MSE in such cases.

This work has been published in [30].

7.3.11. *The visual word form area (VWFA) is part of both language and attention circuitry*

Participants: Lang Chen, Demian Wasserman, Daniel Abrams, John Kochalka, Guillermo Gallardo-Diez, Vinod Menon.

While predominant models of visual word form area (VWFA) function argue for its specific role in decoding written language, other accounts propose a more general role of VWFA in complex visual processing. However, a comprehensive examination of structural and functional VWFA circuits and their relationship to behavior has been missing. Here, using high-resolution multimodal imaging data from a large Human Connectome Project cohort (N=313), we demonstrate robust patterns of VWFA connectivity with both canonical language and attentional networks. Brain-behavior relationships revealed a striking pattern of double dissociation: structural connectivity of VWFA with lateral temporal language network predicted language, but not visuo-spatial attention abilities, while VWFA connectivity with dorsal fronto-parietal attention network predicted visuo-spatial attention, but not language abilities. Our findings support a multiplex model of VWFA function characterized by distinct circuits for integrating language and attention, and point to connectivity-constrained cognition as a key principle of human brain organization.

This work has been published in [10].

7.4. Brain Computer Interfaces

7.4.1. *Augmenting Motor Imagery Learning for Brain–Computer Interfacing Using Electrical Stimulation as Feedback*

Participants: Saugat Bhattacharyya [School of Bio-Science and Engineering, Calcutta], Mitsuhiro Hayashibe [Tohoku University, Sendai], Maureen Clerc.

Brain-computer Interfaces (BCI) and Functional electrical stimulation (FES) contribute significantly to induce cortical learning and to elicit peripheral neuronal activation processes and thus, are highly effective to promote motor recovery. This study aims at understanding the effect of FES as a neural feedback and its influence on the learning process for motor imagery tasks while comparing its performance with a classical visual feedback protocol. The participants were randomly separated into two groups: one group was provided with visual feedback (VIS) while the other received electrical stimulation (FES) as feedback. Both groups performed various motor imagery tasks while feedback was provided in form of a bi-directional bar for VIS group and targeted electrical stimulation on the upper and lower limbs for FES group. The results shown in this paper suggest that the FES based feedback is more intuitive to the participants, hence, the superior results as compared to the visual feedback. The results suggest that the convergence of BCI with FES modality could improve the learning of the patients both in terms of accuracy and speed and provide a practical solution to the BCI learning process in rehabilitation.

This work, obtained in the context of the BCI-LIFT IPL, has been published in [9].

7.4.2. *Adaptive parameter setting in a code modulated visual evoked potentials BCI*

Participants: Federica Turi, Maureen Clerc.

Code-modulated visual evoked potentials (c-VEPs) BCI are designed for high-speed communication. The setting of stimulus parameters is fundamental for this type of BCI, because stimulus parameters have an influence on the performance of the system. In this work we design a c-VEP BCI for word spelling, in which it is possible to find the optimal stimulus presentation rate per each subject thanks to an adaptive setting parameter phase. This phase takes place at the beginning of each session and allows to define the stimulus parameters that are used during the spelling phase. The different stimuli are modulated by a binary m-sequence circular-shifted by a different time lag and a template matching method is applied for the target detection. We acquired data from 4 subjects in two sessions. The results obtained for the offline spelling show the variability between subjects and therefore the importance of subject-dependent adaptation of c-VEP BCI.

This work has been published in [32].

7.4.3. *Participation to the Cybathlon BCI Series*

Participants: Karine Leclerc [Centre René Labreuil, Le Cannet], Magali Mambrucchi [Centre René Labreuil, Le Cannet], Amandine Audino, Pierre Giacalone, Federica Turi, Maureen Clerc, Théodore Papadopoulo.

The CYBATHLON is a unique championship in which people with physical disabilities compete against each other to complete everyday tasks using state-of-the-art technical assistance systems. Athena participated in the CYBATHLON BCI Series that took place on September 8th, 2019 as a satellite event of the Graz Brain-Computer Interface Conference. Athena was part of a bigger Inria team which encompassed also the Inria Bordeaux Sud-Ouest Potioc team (participants from Bordeaux are not listed). For both Inria sub-teams, it was a first participation to such a competition : we learned a lot about the practical issues of working with people with physical disabilities and on all the practical issues that can encounter a BCI user out of the lab. The actual competition consisted of driving a car on a track by issuing three types of commands (Left, Right, Lights) using mental imagery. Even though our pilot finished last, she was for each run leading the race till a few seconds before its end. A great satisfaction was to see that the software that we built worked reliably out of the lab (many teams have had troubles in issuing commands and had to redo a race). Yet, this required a lot of last minute work to integrate smoothly in the competition system: we learned a lot in this respect. The poster [36] summarises this effort.

7.4.4. *BCI Performance prediction*

Participants: Maureen Clerc, Nathalie Gayraud, Laurent Bougrain [NeuroSys Project-Team], Sébastien Rimbert [NeuroSys Project-Team], Stéphanie Fleck [Perseus].

Predicting a subject's ability to use a Brain Computer Interface (BCI) is one of the major issues in the BCI domain. Relevant applications of forecasting BCI performance include the ability to adapt the BCI to the needs and expectations of the user, assessing the efficiency of BCI use in stroke rehabilitation, and finally, homogenizing a research population. A limited number of recent studies have proposed the use of subjective questionnaires, such as the Motor Imagery Questionnaire Revised-Second Edition (MIQ-RS). Our results showed no significant correlation between BCI performance and the MIQ-RS scores. However, we reveal that BCI performance is correlated to habits and frequency of practicing manual activities. This work is an outcome of the BCI-LIFT IPL and was published in [18]. Another joint publication [19] investigated median nerve stimulation as a new approach to detect intraoperative awareness during General Anesthesia.

7.4.5. *EEG Classification of Auditory Attention*

Participants: Joan Belo, Johann Benerradi, Maureen Clerc, Michel Pascal [Nice Music Conservatory], Daniele Schön [Institut de Neurosciences des Systèmes].

In a Master's thesis [33] in collaboration with Nice Music Conservatory and Institut de Neurosciences des Systèmes, we focused on analyzing auditory attention of human participants who are presented two auditory streams, simultaneously on left and right. By analyzing the EEG signals measured, the problem is to detect to which stream the participant is attending. Auditory Attention is also the topic of the PhD thesis of Joan Belo, funded by a CIFRE with Oticon Medical.

7.4.6. *Innovative Brain-Computer Interface based on motor cortex activity to detect accidental awareness during general anesthesia*

Participants: Sébastien Rimbert, Philippe Guerci, Nathalie Gayraud, Claude Meistelman, Laurent Bougrain.

Accidental Awareness during General Anesthesia (AAGA) occurs in 1-2% of high-risk practice patients and is responsible for severe psychological trauma, termed post-traumatic stress disorder (PTSD). Currently, monitoring techniques have limited accuracy in predicting or detecting AAGA. Since the first reflex of a patient experiencing AAGA is to move, a passive Brain-Computer Interface (BCI) based on the detection of an intention of movement would be conceivable to alert the anesthetist and prevent this phenomenon. However, the way in which the propofol (an anesthetic drug commonly used for inducing and maintaining general anesthesia) affects the motor brain activity and is reflected by the electroencephalo-graphic (EEG)

signal has been poorly investigated and is not clearly understood. The goal of this forward-looking study is to investigate the motor activity behavior with step-wise increase of propofol doses in 4 healthy subjects and provide a proof of concept for such an innovative BCI.

This work has been published in [26].

8. Partnerships and Cooperations

8.1. National Initiatives

8.1.1. ADT

8.1.1.1. 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.

8.1.1.2. 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.

8.2. European Initiatives

8.2.1. FP7 & H2020 Projects

8.2.1.1. 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.

8.3. International Initiatives

8.3.1. Inria International Partners

8.3.1.1. 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.

8.3.2. Participation in Other International Programs

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

8.4. International Research Visitors

8.4.1. Visits of International Scientists

- Pr Gloria Menegaz, Department of Computer Science, University of Verona (March 23 - Sept 20, 2019)

8.4.1.1. Internships

- Imogen Den otter-Moore - Queen's University, Kingston, Canada, From early May to late July, 2019
- Federica Cruciani - Department of Computer Science, University of Verona (March 1 - June 30, 2019)
- Enes Albay - Ph.D. student in Computer Engineering (Cont.), Istanbul Technical University, From Nov. 4, 2019 to Oct. 3, 2020.

9. Dissemination

9.1. Promoting Scientific Activities

9.1.1. Scientific Events: Organisation

9.1.1.1. Member of the Organizing Committees

- M. Zucchelli is one of the organizer of the summer school on Brain Connectomics at the University of Verona, September 2019.

9.1.2. Scientific Events: Selection

9.1.2.1. Member of the Conference Program Committees

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

9.1.2.2. 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 (GRETSI, ICIP, ISBI, ICASSP, VISAPP).

9.1.3. Journal

9.1.3.1. Member of the 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
- M. Clerc, R. Deriche and T. Papadopoulo serve as Guest Editor for the special issue on Non-invasive brain imaging of the Journal of Neural Engineering.

9.1.3.2. 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 (Pattern Recognition, NeuroImage, Frontiers in Neuroscience, Brain Topography, Journal of Neural Engineering).
- S. Deslauriers-Gauthier serves several international journals (NeuroImage, IEEE Transactions on Biomedical Engineering, Journal of Neural Engineering).
- M. Zucchelli serves several international journals (NeuroImage, BioMedical Engineering OnLine).

9.1.4. Invited Talks

- M. Clerc gave a talk in front of the French Academy of Sciences on June 21 2019.
- M. Clerc gave a keynote talk at the INCF conference in Warsaw on Sep 2, 2019.
- M. Clerc gave a keynote talk at the ACM Multimedia HealthMedia workshop in Nice on October 21, 2019.
- R. Deriche gave an invited keynote speech at Hassan II Academy of Sciences and Technology, Kingdom of Morocco (Feb. 27, 2019).

9.1.5. Leadership within the Scientific Community

- M. Clerc is vice-president of the CORTICO association <https://www.cortico.fr>
- M. Clerc is vice-president of the NeuroMod institute of Université Côte d'Azur

9.1.6. Scientific Expertise

- M. Clerc is member of the COERLE and CERNA committees.
- R. Deriche serves several international institutions in reviewing applications : ERC Grants, Swiss National Science Foundation, EPFL, the Netherlands Organisation for Scientific Research (NWO).
- T. Papadopoulo serves several international (Cordis-H2020 for FET-OPEN), national (ANR) and local (NeuroMod in Nice, iSite NEXt in Nantes) institutions in reviewing applications.

9.1.7. Research Administration

- M. Clerc was appointed director of the Inria Sophia Antipolis research Center in November 2019.
- M. Clerc was president of the CRCN hiring committee at Inria Bordeaux in 2019.
- M. Clerc was vice-president of the Inria Evaluation committee from September to October 2019.
- 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 (<https://www.olea-medical.com/en>).

9.2. Teaching - Supervision - Juries

9.2.1. Teaching

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

M. Clerc teaches Functional Brain Imaging in the MSc Mod4NeuCog of Université Côte d'Azur (30 hours).

M. Clerc gave two lectures in a summer school on Brain Connectomics at the University of Verona, September 2019.

M. Zucchelli gave one lecture and one hands-on session in a summer school on Brain Connectomics at the University of Verona, September 2019.

9.2.2. Supervision

PhD defended on May 7th, 2019: Thinhinane Megherbi, “HARDI & High Order Tensors”, 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 defended on Dec. 19th, 2019: Kostiantyn Maksymenko, “Inverse problem in EEG/MEG/SSEG: towards a better consideration of anatomo-functional constraints”, Université Côte d’Azur, Supervisors: Théodore Papadopoulo and 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.

PhD in progress: Côme Le Breton, "Non invasive analysis of epileptogenic networks and their response to neurofeedback", started June 2019. Supervisors: Maureen Clerc and Théodore Papadopoulo.

PhD in progress: Joan Belo, "Electroencephalography analysis of auditory attention when listening to music", started June 2019. Supervisors: Maureen Clerc and Daniele Schön.

9.2.3. Juries

- M. Clerc participated in the PhD Jury of Maria-Carla Piastra at University of Genova in March 2019.
- M. Clerc participated in the PhD Jury of Jelena Mladenovic at University of Bordeaux in September 2019.
- R. Deriche participated in the PhD Jury of L. El Gueddari at University Paris Saclay on Dec. 13th, 2019.
- R. Deriche participated in the PhD Jury of A. Mendoza Quispe at Ecole Normale Supérieure Paris-Saclay on Feb. 5th, 2019.
- R. Deriche participated in the PhD Jury of T. Megherbi at USTHB (Algiers) on May 7th, 2019.
- R. Deriche participated as a reviewer in the PhD Jury of M. Kchaou at ENIT (Tunis) defended on July, 2019.
- T. Papadopoulo participated as a reviewer in the PhD Jury of L. Uro at Sorbonne University Paris 6 on Nov. 25th, 2019.
- T. Papadopoulo participated as a reviewer in the HDR Jury of S. Bonnet at CEA Cinatec, Grenoble on Dec. 2nd, 2019.
- T. Papadopoulo and M. Clerc participated in the PhD Jury of K. Maksymenko at Université Côte d’Azur on Dec. 19th, 2019.

9.3. Popularization

- Demonstration of the P300 speller and of the subject adapted dry EEG cap to the local and national instances, M. Clerc, T. Papadopoulo, F. Turi, S. Guebba.
- Participation to the Cybathlon BCI Series, Graz. September 2019 [36].

9.3.1. Articles and contents

- An article mentioned the BCI projects of Athena in a special issue from magazine Le Point https://www.lepoint.fr/sante/connecter-son-cerveau-a-un-ordinateur-pour-quoi-faire-18-03-2019-2301895_40.php

9.3.2. Interventions

- National events: Brain Awareness Week, two wide audience talks in Biot, Mouans Sartoux, and demonstration of Brain-Computer interfaces, M. Clerc, T. Papadopoulo.

10. Bibliography

Major publications by the team in recent years

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