RESEARCH CENTRE

Sophia Antipolis - Méditerranée

2020 ACTIVITY REPORT

Project-Team ATHENA

Computational Imaging of the Central Nervous System

DOMAIN

Digital Health, Biology and Earth

THEME

Computational Neuroscience and Medicine

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Project-Team ATHENA

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

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1 Team members, visitors, external collaborators

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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 primarly 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 primarly 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 [65], Merboldt et al [70] and Taylor et al [84]. 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.

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) [83, 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 [66, 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 [68] and [67]).

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) [87] and High Angular Resolution Diffusion Imaging (HARDI) methods such as Q-ball imaging [85] and other multi-tensors and compartment models [80, 82, 63, 62, 77] were developed to resolve the orientationnality of more complicated fiber bundle configurations.

Q-Ball imaging (QBI) has been proven very successful in resolving multiple intravoxel fiber orientations in MR images, thanks to its ability to reconstruct the Orientation Distribution Function (ODF, the probability of diffusion in a given direction). These tools play a central role in our work related to the development of a robust and linear spherical harmonic estimation of the HARDI signal and to our development of a regularized, fast and robust analytical QBI solution that outperforms the state-of-the-art ODF numerical technique developed by Tuch [85]. Those contributions are fundamental and have already started to impact on the Diffusion MRI, HARDI and Q-Ball Imaging community [51]. They are at the core of our probabilistic and deterministic tractography algorithms devised to best exploit the full distribution of the fiber ODF (see [52], [3] and [53], [4]).

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 [75, 76] or 4th order Tensor Model [43]. For more details, we refer the reader to our articles in [59, 80] where we review HOT models and to our articles in [67], 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 [62, 63]. They have also opened up a landscape of extremely exciting research fields for medicine and neuroscience. Hence, due to the complexity of the CNS data and as the magnetic field strength of scanners 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 [57, 80].

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 [71].

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 [71, 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 download[1], have been selected for use in the HCP (Human Connectome Project)[2].

We think that such kind of contributions open new perspectives for dMRI applications including, for example, tractography where the improved characterization of the fiber orientations is likely to greatly and quickly help tracking through regions with and/or without crossing fibers [58].

[1] http://www.emmanuelcaruyer.com/

[2] http://humanconnectome.org/documentation/Q1/imaging-protocols.html

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 [88] 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 [41, 42], the Solid Harmonic (SoH) basis [54], the Simple Harmonic Oscillator based Reconstruction and Estimation (SHORE) basis [73] and more recent Mean Apparent Propagator or MAP-MRI basis [74].

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 [7].

Towards microstructural based tractography In order to go far beyond traditional fiber-tracking techniques, we believe that first order information, i.e. fiber orientations, has to be superseeded by second and third order information, such as microstructure details, to improve tractography. However, many of these higher order information methods are relatively new or unexplored and tractography algorithms based on these high order based methods have to be conceived and designed. In this aim, we propose to work with multiple-shells to reconstruct the Ensemble Average Propagator (EAP), which represents the whole 3D diffusion process and use the possibility it offers to deduce valuable insights on the microstructural properties of the white matter. Indeed, from a reconstructed EAP one can compute the angular features of the diffusion in an diffusion Orientation Distribution Function (ODF), providing insight in axon orientation, calculate properties of the entire diffusion in a voxel such as the Mean Squared Diffusivity (MSD) and Return-To-Origin Probability (RTOP), or come forth with bio-markers detailing diffusion along a particular white matter bundle direction such as the Return-to-Axis or Return-to-Plane Probability (RTAP or RTPP). This opens the way to a ground-breaking computational and unified framework for tractography based on EAP and microstructure features [8]. Using additional a priori anatomical and/or functional information, we could also constrain the tractography algorithm to start and terminate the streamlines only at valid processing areas of the brain.

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

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 groundbreaking 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 ODYSSÉE/ATHENA have participated in the acquisition of one such machine installed in the hospital "La Timone" in Marseille.

MEG and EEG can be measured simultaneously (M/EEG) and reveal complementary properties of the electrical fields. The two techniques have temporal resolutions of about the millisecond, which is the typical granularity of the measurable electrical phenomena that arise within the brain. This high temporal resolution makes MEG and EEG attractive for the functional study of the brain. The spatial resolution, on the contrary, is somewhat poor as only a few hundred data points can be acquired simultaneously (about 300-400 for MEG and up to 256 for EEG). MEG and EEG are somewhat complementary with fMRI (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 [64], [9] and means to calibrate them [86] 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 [81].

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 [69, 72], but to our knowledge there are very few studies merging data coming both from M/EEG and dMRI at the analysis level [79, 56, 46, 78].

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 develops new generation of computational dMRI and M/EEG models and methods for identifying and characterizing the connectivities on which the joint network is built [5, 6].

Capitalizing on the strengths of dMRI & M/EEG and building on the bio-physical and mathematical foundations of our models, CoBCoM contributes 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).

The 3IA UCA Chair AI-BASED OMPUTATIONAL BRAIN CONNECTOMICS project aims to reconstruct and analyse the network of neural connections of the brain, called the connectome via a computational brain connectomics framework based on ground-breaking AI algorithms and machine learning tools to gain insight into brain architecture, functioning and neurodegenerative diseases. The avalanche of big data required to reconstruct the connectome and the study of the high complexity of structural and functional interactions within the connectome clearly position brain connectomics as a big data problem where AI & machine learning in particular, represent a very promising trend, as recently demonstrated in computer vision and in some biomedical image data-driven analysis. Partly related to the ERC Advanced Grant CoBCoM this project aims to construct networks specifically built on new generation of AI algorithms and machine learning tools to reconstruct structural and functional connectomes using advanced and integrated diffusion MRI, Electro and Magneto-Encephalography (EEG & MEG) methods [10].

Capitalizing on the strengths of dMRI & M/EEG and building on the bio-physical and mathematical foundations of our models, COBCOM and the 3IA UCA Chair AI-BASED COMPUTATIONAL BRAIN CONNECTOMICS 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 microstructure 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 https://ins-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 ALS[3] patients.

5 New software and platforms

5.1 New software

5.1.1 Dmipy

Name: Diffusion MRI Multi-Compartment Modeling and Microstructure Recovery Made Easy

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

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(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.

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5.1.2 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 Contributions: 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: The python interface of OpenMEEG has been improved and now allows to pass python data structures (meshes, conductivities) to characterize the gain matrices to be calculated without going through files. This is done to ease a future integration of OpenMEEG in MNE-python. A code factorization also took place to allow in the long term to facilitate the integration in OpenMEEG of the work of K. Maksymenko on the efficient calculation of gain matrices for several conductivity values. This work has not yet been released.

URL: http://openmeeg.github.io/

Publications: inria-00467061v2, inria-00584205v1, hal-01278377v1

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Participants: Alexandre Gramfort, Emmanuel Olivi, Geoffray Adde, Jan Kybic, Kai Dang, Maureen Clerc, Perrine Landreau, Renaud Keriven, Théodore Papadopoulo

5.1.3 BCI-VIZAPP

Name: 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 deep transmutation following, among other things, the impulse of the SED of CRISAM in the ADT BciBrowser. Signal processing which was once based only on OpenViBE can now be done internally by the software. This has led to the development of different substitutable "backends" which can do this processing. This signal processing capability was also used to implement an interface intended for participation in 2020 in the Athena Cybathlon (which did not take place for health reasons). Indeed, the use of an external software such as OpenViBE turned out to be a weak point of the system which was tested during the Cybathlon BCI series in 2019.

Contact: Théodore Papadopoulo

Participants: Nathanaël Foy, Romain Lacroix, Maureen Clerc, Théodore Papadopoulo, Yang Ji, Come Le Breton

5.1.4 Talon

Name: Tractograms As Linear Operators in Neuroimaging

Keywords: Diffusion imaging, Diffusion MRI, Brain MRI, Brain

Scientific Description: Talon is a Python package that implements Tractograms As Linear Operators in Neuroimaging. It is a general tool which allows users to transform a collection of streamlines (a tractogram) obtained from diffusion magnetic resonance imaging (MRI) into a linear forward model of neuroimaging data. A particularity of Talon is that it allows the user to specify the forward model, therefore being very flexible on the definition of the linear operator. The structure of the operator is exploited, allowing Talon to solve problems with millions of variables and hundreds of millions of data points. By solving a linear system this operator, Talon assigns a weight to each streamline which represents its contribution to imaging data. The current version is directed at diffusion MRI data and supports solving linear systems with non-negative least squares, group sparsity, and hierarchical sparsity. In the future, it will be updated to support more varied structural and functional data.

Functional Description: Talon is a Python package that implements Tractograms As Linear Operators in Neuroimaging. It is a general tool that assigns a weight to each streamline of a collection (referred to as a tractogram) by fitting the diffusion MRI data. This allows, among other things, to filter a tractogram and remove redundant streamlines. The current version is directed at diffusion MRI data and supports solving linear systems with non-negative least squares, group sparsity, and hierarchical sparsity. In the future, it will be updated to support more varied structural and functional data.

Release Contributions: Initial version that implements the minimum requirements.

News of the Year: This first version contains the base functionality of the software.

Publication: hal-03116143

Authors: Matteo Frigo, Samuel Deslauriers-Gauthier, Mauro Zucchelli, Rachid Deriche

Contact: Samuel Deslauriers-Gauthier

6 New results

6.1 Computational Diffusion MRI

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 [18, 10].

Diffusion MRI Tractography Filtering Techniques Change the Topology of Structural 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 use of non-invasive techniques for the estimation of structural brain networks (i.e. connectomes) opened the door to large-scale investigations on the functioning and the architecture of the brain, unveiling the link between neurological disorders and topological changes of the brain network. This

study aims at assessing if and how the topology of structural connectomes estimated non-invasively with diffusion MRI is affected by the employment of tractography filtering techniques in structural connectomic pipelines. Additionally, this work investigates the robustness of topological descriptors of filtered connectomes to the common practice of density-based thresholding. In this approach, we investigate the changes in global efficiency, characteristic path length, modularity and clustering coefficient on filtered connectomes obtained with the spherical deconvolution informed filtering of tractograms and using the convex optimization modelling for microstructure informed tractography. The analysis is performed on both healthy subjects and patients affected by traumatic brain injury and with an assessment of the robustness of the computed graph-theoretical measures with respect to density-based thresholding of the connectome. Our results demonstrate that tractography filtering techniques change the topology of brain networks, and thus alter network metrics both in the pathological and the healthy cases. Moreover, the measures are shown to be robust to density-based thresholding. Significance. The present work highlights how the inclusion of tractography filtering techniques in connectomic pipelines requires extra caution as they systematically change the network topology both in healthy subjects and patients affected by traumatic brain injury. Finally, the practice of low-to-moderate density-based thresholding of the connectomes is confirmed to have negligible effects on the topological analysis.

This work has been published in [16].

Fully-Connected Neural Network and Spherical-Harmonics Rotation Invariant Features Improve the Estimation of Brain Tissue Microstructure in Diffusion MRI

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

Fully connected neural networks (FC-NN) have been successfully trained on the diffusion signal in each brain voxel to fit microstructural indices. In this work, we propose to combine the Fully Connected Neural Networks and the new series of algebraic independent rotation-invariant features (RIF) our group derived from the diffusion signal Spherical Harmonics (SH) expansion, testing if the combination of these two approaches improves the estimation of the microstructural indices with respect to each method taken by itself. In order to test this hypothesis, we created a set of 300000 synthetic voxels simulated using the state of the art multi-compartment models to train 12 FC-NN with an increasing number of perceptrons and hidden layers. Our results show that all the networks are able to outperform the classical fitting using multi-compartment models. RIF-based FC-NN is able to obtain better performances with respect to SH-coefficients and signal based FC-NN for all the networks with less than 64 perceptrons per hidden layer. Increasing the number of perceptrons leads to a convergence of the accuracy of the estimation of the microstructural indices for the three networks. In conclusion, increasing the number of hidden layers from 2 to 5 leads to a general improvement of the estimation of the indices for all the inputs

This work has been published in [27].

Diffusion MRI Fiber Orientation Distribution Function Estimation Using Voxel-wise Spherical U-net

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

Diffusion Magnetic Resonance Imaging (dMRI) is an imaging technique which enables analysis of the brain tissue at a microscopic scale, particularly the analysis of white matter. Given a high enough angular resolution, a common way to explain the measured signal is via fiber orientation distribution function (fODF). This function describes the orientation and volume fraction of axon bundles within each voxel and is an essential ingredient of tractography. In this work, we have investigated a deep learning approach for the fODF estimation. U-nets enable fast and high resolution inference by combining multi-scale features from contracting and expanding parts of the network. As dMRI signals are most commonly acquired on spheres, we propose a spherical U-net which is adjusted to the properties of the dMRI data, namely its real nature, antipodal symmetry, uniform sampling and axial symmetry of the

signals corresponding to individual fibers. We compared our model with another deep learning approach based on a 3D convolutional neural network and a state-of-the-art approach-multi-shell multi-tissue constrained spherical deconvolution, on real data from Human Connectome Project and synthetic data generated using ball and stick model. The methods are compared in terms of mean square error and mean angular error for dMRI signals of different angular resolutions. Provided quantitative analyses show improved performance with our approach even with significantly reduced number of parameters and results obtained on synthetic data indicate its robustness with respect to noise. Qualitative results illustrating the performance of the methods are also presented.

This work has been published in [21]

Multi Tissue Modelling of Diffusion MRI Signal Reveals Volume Fraction Bias

Participants Matteo Frigo, Rutger Fick *(TheraPanacea)*, Mauro Zucchelli, Samuel Deslauriers-Gauthier, Rachid Deriche.

This paper highlights a systematic bias in white matter tissue microstructure modelling via diffusion MRI that is due to the common, yet inaccurate, assumption that all brain tissues have a similar T2 response. We show that the concept of "signal fraction" is more appropriate to describe what have always been referred to as "volume fraction". This dichotomy is described from the theoretical point of view by analysing the mathematical formulation of the diffusion MRI signal. We propose a generalized multi tissue modelling framework that allows to compute the actual volume fractions. The Dmipy implementation of this framework is then used to verify the presence of this bias in two classical tissue microstructure models computed on two subjects from the Human Connectome Project database. The proposed paradigm shift exposes the research field of brain tissue microstructure estimation to the necessity of a systematic review of the results obtained in the past that takes into account the difference between the concepts of volume fraction and signal fraction.

This work has been published in [24]

Multi-Compartment Modelling of Diffusion MRI Signal Shows TE-Based Volume Fraction Bias

Participants Matteo Frigo, Mauro Zucchelli, Rutger Fick *(TheraPanacea)*, Samuel Deslauriers-Gauthier, Rachid Deriche.

Diffusion MRI (dMRI) has been widely used to estimate brain tissue microstructure in-vivo.Two of the most widely used microstructural indices are the white matter (WM) andintra-cellular (IC) volume fractions (VF). In estimating these fractions, acommon assumption of dMRI-based signal modeling is to assume that the T2-relaxation foreach compartment is equal. However, it has been shown that this assumption is inaccurate. Here, we characterize the bias introduced by this assumption using a generalmulti-compartmental model of the dMRI signal in three distinct scenarios:3-S0) the realistic-case, where each compartment has its T2-dependent signal at b-value 0(S0).2-S0) in which we consider only two separated S0, one for WM and one for CSF.1-S0) a single average S0 is considered for all the compartments, as commonly done indMRI.Our simulations and experiments on real data show fitting the WM and IC VF using the moresimplistic 2-S0 and 1-S0 model, a systematic bias appears that potentially alters the interpretation of conclusions drawn from studies focusing on WM and IC VF.

This work has been published in [25].

Network Alignment and Similarity Reveal Atlas-Based Topological Differences in Structural Connectomes

Participants Matteo Frigo, Emilio Cruciani *(Inria Coati)*, David Coudert *(Inria Coati)*, Rachid Deriche, Emanuele Natale *(Inria Coati)*, Samuel Deslauriers-Gauthier.

Brain atlases are central objects in network neuroscience, where the interactions between different brain regions are modeled as a graph called connectome. In structural connectomes, nodes are parcels from a predefined cortical atlas and edges encode the strength of the axonal connectivity between regions measured via diffusion Magnetic Resonance Imaging (MRI) tractography. Herein, we aim at providing a novel perspective on the evaluation of brain atlases by modeling it as a network alignment problem, with the goal of tackling the following question: given an atlas, how robustly does it capture the network topology across different subjects? To answer such a question, we introduce two novel concepts arising as natural generalizations of previous ones. First, the graph Jaccard index (GJI), a graph similarity measure based on the well-established Jaccard index between sets; the GJI exhibits natural mathematical properties that are not satisfied by previous approaches. Second, we devise WL-align, a new technique for aligning connectomes obtained by adapting the Weisfeiler-Lehman (WL) graph-isomorphism test. We validated the GJI and WL-align on data from the Human Connectome Project database, inferring a strategy for choosing a suitable parcellation for structural connectivity studies. Code and data are publicly available.

A preprint of this work, currently submitted to a journal and under review, has been published in [34].

Explainable 3D-CNN for Multiple Sclerosis Patients Stratification

Participants Federica Cruciani *(University of Verona)*, Lorenza Brusini *(University of Verona)*, Mauro Zucchelli, Gustavo Retuci Pinheiro *(UNICAMP - Universidade Estadual de Campinas)*, Francesco Setti *(University of Verona)*, Ilaria Boscolo Galazzo *(University of Verona)*, Leticia Rittner *(University of Verona)*, Massimiliano Calabrese *(University of Verona)*, Rachid Deriche, Gloria Menegaz *(University of Verona)*.

The growing availability of novel interpretation techniques opened the way to the application of deep learning models in the clinical field, including neuroimaging, where their use is still largely underexploited. In this framework, we focus the stratification of Multiple Sclerosis (MS) patients in the Primary Progressive versus the Relapsing- Remitting state of the disease using a 3D Convolutional Neural Network trained on structural MRI data. Within this task, the application of Layer-wise Relevance Propagation visualization allowed detecting the voxels of the input data mostly involved in the classification decision, potentially bringing to light brain regions which might reveal disease state.

This work has been published in [32, 33].

Multi-Tissue Multi-Compartment Models of Diffusion MRI

Participants Matteo Frigo, Rutger Fick *(TheraPanacea)*, Mauro Zucchelli, Samuel Deslauriers-Gauthier, Rachid Deriche.

State-of-the-art multi-compartment microstructural models of diffusion MRI in the human brain have limited capability to model multiple tissues at the same time. In particular, the available techniques that allow this multi-tissue modelling are based on multi-TE acquisitions. In this work we propose a novel multi-tissue formulation of classical multi-compartment models that relies on more common single-TE acquisitions and can be employed in the analysis of previously acquired datasets. We show how modelling multiple tissues provides a new interpretation of the concepts of signal fraction and volume fraction in the context of multi-compartment modelling. The software that allows to inspect single-TE diffusion MRI data with multi-tissue multi-compartment models is included in the publicly available Dmipy Python package.

This work has been submitted to a journal and is currently under review.

On the Generalizability of Diffusion MRI Signal Representations Across Acquisition Parameters, Sequences, and Tissue Types: Chronicles of the MEMENTO Challenge.

Participants Alberto De Luca *(PROVIDI Lab, Image Sciences Institute, University Medical Center Utrecht)*, , Matteo Frigo, Rutger Fick *(TheraPanacea)*, Sara Sedlar, Abib Alimi, Enes Alpay, Mauro Zucchelli, Samuel Deslauriers-Gauthier, Rachid Deriche, Kurt Schilling *(Department of Neurology, Brain Center Rudolf Magnus, University Medical Center Utrecht)*.

Diffusion MRI (dMRI) has become an invaluable tool to assess the microstructural organization of brain tissue. Depending on the specific acquisition settings, the dMRI signal encodes specific properties of the underlying diffusion process. In the last two decades, several signal representations have been proposed to fit the dMRI signal and decode such properties. Most methods, however, are tested and developed on a limited amount of data, and their applicability to other acquisition schemes remains unknown. With this work, we aimed to shed light on the generalizability of existing dMRI signal representations to different brain tissue types for diffusion encoding parameters. To this end, we organized a community challenge - named MEMENTO, making available the same datasets for fair comparisons across algorithms and techniques. We considered two state-of-the-art diffusion datasets, including single-diffusion-encoding (SDE) spin-echo data from a human brain with over 3820 unique diffusion weightings (the MASSIVE dataset), and double (oscillating) diffusion encoding data (DDE/DODE) of a mouse brain including over 2520 unique data points. A subset of the data sampled in 5 different voxels was openly distributed, and the challenge participants were asked to predict the remaining part of the data. After one year, eight participant teams submitted a total of 80 signal fits. For each submission, we evaluated the mean squared error, the variance of the prediction error and the Bayesian information criteria. Most predictions predicted either multi-shell SDE data (39%) or DODE data (22,5%), followed by cartesian SDE data (20%) and DDE (22,5%). Most submissions predicted the signals measured with SDE remarkably well, with the exception of low and very strong diffusion weightings. The prediction of DDE and DODE data seemed more challenging, likely because none of the submissions explicitly accounted for diffusion time and frequency. Next to the choice of the model, decisions on fit procedure and hyperparameters play a major role in the prediction performance, highlighting the importance of optimizing and reporting such choices. This work is a community effort to highlight strength and limitations of the field at representing dMRI acquired with trending encoding schemes, gaining insights into how different models generalize to different tissue types and fiber configurations over a large range of diffusion encodings.

This work is currently under review.

Lesion-Robust White-Matter Bundle Identification Through Diffusion Driven Label Fusion

Participants Guillermo Gallardo *(IMPNSC - Max Planck Institute for Human Cognitive and Brain Sciences,Leipzig)*, Gaston Zanitti *(Inria Parietal)*, Alfred Anwander *(IMPNSC - Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig)*, Mat Higger *(BWH - Brigham & Women's Hospital, Boston)*, Sylvain Bouix *(BWH - Brigham & Women's Hospital, Boston)*, Samuel Deslauriers-Gauthier, Demian Wassermann *(Inria Parietal)*.

Pathologies such as infiltrative tumors disrupt the structure of white matter in the brain, resulting in cognitive deficits. Inferring which pathways are affected by the lesion is key for both pre and post-treatment planning. In the presence of lesions, tractography algorithms fail to wholly track white matter pathways, regardless if these are unaffected by the lesion. In this work, we develop a label fusion technique to localize fiber bundles when whole-bundle tracking is hampered. we solve this by harnessing aggregated healthy subject information. Given a set of labeled major bundles in a group of healthy subjects, we non-linearly register them to our patient's brain and combine them using a novel label fusion algorithm. A major advantage of label fusion techniques is their high accuracy even when inferring from few subjects. Extant label fusion techniques rely on tissue contrast, not taking into account the fibrous structure of

white matter. Leveraging that brain structures constrain the diffusion of water particles differently, we propose a novel diffusion driven technique to improve the localization of brain pathways. We show its feasibility and advantages in both synthetic and human data.

This work has been published in [26].

6.2 Unveiling brain activity using M/EEG

A Comprehensive Study on Electroencephalography and Magnetoencephalography Sensitivity to Cortical and Subcortical Sources

Participants Maria Carla Piastra *(Institute for Biomagnetism and Biosignalanalysis, University of Münster, Münster, Germany)*, Andreas Nüßing *(Institute for Biomagnetism and Biosignalanalysis, University of Münster, Münster, Germany)*, Johannes Vorwerk *(Institute of Electrical and Biomedical Engineering, University for Health Sciences, Medical Informatics and Technology, Hall in Tirol, Austria)*, Maureen Clerc, Christian Engwer *(Institute for Computational and Applied Mathematics, University of Münster, Münster, Germany)*, Carsten Wolters *(Institute for Biomagnetism and Biosignalanalysis, University of Münster, Münster, Germany)*.

Signal-to-noise ratio (SNR) maps are a good way to visualize electroencephalography (EEG) and magnetoencephalography (MEG) sensitivity. SNR maps extend the knowledge about the modulation of EEG and MEG signals by source locations and orientations and can therefore help to better understand and interpret measured signals as well as source reconstruction results thereof. Our work has two main objectives. First, we investigated the accuracy and reliability of EEG and MEG finite element method (FEM)-based sensitivity maps for three different head models, namely an isotropic three and four-compartment and an anisotropic six-compartment head model. As a result, we found that ignoring the cerebrospinal fluid leads to an overestimation of EEG SNR values. Second, we examined and compared EEG and MEG SNR mappings for both cortical and subcortical sources and their modulation by source location and orientation. Our results for cortical sources show that EEG sensitivity is higher for radial and deep sources and MEG for tangential ones, which are the majority of sources. As to the subcortical sources, we found that deep sources with sufficient tangential source orientation are recordable by the MEG. Our work, which represents the first comprehensive study where cortical and subcortical sources are considered in highly detailed FEM-based EEG and MEG SNR mappings, sheds a new light on the sensitivity of EEG and MEG and might influence the decision of brain researchers or clinicians in their choice of the best modality for their experiment or diagnostics, respectively.

This work has been published in [17].

Convolutional Autoencoder for Waveform Learning

Participants Sara Sedlar, Sandra Ayas, 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.

Automatic Detection of Epileptic Spikes in EEG Signals

Participants Pierre Guetschel, Fabrice Duprat *(IPMC)*, Massimo Mantegazza *(IPMC)*, 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 software tools to automate EEG analysis in long recording sequences. We started from the "Adaptive Waveform Learning" method that was developed in the group a few years ago [61]. In the context of video EEG recordings, the method proved to work poorly due to the motion artifacts generated by the mice activities. The method was thus revisited and re-implemented using the alphacsc code base and used along with some outlier suppression techniques

Embeddings for EEG Signals

Participants Pierre Guetschel, Yang Ji, Michael Tangerman *(University of Tübingen/University of Freiburg)*, Théodore Papadopoulo.

The goal of this work is to generate embedding for EEG recordings in order to use them in various BCI tasks. To produce them, we used EEGNet, a CNN model that was originally designed for EEG classification where we just changed the output size. We chose it for it's light weight, allowing relatively fast training and experimentation. We introduced a new loss function to train this model that can be seen as a generalization of the triplet loss. It can encode in the embeddings multiple independent labels (ie. all the metadata coming with EEG recordings), their relative importance and their weight. The flexibility of this new loss allows us to express some expert knowledge in the embeddings. To evaluate if the desired information is actually encoded in the embeddings, we test if simple models (i.e. linear classifier or KNN) can classify them according to one of the labels, and we do so for all the labels independently. In the future, we will investigate whether some interesting properties might have been encoded in these embeddings without having explicitly been trained for (like it was the case for word embeddings in NLP). These could include, for example, one of the metadata that has been ignored during the training phase.

This is work in progress.

6.3 Combined fMRI, M/EEG and dMRI

A Unified Framework for Multimodal Structure-function Mapping Based on Eigenmodes

Participants Samuel Deslauris-Gauthier, Mauro Zucchelli, Matteo Frigo, Rachid Deriche.

Characterizing the connection between brain structure and brain function is essential for understanding how behaviour emerges from the underlying anatomy. A number of studies have shown that the network structure of the white matter shapes functional connectivity. Therefore, it should be possible to predict, at least partially, functional connectivity given the structural network. Many structure–function mappings have been proposed in the literature, including several direct mappings between the structural and functional connectivity matrices. However, the current literature is fragmented and does not provide a uniform treatment of current methods based on eigendecompositions. In particular, existing methods have never been compared to each other and their relationship explicitly derived in the context of brain structure–function mapping. In this work, we propose a unified computational framework that generalizes recently proposed structure–function mappings based on eigenmodes. Using this unified framework, we highlight the link between existing models and show how they can be obtained by specific choices of the parameters of our framework. By applying our framework to 50 subjects of the Human Connectome Project, we reproduce 6 recently published results, devise two new models and provide a direct comparison between all mappings. Finally, we show that a glass ceiling on the performance of mappings based on eigenmodes seems to be reached and conclude with possible approaches to break this performance limit.

This work has been published in [14, 37].

Connectivity-Informed M/EEG Inverse Problem

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

In the context of regularizing the dynamics of M/EEG and recovering electrical activity of the brain from M/EEG measurements, traditional linear inverse methods deploy different constraints such as minimum norm, maximum-smoothness in space and/or time along the cortical surface. However, they usually do not take into account the structural connectivity and very few include delays supported by dMRI as a prior information. The goal of this work is to include these delays into the MEG source reconstruction process by imposing temporal smoothness in structurally connected sources, with the corresponding delays. We propose to encapsulate delays provided by dMRI in a graph representation and show their potential in improving the MEG source reconstruction when compared to a state-of-the-art approach. Our preliminary results show that including the conduction delays provided by dMRI encapsulated in a graph representation improves MEG source localization when compared to the state-of-the-art Cortical Graph Smoothing (CGS) method.

This work has been published in [20].

Using Structural Connectivity to Reconstruct Brain Activation and Effective Connectivity

Participants Brahim Belaoucha, , Théodore Papadopoulo.

Understanding how brain regions interact to perform a specific task is very challenging. EEG and MEG are two noninvasive 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 informa on to do so. We present a source estimation algorithm that uses brain structural connectivity,

obtained 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 auto-regressive model that explains the data in further time instants. This auto-regressive 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 work 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 shows that complex EEG/MEG datasets can be explained by an initial state and a MAR model for effective connectivity. This is a compact way to describe brain dynamics and offers a direct access to effective connectivity

This work has been published in [36] and [12].

Non–invasive Inference of Information Flow Using Diffusion MRI, Functional MRI, and MEG

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

To infer information flow in the white matter of the brain and recover cortical activity using functional MRI, diffusion MRI, and MEG without a manual selection of the white matter connections of interest. A Bayesian network which encodes the priors knowledge of possible brain states is built from imaging data. Diffusion MRI is used to enumerate all possible connections between cortical regions. Functional MRI is used to prune connections without manual intervention and increase the likelihood of specific regions being active. MEG data is used as evidence into this network to obtain a posterior distribution on cortical regions and connections. We show that our proposed method is able to identify connections associated with the a sensory–motor task. This allows us to build the Bayesian network with no manual selection of connections of interest. Using sensory–motor MEG evoked response as evidence into this network, our method identified areas known to be involved in a visuomotor task. In addition, information flow along white matter fiber bundles connecting those regions was also recovered. Significance. Current methods to estimate white matter information flow are extremely invasive, therefore limiting our understanding of the interaction between cortical regions. The proposed method makes use of functional MRI, diffusion MRI, and M/EEG to infer communication between cortical regions, therefore opening the door to the non–invasive exploration of information flow in the white matter.

This work has been published in [13] and is part of the PhD thesis [29]

Towards Linking Diffusion MRI Based Macro- and Microstructure Measures with Cortico-Cortical Transmission in Brain Tumor Patients

Participants Patryk Filipiak, Fabien Almairac *(CHU Nice, UCA)*, Marie Onno *(CHU Nice, UCA)*, Theo Papadopoulo, Denys Fontaine *(CHU Nice, UCA)*, Lydiane Mondot *(CHU Nice, UCA)*, Stéphane Chanalet *(CHU Nice, UCA)*, Rachid Deriche, Maureen Clerc, Demian Wassermann *(INRIA Parietal)*.

We aimed to link macro- and microstructure measures of brain white matter obtained from diffusion MRI with effective connectivity measures based on a propagation of cortico-cortical evoked potentials induced with intrasurgical direct electrical stimulation. For this, we compared streamline lengths and log-transformed ratios of streamlines computed from presurgical diffusion-weighted images, and the delays and amplitudes of N1 peaks recorded intrasurgically with electrocorticography electrodes in a pilot study of 9 brain tumor patients. Our results showed positive correlation between these two modalities in the vicinity of the stimulation sites (Pearson coefficient 0.54±0.13 for N1 delays, and 0.47±0.23 for N1

amplitudes), which could correspond to the neural propagation via U-fibers. In addition, we reached high sensitivities (0.78±0.07) and very high specificities (0.93±0.03) in a binary variant of our comparison. Finally, we used the structural connectivity measures to predict the effective connectivity using a multiple linear regression model, and showed a significant role of brain microstructure-related indices in this relation.

Part of this work has been published in [15].

A Paradigm Free Regularization Approach to Recover Brain Activations: Validation on Task fMRI

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

Resting-state functional MRI (rs-fMRI) provides insight into brain function in the absence of stimuli and allows to map brain activity for subjects whose condition does not allow to perform tasks. This has emphasized the need to recover neural activations from fMRI signals in the absence of an experimental paradigm. To avoid the need for prior information on the timing of the activations, techniques to deconvolve brain activity from the blood-oxygen-level-dependent (BOLD) response have been proposed. In particular, by supposing the brain activates in constant blocks, Farouj et al. developed an approach which involves both spatial and temporal regularization (Total Activation, TA). However, it splits the optimization problem into two decoupled spatial and temporal regularization which doubles the number of parameters to set and requires the solver to alternate between the constraints. Starting from the idea that large image variations should be preserved as they occur during brain activation, whereas small variations should be smoothed to remove noise, we previously proposed an alternative paradigm-free algorithm based on partial differential equations (PDEs) named PFFMRI (Paradigm-Free fMRI). In this work, we validate PFFMRI on task-fMRI data from 51 subjects using the experimental paradigm as ground truth and compare its performance to TA. We also show that PFFMRI recovers activity that agrees with the general linear model (GLM) without knowledge of the experimental paradigm.

This work has been published in [23].

Diffusion MRI-Based Connectivity Enriched with Microstructure Information Predicts the Propagation of Cortico-Cortical Evoked Potentials

Participants Patryk Filipiak, Fabien Almairac *(CHU Nice, UCA)*, Theodore Papadopoulo, Denys Fontaine *(CHU Nice, UCA)*, Lydiane Mondot *(CHU Nice, UCA)*, Stéphane Chanalet *(CHU Nice, UCA)*, Rachid Deriche, Maureen Clerc, Demian Wassermann *(INRIA Parietal)*.

Propagation of Cortico-Cortical Evoked Potentials (CCEPs) varies depending on numerous structural features of brain tissue. In this work, we show that dMRI-based connectivity enriched with microstructure data has the potential to measure cortico-cortical communication as it predicts CCEP-based effective connectivity. Our multiple linear regression model incorporates q-space indices like Q-space Inverse Variance, Non-Gaussianity and Return to Plane Probability with minimum streamline lengths obtained from tractography to predict delays and amplitudes of the N1 peaks in CCEPs. In our experiment, we use presurgical dMRI and intrasurgical ECoG recordings of 9 patients operated on brain tumor in the awake condition.

This work has been published in [19].

Analytical and Fast Fiber ODF Reconstruction in 3D Polarized Light Imaging

Participants Abib Olushola Yessouffou Alimi, Samuel Deslauriers-Gauthier, Felix Matuschke *(INM-1 - Institute of Neuroscience and Medicine, Jülich)*, Andreas Muller *(Simulation Lab Neuroscience - Institute for Advanced Simulation. Jülich)*, Sacha Muenzing *(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) is an optical technique which allows mapping the spatial fiber architecture of fibrous postmortem tissues, at sub-millimeter resolutions. Here, we propose an analytical and fast approach to compute the fiber orientation distribution (FOD) from high-resolution vector data provided by 3D-PLI. The FOD is modeled as a sum of K orientations/Diracs on the unit sphere, described on a spherical harmonics basis and analytically computed using the spherical Fourier transform. Experiments are performed on rich synthetic data which simulate the geometry of the neuronal fibers and on human brain data. Results indicate the analytical FOD is computationally efficient and very fast, and has high angular precision and angular resolution. Furthermore, investigations on the right occipital lobe illustrate that our strategy of FOD computation enables the bridging of spatial scales from microscopic 3D-PLI information to macro-or mesoscopic dimensions of diffusion Magnetic Resonance Imaging (MRI), while being a means to evaluate prospective resolution limits for diffusion MRI to reconstruct regionspecific white matter tracts. These results demonstrate the interest and great potential of our analytical approach.

This work has been published in [11] and is part of the PhD thesis [28].

Quantitative Assessment of Multi-Scale Tractography: Bridging the Resolution Gap With 3D-PLI

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

The in vivo validation of diffusion MRI (dMRI)-based tractography has been shown to be a challenging task. Therefore, we have been investigating how 3D Polarized Light Imaging (3D-PLI) could be used as a validation tool for dMRI-based fiber orientation estimation and tractography. PLI is an optical imaging technique that provides us with high-resolution fiber orientation measurements at micrometer scale. For this reason, it has been presented as a good candidate for the afore mentioned validation tasks. In some previous works, we introduced an approach to close the resolution gap between dMRI and 3D-PLI. The study of the brain network from the topological point of view has seen an increasing interest in the last years. In this work, we show how tractograms obtained at different spatial scales using 3D-PLI human brain datasets can bein spected using homology theory to perform a quantitative comparison between them. In particular, we investigate the persistence of the number of connected components in brain networks estimated from data at different resolutions.

This work has been published in [22].

Improving Auto-Encoders' Self-Supervised Image Classification Using Pseudo-Labelling via Data Augmentation and the Perceptual Loss

Participants Aymene Mohamed Bouayed *(USTHB - Université des Sciences et de la Technologie Houari Boumediene, Alger)*, Karim Atif *(USTHB - Université des Sciences et de la Technologie Houari Boumediene, Alger)*, Rachid Deriche, Abdelhakim Saim *(USTHB - Université des Sciences et de la Technologie Houari Boumediene, Alger)*.

In this work, developed within the framework of a collaboration on a AI based subject, not yet related to brain imaging, we introduce a novel method to pseudo-label unlabelled images and train an Auto-Encoder to classify them in a self-supervised manner that allows for a high accuracy and consistency

across several datasets. The proposed method consists of first applying a randomly sampled set of data augmentation transformations to each training image. As a result, each initial image can be considered as a pseudo-label to its corresponding augmented ones. Then, an Auto-Encoder is used to learn the mapping between each set of the augmented images and its corresponding pseudo-label. Furthermore, the perceptual loss is employed to take into consideration the existing dependencies between the pixels in the same neighbourhood of an image. This combination encourages the encoder to output richer encodings that are highly informative of the input's class. Consequently, the Auto-Encoder's performance on unsupervised image classification is improved both in termes of stability and accuracy becoming more uniform and more consistent across all tested datasets. Previous state-of-the-art accuracy on the MNIST, CIFAR-10 and SVHN datasets is improved by 0.3%, 3.11% and 9.21% respectively.

This work has been published in [31].

6.4 Brain Computer Interfaces

Auto-Calibration of c-VEP BCI by Word Prediction

Participants Federica Turi, Nathalie Gayraud, Maureen Clerc.

A code-modulated Visual Evoked Potential Brain Computer Interface (c-VEP BCI) allows for spelling from a virtual keyboard of flashing characters. All characters flash simultaneously, and each character flashes according to a predefined pseudo-random binary sequence, circular-shifted by a different time lag. For a given character, the pseudo-random stimulus sequence evokes a VEP in the electroencephalogram (EEG) of the subject, which can be used as a template. This template is usually obtained during a calibration phase and it is applied for the target identification during the spelling phase. A downside of a c-VEP BCI system is that it needs a long calibration phase to reach good performance. This work proposes an unsupervised method that avoids the calibration phase in a c-VEP BCI, by extracting relative lags from the VEP responses, between successive characters, and predicting the full word using a dictionary. We tested it in offline experiments on a public dataset. We simulated the spelling of four groups of words with a different total number of characters selected from an English dictionary. Each experiment is parameterized by the number of stimulus cycles. The obtained results show that a word-prediction-based auto-calibration method in c-VEP BCIs can be efficient and effective. This work has been published in [35] and is part of the PhD thesis [30].

Finding the Best Classifier for the Cybathlon Competition

Participants Yang Ji, Paul-Emmanuel Ponsenard, Amandine Audino, Maureen Clerc, Théodore Papadopoulo.

In 2020, the ATHENA team was supposed to participate to the Cybathlon BCI competition. For this, the team had developped a mental imagery based protocol which was relying on four mental tasks that were used to drive a car on a track in a virtual game. Each mental task corresponds to one of the simple actions (go straight, go left, go right, put lights on) that were needed to play the game. The data that the team gathered during 2019 was used in this study to find the best combination of classification method and parameters that led to the best classification scores. The study was based on the classifiers available in sckit-learns. The winning method was a Random Forest Classifier. In order to use it in a BCIO setup, this classifier has been re-implemented in C++. This will be useful for the BCI developments in the team, even if, in the end, due to the COVID-19 crisis the team has not participated to the virtual Cybathlon BCI race.

An Integrated BCI System for Cybathlon

Participants Yang Ji, Côme Le Breton, Théodore Papadopoulo.

In 2019, the ATHENA team participated to a BCI competition preparatory to the 2020 Cybathlon BCI competition. The system that was used proved to be too complex: the solution was based on OpenViBE and was running on a small network of two computers. This complexity and the modularity that it brought was needed in the development phase of the system, but was counterproductive during the competition as the team had to struggle to deal with networking problems instead of concentrating on the competition and training the pilot. With the principles of the system fixed, it seemed valuable to develop a simplified system less modular but completely architectured around the needs of a competition to prepare the 2020 Cybathlon competition. Even though, in the end, the team had to cancell its participation due to the COVID-19 crisis, most of the work for such an integrated system has been done and will be valuable for the future BCI developments of the team.

EEG Neurofeeback for Epilepsy

Participants Côme Le Breton, Jeanne Benoît, Fabrice Bartolomei *(INS, Hospital La Timone, Marseille)*, Christian Bénar *(INS, Hospital La Timone, Marseille)*, Maureen Clerc, Théodore Papadopoulo.

This work in progress is in collaboration with "Institut de Neurosciences des Systèmes" (Marseille). It focusses on alternative ways – without medication – to ease epilepsy symptoms. The team in Marseille had recently observed positive outcomes to Galvanic Skin Response (skin conductance) biofeedback.Given the relatively slow latency of this response (approx 3s), and the fact that this derived neural information is condensed in a single property varying with time, a scalp EEG informed biofeedback (neurofeedback) seems interesting to explore with the hope of getting better results. A review of the litterature for clues of neural synchrony in scalp EEG signals revealed in particular a paper discussing analysis of long range / short range synchrony in epileptic patients and control group. This paper claimed a reduced long range synchrony in epileptic patients. Such a claim seemed a good base to develop a neuromarker based on measuring this impaired long range synchrony. The different algorithms used in the paper were implemented and applied to both a Nice hospital database of recordings of epileptic patients EEG, and some new EEG recordings on healthy subjects. Unfortunately, the claims made in the paper were by no mean reproducible on their data, the variability of synchrony inside either group beeing way to strong to statistically infer differences based on the group. They are still investigating intra/interhemispheric synchrony with regard to the lateralisation of the epileptic focus, on the same dataset.

7 Partnerships and Cooperations

7.1 International initiatives

Informal international partners

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

7.2 International research visitors

7.2.1 Visits of international scientists

- Enes Albay - Ph.D. student in Computer Engineering (Cont.), Istanbul Technical University, From Nov. 2019 to March 2020.

7.3 European initiatives

7.3.1 ERC AdG CoBCoM

- Program: H2020-EU.1.1. (ERC-ADG-2015 - ERC Advanced Grant)
- Project acronym: CoBCoM - **ID:** 694665
- Project title: *Computational Brain Connectivity Mapping*
- Start date: 2016-09-01, End date: 2021-08-31
- P.I. : R. Deriche
- Partners: ATHENA project-team
- Abstract:

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

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

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

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

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

7.4 National initiatives

3IA UCA Chair : AI-Based Computational Brain Connectomics

Participants	Rachid Deriche, Samuel Deslauriers-Gauthier, Sara Sedlar, Mauro Zuccheli.

Start date: 2019-10-01 **Duration:** *48 months.*

This project aims to reconstruct and analyse the network of neural connections of the brain, called the connectome via a computational brain connectomics framework based on ground-breaking AI algorithms and machine learning tools to gain insight into brain architecture, functioning and neurodegenerative diseases.

The avalanche of big data required to reconstruct the connectome and the study of the high complexity of structural and functional interactions within the connectome clearly position brain connectomics as a big data problem where AI & machine learning in particular, represent a very promising trend, as recently demonstrated in computer vision and in some biomedical image data-driven analysis. Partly related to the ERC AdG CoBCoM, the computational brain connectomics framework we develop in this project will construct networks specifically built on new generation of AI algorithms and machine learning tools to reconstruct a structural and functional connectome using advanced and integrated dMRI, EEG & MEG methods. This project completes CoBCoM by specifically investigating the AI added value in brain mapping, opens also exciting prospects and paves the way to translate the large amounts of high dimensional heterogeneous and complex brain data into knowledge for better contribute to neurodegenerative diseases detection and diagnosis.

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:

- Offer a user interface for the creation and verification of head models most importantly for a simpler management of non-nested head models.
- Improve the Python interface (extension and reliability). This will also be useful to develop new research axes (in connection with point 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 Dissemination

8.1 Promoting scientific activities

Member of the organizing committees

- T. Papadopoulo is member of the Program Commitee of Soph.IA 2020.

8.1.1 Scientific events: selection

Reviewer

- R. Deriche serves several international conferences (ISBI, MICCAI, ISMRM, ...) and international workshops (CD-MRI MICCAI, MFCA Miccai...)
- T. Papadopoulo served for the ISBI international conference.

8.1.2 Journal

Member of the editorial boards

- 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.

Reviewer - reviewing activities

- R. Deriche serves several international journals (NeuroImage, IEEE Transactions on Medical Imaging, Magnetic Resonance in Medicine,Journal of Mathematical Imaging and Vision, Medical Image Analysis Journal, ...).

- T. Papadopoulo served several international journals (Frontiers in Neuroscience, Brain Computer Interfaces, Journal of Neural Engneering, Medical & Biological Engineering & Computing).

- 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).

8.1.3 Invited talks

- T. Papadopoulo has been invited to give a pretentation on Brain Computer Interfaces at Institute for Language, Communication and the Brain (ILCB), on Sep. 1st, 2020

8.1.4 Leadership within the scientific community

- T. Papadopoulo is a member of the scientific committee of the NeuroMod institute of Université Côte d'Azur.

- T. Papadopoulo is a member of the COSP of the EUR Healthy of Université Côte d'Azur.

8.1.5 Scientific expertise

- T. Papadopoulo served in reviewing applications for the Neuromod institute of Université Côte d'Azur.

- R. Deriche served several national and international institutions in reviewing applications : 3IA UCA Chairs, ERC AdG and StG Grants, Swiss National Science Foundation, EPFL, the Netherlands Organisation for Scientific Research (NWO).

8.1.6 Research administration

- T. Papadopoulo was a member of the CRCN/ISFP hiring committee at Inria Sophia Antipolis.

- T. Papadopoulo has been appointed as the head of the Inria Sophia Software committeee (CDT) since June, 1st, 2020.

- T. Papadopoulo is a member of the Computer Users committee (CUMI) since September, 2020.

8.2 Teaching - Supervision - Juries

8.2.1 Teaching

- Master: T. Papadopoulo, *Inverse problems for brain functional imaging*, 24 ETD, M2, Mathématiques, Vision et Apprentissage, ENS Cachan, France.
- Master: T. Papadopoulo, *Functional Brain Imaging*, 20ETD, M1,M2 in the MSc Mod4NeuCog of Université Côte d'Azur.

8.2.2 Supervision

- PhD defended on May 27th, 2020: Abib Alimi, "3D Polarized Light Imaging : Towards Multiscale and Multimodal Analysis with Diffusion MRI. Université Côte d'Azur. Supervisors: Rachid Deriche and Samuel Deslauriers-Gauthier.
- PhD in progress: To be defended on Feb. 22th, 2021 Matteo Frigo, "Computational brain connectivity mapping: from multi-compartment modeling to network topology via tractography filtering" started Nov, 1st, 2017, Université Côte d'Azur. Supervisors: Rachid Deriche and Samuel Deslauriers-Gauthier.
- PhD defended on May 28th, 2020: Isa Costantini, "Paradigm Free Regularization for fMRI Brain Activation Recovery" Université Côte d'Azur. Supervisors: Rachid Deriche and Samuel Deslauriers-Gauthier.
- PhD defended on Sep. 23rd, 2020: 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 epileptogenetic 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.

8.2.3 Juries

- R. Deriche, S. Deslauriers-Gauthier and T. Papadopoulo participated in the PhD Jury of A. Alimi at Université Côte d'Azur on May. 27th, 2020.
- R. Deriche, S. Deslauriers-Gauthier and T. Papadopoulo participated in the PhD Jury of I. Costantini at Université Côte d'Azur on May. 28th, 2020.
- T. Papadopoulo and M. Clerc participated in the PhD Jury of F. Turi at Université Côte d'Azur on Sep. 23rd, 2020.

9 Scientific production

9.1 Major publications

[1] C. Bénar, T. Papadopoulo, B. Torrésani and M. Clerc. 'Consensus Matching Pursuit for Multi-Trial EEG Signals'. In: *Journal of Neuroscience Methods* 180 (2009), pp. 161–170. DOI: DOI:10.1016/j.jneumeth.2009.03.005.

[2] E. Caruyer, C. Lenglet, G. Sapiro and R. Deriche. 'Design of multishell sampling schemes with uniform coverage in diffusion MRI'. In: *Magnetic Resonance in Medicine* 69.6 (June 2013), pp. 1534–1540. DOI: 10.1002/mrm.24736. URL: http://hal.inria.fr/hal-00821688/.

[3] M. Descoteaux, E. Angelino, S. Fitzgibbons and R. Deriche. 'Regularized, Fast, and Robust Analytical Q-Ball Imaging'. In: *Magnetic Resonance in Medicine* 58.3 (2007), pp. 497–510. URL: ftp://ftp-sop.inria.fr/odyssee/Publications/2007/descoteaux-angelino-etal:07.pdf.

[4] M. Descoteaux, R. Deriche, T. R. Knosche and A. Anwander. 'Deterministic and Probabilistic Tractography Based on Complex Fibre Orientation Distributions'. In: *IEEE Transactions in Medical Imaging* 28.2 (Feb. 2009), pp. 269–286. URL: ftp://ftp-sop.inria.fr/odyssee/Publications/2009/descoteaux-deriche-etal:09.pdf.

[5] S. Deslauriers-Gauthier, J.-M. Lina, R. Butler, K. Whittingstall, P.-M. Bernier, R. Deriche and M. Descoteaux. 'White Matter Information Flow Mapping from Diffusion MRI and EEG'. In: *NeuroImage* (July 2019). DOI: 10.1016/j.neuroimage.2019.116017. URL: https://hal.inria.fr/hal-02187859.

[6] S. Deslauriers-Gauthier, M. Zucchelli, M. Frigo and R. Deriche. 'A Unified Framework for Multimodal Structure-function Mapping Based on Eigenmodes'. In: *Medical Image Analysis* (Aug. 2020), p. 22. DOI: 10.1016/j.media.2020.101799. URL: https://hal.inria.fr/hal-02925913.

[7] R. H. Fick, D. Wassermann, E. Caruyer and R. Deriche. 'MAPL: Tissue microstructure estimation using Laplacian-regularized MAP-MRI and its application to HCP data'. In: *Neuroimage* 134 (July 2016), pp. 365–385. DOI: \url{http://dx.doi.org/10.1016/j.neuroimage.2016.03.046}. URL: https://hal.inria.fr/hal-01291929.

[8] G. Girard, A. Daducci, L. Petit, J.-P. Thiran, K. Whittingstall, R. Deriche, D. Wassermann and M. Descoteaux. 'AxTract: Toward microstructure informed tractography'. In: *Human Brain Mapping* 38.11 (Nov. 2017), pp. 5485–5500. DOI: 10.1002/hbm.23741. URL: http://onlinelibrary.wiley.com/doi/10.1002/hbm.23741/abstract.

[9] S. Vallaghé and T. Papadopoulo. 'A Trilinear Immersed Finite Element Method for Solving the Electroencephalography Forward Problem'. In: *SIAM Journal on Scientific Computing* 32.4 (2010), pp. 2379–2394. DOI: 10.1137/09075038X. URL: https://epubs.siam.org/doi/pdf/10.1137/09075038X.

[10] M. Zucchelli, S. Deslauriers-Gauthier and R. Deriche. 'A Computational Framework For Generating Rotation Invariant Features And Its Application In Diffusion MRI'. In: *Medical Image Analysis* (Feb. 2020). DOI: 10.1016/j.media.2019.101597. URL: https://hal.inria.fr/hal-02370077.

9.2 Publications of the year

International journals

[11] A. Alimi, S. Deslauriers-Gauthier, F. Matuschke, A. Müller, S. E. Muenzing, M. Axer and R. Deriche. 'Analytical and fast Fiber Orientation Distribution reconstruction in 3D-Polarized Light Imaging'. In: *Medical Image Analysis* 65 (Oct. 2020), p. 101760. DOI: 10.1016/j.media.2020.101760. URL: https://hal.inria.fr/hal-03078848.

[12] B. Belaoucha and T. Papadopoulo. 'Structural connectivity to reconstruct brain activation and effective connectivity between brain regions'. In: *Journal of Neural Engineering* 17.3 (1st June 2020), p. 035006. DOI: 10.1088/1741-2552/ab8b2b. URL: https://hal.inria.fr/hal-02945585.

[13] S. Deslauriers-Gauthier, I. Costantini and R. Deriche. 'Non-invasive inference of information flow using diffusion MRI, functional MRI, and MEG'. In: *Journal of Neural Engineering* 17.4 (1st Aug. 2020), p. 19. DOI: 10.1088/1741-2552/ab95ec. URL: https://hal.inria.fr/hal-02925937.

[14] S. Deslauriers-Gauthier, M. Zucchelli, M. Frigo and R. Deriche. 'A Unified Framework for Multimodal Structure-function Mapping Based on Eigenmodes'. In: *Medical Image Analysis* (20th Aug. 2020), p. 22. DOI: 10.1016/j.media.2020.101799. URL: https://hal.inria.fr/hal-02925913.

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[18] M. Zucchelli, S. Deslauriers-Gauthier and R. Deriche. 'A Computational Framework For Generating Rotation Invariant Features And Its Application In Diffusion MRI'. In: *Medical Image Analysis* (1st Feb. 2020). DOI: 10.1016/j.media.2019.101597. URL: https://hal.inria.fr/hal-02370077.

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