



Activity Report 2015

Project-Team ATHENA

Computational Imaging of the Central
Nervous System

RESEARCH CENTER
Sophia Antipolis - Méditerranée

THEME
**Computational Neuroscience and
Medicine**

Table of contents

1. Members	2
2. Overall Objectives	2
3. Research Program	4
3.1. Computational diffusion MRI	4
3.1.1. Diffusion Tensor Imaging & High Angular Resolution Diffusion Imaging	4
3.1.2. Beyond DTI with high order tensors	4
3.1.3. Improving dMRI acquisitions	5
3.1.4. dMRI modelling, tissue microstructures features recovery & applications	5
3.1.5. Towards microstructural based tractography	6
3.2. MEG and EEG	6
4. Application Domains	7
4.1. Applications of diffusion MRI	7
4.2. Applications of M/EEG	8
5. New Software and Platforms	8
5.1. High Performance Diffusion MRI	8
5.2. DIPY	9
5.3. The White Matter Query Language	9
5.4. MedInria	9
5.5. Coadapt P300 Stimulator	10
5.6. FindSources3D	10
5.7. OpenMEEG	10
5.8. OpenVIBE	11
6. New Results	11
6.1. Modeling in Diffusion MRI	11
6.1.1. Improving fiber alignment in HARDI by combining contextual PDE flow with constrained spherical deconvolution	11
6.1.2. Sparse reconstruction challenge for diffusion MRI: Validation on a physical phantom to determine which acquisition scheme and analysis method to use?	12
6.1.3. A Unifying framework for spatial and temporal diffusion in dMRI	12
6.1.4. Exploiting the phase in dMRI for microstructure recovery: Towards axonal tortuosity via asymmetric diffusion processes	13
6.1.5. A temperature phantom to probe the Ensemble Average Propagator asymmetry: an in-silico study	13
6.1.6. How to get more out of a clinically feasible 64 gradient dMRI acquisition: multi-shell versus single-shell	13
6.2. Tissue Microstructures features recovery & applications	14
6.2.1. Laplacian-regularized MAP-MRI : Improving axonal caliber estimation	14
6.2.2. Using 3D-SHORE and MAP-MRI to obtain both tractography and microstructural contrasts from a clinical dMRI acquisition	14
6.2.3. A sensitivity analysis of Q-space Indices with respect to changes in axonal diameter, dispersion and tissue composition	14
6.2.4. MAPL: Tissue microstructure estimation using Laplacian-regularized MAP-MRI and its application to HCP data	15
6.3. Towards microstructural based tractography	15
6.3.1. AxTract: Microstructure-driven tractography based on the Ensemble Average Propagator	15
6.3.2. Studying white matter tractography reproducibility through connectivity matrices	16
6.3.3. Structural connectivity reproducibility through multiple acquisitions	16
6.4. Computational Diffusion MRI	16

6.4.1.	Robust and efficient linear registration of white-matter fascicles in the space of streamlines	16
6.4.2.	Cortical surface parcellation via dMRI using mutual nearest neighbor condition	16
6.5.	Clinical and Neurocognitive Applications of Diffusion MRI	17
6.5.1.	Plasticity of left perisylvian white-matter tracts is associated with individual differences in math learning brain structure and function	17
6.5.2.	Prefrontal cortex white matter tracts in prodromal Huntington disease	17
6.6.	Perfusion MRI	18
6.6.1.	Perfusion MRI deconvolution with delay estimation and non-negativity constraints	18
6.6.2.	Elucidating dispersion effects in perfusion MRI by means of dispersion-compliant bases	18
6.6.3.	Unveiling the dispersion kernel in DSC-MRI by means of dispersion-compliant bases and control point interpolation techniques	18
6.6.4.	Improved vascular transport function characterization in DSC-MRI via deconvolution with dispersion-compliant bases	19
6.7.	MEG, EEG and cochlear modeling	19
6.7.1.	MEM-diffusion MRI framework to solve MEEG inverse problem	19
6.7.2.	MEG/EEG reconstruction in the reduced source space	19
6.7.3.	Realistic simulation of electric potential distributions of different stimulation modes in an implanted cochlea	20
6.7.4.	Influence of skull modelling on conductivity estimation for EEG source analysis	20
6.7.5.	Dictionary learning for M/EEG multidimensional data	20
6.8.	Brain Computer Interfaces	21
6.8.1.	Decoding covert shifts of attention induced by ambiguous visuospatial cues	21
6.8.2.	Online extraction and single trial analysis of regions contributing to erroneous feedback detection	21
7.	Bilateral Contracts and Grants with Industry	22
8.	Partnerships and Cooperations	22
8.1.	National Initiatives	22
8.1.1.	ANR	22
8.1.1.1.	ANR MRSEI LEMONS	22
8.1.1.2.	ANR MOSIFAH	22
8.1.1.3.	ANR VIBRATIONS	23
8.1.2.	ADT	23
8.1.2.1.	ADT BOLIS	23
8.1.2.2.	ADT OpenViBE-X	24
8.2.	European Initiatives	24
8.3.	International Initiatives	24
8.4.	International Research Visitors	25
9.	Dissemination	25
9.1.	Promoting Scientific Activities	25
9.1.1.	Scientific events organisation	25
9.1.2.	Scientific events selection	25
9.1.2.1.	Member of the conference program committees	25
9.1.2.2.	Reviewer	26
9.1.3.	Journal	26
9.1.3.1.	Member of the editorial boards	26
9.1.3.2.	Reviewer - Reviewing activities	26
9.1.4.	Invited talks	26
9.1.5.	Leadership within the scientific community	27
9.1.6.	Scientific expertise	27
9.1.7.	Research administration	27

9.2. Teaching - Supervision - Juries	27
9.2.1. Teaching	27
9.2.2. Supervision	28
9.2.3. Juries	28
9.3. Popularization	28
10. Bibliography	29

Project-Team ATHENA

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

Keywords:

Computer Science and Digital Science:

- 3.1.1. - Modeling, representation
- 3.1.4. - Uncertain data
- 3.3.3. - Big data analysis
- 3.4.1. - Supervised learning
- 3.4.2. - Unsupervised learning
- 3.4.3. - Reinforcement learning
- 3.4.4. - Optimization and learning
- 3.4.5. - Bayesian methods
- 3.4.7. - Kernel methods
- 5.1.4. - Brain-computer interfaces, physiological computing
- 5.2. - Data visualization
- 5.3.2. - Sparse modeling and image representation
- 5.3.4. - Registration
- 5.9.1. - Sampling, acquisition
- 5.9.2. - Estimation, modeling
- 5.9.3. - Reconstruction, enhancement
- 5.9.4. - Signal processing over graphs
- 5.9.5. - Sparsity-aware processing
- 5.9.6. - Optimization tools
- 6.1.1. - Continuous Modeling (PDE, ODE)
- 6.1.4. - Multiscale modeling
- 6.1.5. - Multiphysics modeling
- 6.2.1. - Numerical analysis of PDE and ODE
- 6.2.3. - Probabilistic methods
- 6.2.4. - Statistical methods
- 6.2.6. - Optimization
- 6.2.8. - Computational geometry and meshes
- 6.3.1. - Inverse problems
- 6.3.2. - Data assimilation
- 6.3.3. - Data processing
- 6.3.4. - Model reduction
- 7.8. - Information theory
- 7.9. - Graph theory
- 8.2. - Machine learning
- 8.3. - Signal analysis

Other Research Topics and Application Domains:

- 1.3.1. - Understanding and simulation of the brain and the nervous system
- 1.3.2. - Cognitive science
- 1.4. - Pathologies
- 2.2.2. - Nervous system and endocrinology
- 2.2.6. - Neurodegenerative diseases
- 2.5.1. - Sensorimotor disabilities
- 2.5.2. - Cognitive disabilities
- 2.5.3. - Assistance for elderly
- 2.6.1. - Brain imaging
- 2.6.2. - Cardiac imaging
- 2.7.1. - Surgical devices

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2. Overall Objectives

2.1. Presentation

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

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

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

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

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

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

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

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

This is implemented through:

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

3. Research Program

3.1. Computational diffusion MRI

Diffusion MRI (dMRI) provides a non-invasive way of estimating in-vivo CNS fiber structures using the average random thermal movement (diffusion) of water molecules as a probe. It's a recent field of research with a history of roughly three decades. It was introduced in the mid 80's by Le Bihan et al [59], Merboldt et al [63] and Taylor et al [71]. As of today, it is the unique non-invasive technique capable of describing the neural connectivity in vivo by quantifying the anisotropic diffusion of water molecules in biological tissues.

3.1.1. Diffusion Tensor Imaging & High Angular Resolution Diffusion Imaging

In dMRI, the acquisition and reconstruction of the diffusion signal allows for the reconstruction of the water molecules displacement probability, known as the Ensemble Average Propagator (EAP) [70], [48]. Historically, the first model in dMRI is the 2nd order diffusion tensor (DTI) [47], [46] which assumes the EAP to be Gaussian centered at the origin. DTI has now proved to be extremely useful to study the normal and pathological human brain [60], [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 [62], [9] and [61]).

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) [74] and High Angular Resolution Diffusion Imaging (HARDI) methods such as Q-ball imaging [72] and other multi-tensors and compartment models [68], [69], [40], [39], [67] were developed to resolve the orientationality of more complicated fiber bundle configurations.

Q-Ball imaging (QBI) has been proven very successful in resolving multiple intravoxel fiber orientations in MR images, thanks to its ability to reconstruct the Orientation Distribution Function (ODF, the probability of diffusion in a given direction). These tools play a central role in our work related to the development of a robust and linear spherical harmonic estimation of the HARDI signal and to our development of a regularized, fast and robust analytical QBI solution that outperforms the state-of-the-art ODF numerical technique developed by Tuch. Those contributions are fundamental and have already started to impact on the Diffusion MRI, HARDI and Q-Ball Imaging community [54]. They are at the core of our probabilistic and deterministic tractography algorithms devised to best exploit the full distribution of the fiber ODF (see [51], [4] and [52],[5]).

3.1.2. Beyond DTI with high order tensors

High Order Tensors (HOT) models to estimate the diffusion function while overcoming the shortcomings of the 2nd order tensor model have also been recently proposed such as the Generalized Diffusion Tensor Imaging (G-DTI) model developed by Ozarslan et al [76], [77] or 4th order Tensor Model [45]. For more details, we refer the reader to our articles in [56], [68] where we review HOT models and to our articles in [8], co-authored with some of our close collaborators, where we review recent mathematical models and computational methods for the processing of Diffusion Magnetic Resonance Images, including state-of-the-art reconstruction of diffusion models, cerebral white matter connectivity analysis, and segmentation techniques.

Recently, we started to work on Diffusion Kurtosis Imaging (DKI), of great interest for the company OLEA MEDICAL. Indeed, DKI is fast gaining popularity in the domain for characterizing the diffusion propagator or EAP by its deviation from Gaussianity. Hence it is an important tool in the clinic for characterizing the white-matter's integrity with biomarkers derived from the 3D 4th order kurtosis tensor (KT) [6].

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 [39], [40]. They have also opened up a landscape of extremely exciting research fields for medicine and neuroscience. Hence, due to the complexity of the CNS data and as the magnetic field strength of scanners increase, as the strength and speed of gradients increase and as new acquisition techniques appear [3], [2], these imaging modalities raise a large amount of mathematical and computational challenges at the core of the research we develop at ATHENA [58], [68].

3.1.3. Improving dMRI acquisitions

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

First, we contributed developing real-time reconstruction algorithm based on the Kalman filter [3]. Then, and more recently, we started to explore the utility of Compressive Sensing methods to enable faster acquisition of dMRI data by reducing the number of measurements, while maintaining a high quality for the results. Compressed Sensing (CS) is a recent technique which has been proved to accurately reconstruct sparse signals from undersampled measurements acquired below the Shannon-Nyquist rate [64].

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 [64], [49], [50]. Compressive sensing as well as the parametric reconstruction of the diffusion signal in a continuous basis of functions such as the Spherical Polar Fourier basis, have been proved through our recent contributions to be very useful for deriving simple and analytical closed formulae for many important dMRI features, which can be estimated via a reduced number of measurements [64], [49], [50].

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 [57]

3.1.4. dMRI modelling, tissue microstructures features recovery & applications

The dMRI signal is highly complex, hence, the mathematical tools required for processing it have to be commensurate in their complexity. Overall, these last twenty years have seen an explosion of intensive

¹<http://www.emmanuelcaruyer.com/>

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

scientific research which has vastly improved and literally changed the face of dMRI. In terms of dMRI models, two trends are clearly visible today: the parametric approaches which attempt to build models of the tissue to explain the signal based on model-parameters such as CHARMED [41], AxCaliber [42] and NODDI [75] 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 [44], [43], the Solid Harmonic (SoH) basis [53], the Simple Harmonic Oscillator based Reconstruction and Estimation (SHORE) basis [65] and more recent Mean Apparent Propagator or MAP-MRI basis [66].

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

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

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

3.1.5. Towards microstructural based tractography

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

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

3.2. MEG and EEG

Electroencephalography (EEG) and Magnetoencephalography (MEG) are two non-invasive techniques for measuring (part of) the electrical activity of the brain. While EEG is an old technique (Hans Berger, a German neuropsychiatrist, measured the first human EEG in 1929), MEG is a rather new one: the first measurements of the magnetic field generated by the electrophysiological activity of the brain were made in 1968 at MIT by D. Cohen. Nowadays, EEG is relatively inexpensive and is routinely used to detect and qualify neural activities (epilepsy detection and characterisation, neural disorder qualification, BCI, ...). MEG is, comparatively, much more expensive as SQUIDS only operate under very challenging conditions (at liquid helium temperature) and as a specially shielded room must be used to separate the signal of interest from the ambient noise. However, as it reveals a complementary vision to that of EEG and as it is less sensitive to the head structure, it also bears great hopes and an increasing number of MEG machines are being installed throughout the world. Inria and ODYSÉE/ATHENA have participated in the acquisition of one such machine installed in the hospital "La Timone" in Marseille.

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

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

- First, as acquisition is continuous and is run at a rate up to 1kHz, the amount of data generated by each experiment is huge. Data selection and reduction (finding relevant time blocks or frequency bands) and pre-processing (removing artifacts, enhancing the signal to noise ratio, ...) are largely done manually at present. Making a better and more systematic use of the measurements is an important step to optimally exploit the M/EEG data [1].
- With a proper model of the head and of the sources of brain electromagnetic activity, it is possible to simulate the electrical propagation and reconstruct sources that can explain the measured signal. Proposing better models [7], [10] and means to calibrate them [73] so as to have better reconstructions are other important aims of our work.
- Finally, we wish to exploit the temporal resolution of M/EEG and to apply the various methods we have developed to better understand some aspects of the brain functioning, and/or to extract more subtle information out of the measurements. This is of interest not only as a cognitive goal, but it also serves the purpose of validating our algorithms and can lead to the use of such methods in the field of Brain Computer Interfaces. To be able to conduct such kind of experiments, an EEG lab has been set up at ATHENA.

4. Application Domains

4.1. Applications of diffusion MRI

Clinical domain: Diagnosis of neurological disorder

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

4.2. Applications of M/EEG

Applications of EEG and MEG:

Clinical domain: Diagnosis of neurological disorders

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

Subtopics include:

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

Cognitive research

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

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

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

5. New Software and Platforms

5.1. High Performance Diffusion MRI

KEYWORDS: Health - Neuroimaging - Medical imaging

FUNCTIONAL DESCRIPTION

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

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

- Participants: Demian Wassermann, Théodore Papadopoulo and Rachid Deriche
- Contact: Demian Wassermann
- URL: <https://gforge.inria.fr/projects/athenadmri2013>

5.2. DIPY

Diffusion Imaging in Python

KEYWORDS: MRI - Medical imaging

FUNCTIONAL DESCRIPTION

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

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

5.3. The White Matter Query Language

KEYWORDS: Health - Neuroimaging - Medical imaging

FUNCTIONAL DESCRIPTION

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

- Participant: Demian Wassermann
- Contact: Demian Wassermann
- URL: <http://tract-querier.readthedocs.org/en/latest/>

5.4. MedInria

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

SCIENTIFIC DESCRIPTION

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

FUNCTIONAL DESCRIPTION

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

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

5.5. Coadapt P300 Stimulator

KEYWORDS: Health - Brain-Computer Interface

FUNCTIONAL DESCRIPTION

In the domain of Brain Computer Interfaces, extracting relevant features requires a precise timing of all events occurring in the system. In particular, when dealing with evoked responses as in the P300 speller, the timing of the visual stimulations must be well controlled. To alleviate some timing issues with the P300 speller initially provided with OpenViBE, we have implemented an external visual stimulator that allows to flash the visual targets, in a time-robust manner.

- Participants: Dieter Devlaminck, Loïc Mahé, Maureen Clerc, Théodore Papadopoulo, Emmanuel Maby and Jérémie Mattout
- Partner: INSERM
- Contact: Maureen Clerc

5.6. FindSources3D

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

FUNCTIONAL DESCRIPTION

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

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

5.7. OpenMEEG

KEYWORDS: Health - Neuroimaging - Medical imaging

FUNCTIONAL DESCRIPTION

OpenMEEG provides state-of-the art tools for processing EEG and MEG data. It incorporates a newly proposed, symmetric BEM for the forward problem, and a distributed source inverse problem, with three different types of regularizations, two of which are original, based on norms of the surface gradient of the source distribution. OpenMEEG is a free, open software written in C++, and can be accessed either through a command line interface or through a user-friendly interface.

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

5.8. OpenViBE

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

FUNCTIONAL DESCRIPTION

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

- Participants: Yann Renard, Anatole Lécuyer, Fabien Lotte, Bruno Renier, Vincent Delannoy, Laurent Bonnet, Baptiste Payan, Jozef Legény, Jussi Tapio Lindgren, Alison Cellard, Loïc Mahé, Guillaume Serriere and Marsel Mano
- Partners: INSERM - CEA-List - GIPSA-Lab
- Contact: Anatole Lécuyer
- URL: <http://openvibe.inria.fr>

6. New Results

6.1. Modeling in Diffusion MRI

6.1.1. *Improving fiber alignment in HARDI by combining contextual PDE flow with constrained spherical deconvolution*

Participants: Jorg Portegies [Department of Mathematics and Computer Science, Eindhoven University of Technology], Rutger Fick, Gonzalo Sanguinetti [Department of Mathematics and Computer Science, Eindhoven University of Technology], Shephan Meesters [Department of Mathematics and Computer Science, Eindhoven University of Technology], Gabriel Girard [Athena, Inria Sophia-A-M & SCIL Lab., Sherbrooke University], Remco Duits [Department of Mathematics and Computer Science, Eindhoven University of Technology].

We propose two strategies to improve the quality of tractography results computed from diffusion weighted magnetic resonance imaging (DW-MRI) data. Both methods are based on the same PDE framework, defined in the coupled space of positions and orientations, associated with a stochastic process describing the enhancement of elongated structures while preserving crossing structures. In the first method we use the enhancement PDE for contextual regularization of a fiber orientation distribution (FOD) that is obtained on individual voxels from high angular resolution diffusion imaging (HARDI) data via constrained spherical deconvolution (CSD). Thereby we improve the FOD as input for subsequent tractography. Secondly, we introduce the fiber to bundle coherence (FBC), a measure for quantification of fiber alignment. The FBC is computed from a tractography result using the same PDE framework and provides a criterion for removing the spurious fibers. We validate the proposed combination of CSD and enhancement on phantom data and on human data, acquired with different scanning protocols. On the phantom data we find that PDE enhancements improve both local metrics and global metrics of tractography results, compared to CSD without enhancements. On the human data we show that the enhancements allow for a better reconstruction of crossing fiber bundles and they reduce the variability of the tractography output with respect to the acquisition parameters. Finally, we show that both the enhancement of the FODs and the use of the FBC measure on the tractography improve the stability with respect to different stochastic realizations of probabilistic tractography. This is shown in a clinical application: the reconstruction of the optic radiation for epilepsy surgery planning.

This work has been published in [19]

6.1.2. *Sparse reconstruction challenge for diffusion MRI: Validation on a physical phantom to determine which acquisition scheme and analysis method to use?*

Participants: Lipeng Ning [Brigham and Women’s Hospital, Harvard Medical School, Boston], Frederik Laun [German Cancer Research Institute], Yogesh Rathi [Brigham and Women’s Hospital, Harvard Medical School, Boston], Thinhinane Megherbi [ParIMed Team, LRPE, USTHB, Algiers], Mario Zuccheli [Dpt of Computer Science, University of Verona], Gloria Menegaz [Dpt of Computer Science, University of Verona], Maxime Descoteaux [SCIL Lab., Sherbrooke University], Aurobrata Ghosh, Rutger Fick, Rachid Deriche.

Diffusion magnetic resonance imaging (dMRI) is the modality of choice for investigating in-vivo white matter connectivity and neural tissue architecture of the brain. The diffusion-weighted signal in dMRI reflects the diffusivity of water molecules in brain tissue and can be utilized to produce image-based biomarkers for clinical research. Due to the constraints on scanning time, a limited number of measurements can be acquired within a clinically feasible scan time. In order to reconstruct the dMRI signal from a discrete set of measurements, a large number of algorithms have been proposed in recent years in conjunction with varying sampling schemes, i.e., with varying b-values and gradient directions. Thus, it is imperative to compare the performance of these reconstruction methods on a single data set to provide appropriate guidelines to neuroscientists on making an informed decision while designing their acquisition protocols. For this purpose, the SPArse Reconstruction Challenge (SPARC) was held along with the workshop on Computational Diffusion MRI (at MICCAI 2014) to validate the performance of multiple reconstruction methods using data acquired from a physical phantom. A total of 16 reconstruction algorithms (9 teams) participated in this community challenge. The goal was to reconstruct single b-value and/or multiple b-value data from a sparse set of measurements. In particular, the aim was to determine an appropriate acquisition protocol (in terms of the number of measurements, b-values) and the analysis method to use for a neuroimaging study. The challenge did not delve on the accuracy of these methods in estimating model specific measures such as fractional anisotropy (FA) or mean diffusivity, but on the accuracy of these methods to fit the data. This work presents several quantitative results pertaining to each reconstruction algorithm. The conclusions in this work provide a valuable guideline for choosing a suitable algorithm and the corresponding data-sampling scheme for clinical neuroscience applications.

This work has been published in [18].

6.1.3. *A Unifying framework for spatial and temporal diffusion in dMRI*

Participants: Rutger Fick, Demian Wassermann, Marco Pizzolato, Rachid Deriche.

We propose a novel framework to simultaneously represent the diffusion-weighted MRI (dMRI) signal over diffusion times, gradient strengths and gradient directions. Current frameworks such as the 3D Simple Harmonic Oscillator Reconstruction and Estimation basis (3D-SHORE) only represent the signal over the spatial domain, leaving the temporal dependency as a fixed parameter. However, microstructure- focused techniques such as Axcaliber and ActiveAx provide evidence of the importance of sampling the dMRI space over diffusion time. Up to now there exists no generalized framework that simultaneously models the dependence of the dMRI signal in space and time. We use a functional basis to fit the 3D+t spatio-temporal dMRI signal, similarly to the 3D-SHORE basis in three dimensional ‘q-space’. The lowest order term in this expansion contains an isotropic diffusion tensor that characterizes the Gaussian displacement distribution, multiplied by a negative exponential. We regularize the signal fitting by minimizing the norm of the analytic Laplacian of the basis. The continuous 3D+t signal representation can provide new insights on the anomalous nature of the dMRI signal in human tissues, i.e., when mean-squared molecular displacements varies slower than linearly with the diffusion time. From the fitting one can also estimate the axon radius distribution parameters along any direction using approaches similar to AxCaliber. We validate our technique on synthetic data generated using the theoretical model proposed by Callaghan et al. We show that our method is robust to noise and can accurately describe the restricted spatio-temporal signal decay originating from tissue models such as cylindrical pores. Moreover, we apply our method on real data from an ActiveAx acquisition. Overall our approach allows to represent the complete 3D+t dMRI signal which should prove helpful in understanding normal and pathologic nervous tissue.

This work has been published in [26]

6.1.4. Exploiting the phase in dMRI for microstructure recovery: Towards axonal tortuosity via asymmetric diffusion processes

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

Microstructure recovery procedures via Diffusion-Weighted Magnetic Resonance Imaging (DW-MRI) usually discard the signal's phase, assuming symmetry in the underlying diffusion process. In this work, we propose to recover the Ensemble Average Propagator (EAP) directly from the complex DW signal in order to describe also eventual diffusional asymmetry, thus obtaining an asymmetric EAP. The asymmetry of the EAP is then related to tortuosity of undulated white matter axons, which are found in pathological scenarios associated with axonal elongation or compression. We derive a model of the EAP for this geometry and quantify its asymmetry. Results show that the EAP obtained when accounting for the DW signal's phase provides useful microstructural information in such pathological scenarios. Furthermore, we validate these results in-silico through 3D Monte-Carlo simulations of white matter tissue that has experienced different degrees of elongation/compression.

This work has been published in [35]

6.1.5. A temperature phantom to probe the Ensemble Average Propagator asymmetry: an in-silico study

Participants: Marco Pizzolato, Demian Wassermann, Tanguy Duval [Institute of Biomedical Engineering, Polytechnique Montréal, Montréal], Jennifer Campbell [Montreal Neurological Institute, McGill University], Timothé Boutelier [Olea Medical, La Ciotat], Julien Cohen-Adad [Institute of Biomedical Engineering, Polytechnique Montréal, Montréal], Rachid Deriche.

The detection and quantification of asymmetry in the Ensemble Average Propagator (EAP) obtained from the Diffusion-Weighted (DW) signal has been shown only for theoretical models. EAP asymmetry appears for instance when diffusion occurs within fibers with particular geometries. However the quantification of EAP asymmetry corresponding to such geometries in controlled experimental conditions is limited by the difficulty of designing fiber geometries on a micrometer scale. To overcome this limitation we propose to adopt an alternative paradigm to induce asymmetry in the EAP. We apply a temperature gradient to a spinal cord tract to induce a corresponding diffusivity profile that alters locally the diffusion process to be asymmetric. We simulate the EAP and the corresponding complex DW signal in such a scenario. We quantify EAP asymmetry and investigate its relationship with the applied experimental conditions and with the acquisition parameters of a Pulsed Gradient Spin-Echo sequence. Results show that EAP asymmetry is sensible to the applied temperature-induced diffusivity gradient and that its quantification is influenced by the selected acquisition parameters.

This work has been published in [36]

6.1.6. How to get more out of a clinically feasible 64 gradient dMRI acquisition: multi-shell versus single-shell

Participants: Rutger Fick, Mario Zuccheli [Dpt of Computer Science, University of Verona], Gabriel Girard [SCIL Lab., Sherbrooke University], Maxime Descoteaux [SCIL Lab., Sherbrooke University], Gloria Menegaz [Dpt of Computer Science, University of Verona], Rachid Deriche.

For clinical applications the number of diffusion MRI (dMRI) samples that can be obtained is often limited by scanner time and patient comfort. For this reason one often uses short scanning protocols that acquire just 32 or 64 gradient directions using a single b-value to obtain diffusion measures such as the fractional anisotropy from Diffusion Tensor Imaging (DTI) or to estimate the white matter orientation using Constrained Spherical Deconvolution (CSD). Using 3D-SHORE and MAP-MRI, we show that by spreading the same number of dMRI samples over different b-shells (sampling angularly and radially) we can estimate not only

the directionality of the white matter using the ODF, but also the radially dependent higher order diffusion measures that SHORE and MAP-MRI provide. This approach lends itself well for situations where acquisition time is limited, and is therefore particularly well suited for clinical applications.

This work has been published in [29].

6.2. Tissue Microstructures features recovery & applications

6.2.1. *Laplacian-regularized MAP-MRI : Improving axonal caliber estimation*

Participants: Rutger Fick, Demian Wassermann, Gonzalo Sanguinetti, Rachid Deriche.

In diffusion MRI, the accurate description of the entire diffusion signal from sparse measurements is essential to enable the recovery of microstructural information of the white matter. The recent Mean Apparent Propagator (MAP)-MRI basis is especially well suited for this task, but the basis fitting becomes unreliable in the presence of noise. As a solution we propose a fast and robust analytic Laplacian regularization for MAP-MRI. Using both synthetic diffusion data and human data from the Human Connectome Project we show that (1) MAP-MRI has more accurate microstructure recovery compared to classical techniques, (2) regularized MAP-MRI has lower signal fitting errors compared to the unregularized approach and a positivity constraint on the EAP and (3) that our regularization improves axon radius recovery on human data.

This work has been published in [27]

6.2.2. *Using 3D-SHORE and MAP-MRI to obtain both tractography and microstructural contrasts from a clinical dMRI acquisition*

Participants: Rutger Fick, Mario Zuccheli [Dpt of Computer Science, University of Verona], Gabriel Girard [Athena, Inria Sophia-A-M & SCIL Lab., Sherbrooke University], Maxime Descoteaux [SCIL Lab., Sherbrooke University], Gloria Menegaz [Dpt of Computer Science, University of Verona], Rachid Deriche.

Diffusion MRI (dMRI) is used to characterize the directionality and microstructural properties of brain white matter (WM) by measuring the diffusivity of water molecules. In clinical practice the number of dMRI samples that can be obtained is limited, and one often uses short scanning protocols that acquire just 32 to 64 different gradient directions using a single gradient strength (b-value). Such 'single shell' scanning protocols restrict one to use methods that have assumptions on the radial decay of the dMRI signal over different b-values, which introduces estimation biases. In this work, we show, that by simply spreading the same number of samples over multiple b-values (i.e. multi-shell) we can accurately estimate both the WM directionality using 3D-SHORE and characterize the radially dependent diffusion microstructure measures using MAP-MRI. We validate our approach by undersampling both noisy synthetic and human brain data of the Human Connectome Project, proving this approach is well-suited for clinical applications.

This work has been published in [28]

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

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

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

(DTI) data, q-space indices have higher sensitivity to tissue changes than DTI indices in large parts of the brain. Based on these results, it may be interesting to revisit older DTI studies using q-space indices as a marker for pathology.

This work has been accepted at the conference ISBI 2016.

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

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

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

This work has been submitted to the journal NeuroImage.

6.3. Towards microstructural based tractography

6.3.1. AxTract: Microstructure-driven tractography based on the Ensemble Average

Propagator

Participants: Gabriel Girard [Athena, Inria Sophia-A-M & SCIL Lab., Sherbrooke University], Rutger Fick, Maxime Descoteaux [SCIL Lab., Sherbrooke University], Demian Wassermann, Rachid Deriche.

In this work, we propose a novel method to simultaneously trace brain white matter (WM) fascicles and estimate WM microstructure characteristics. Recent advancements in diffusion-weighted imaging (DWI) allow multi-shell acquisitions with b-values of up to 10,000 s/mm² in human subjects, enabling the measurement of the ensemble average propagator (EAP) at distances as short as 10 micro-meters. Coupled with continuous models of the full 3D DWI signal and the EAP such as Mean Apparent Propagator (MAP) MRI, these acquisition schemes provide unparalleled means to probe the WM tissue in vivo. Presently, there are two complementary limitations in tractography and microstructure measurement techniques. Tractography techniques are based on models of the DWI signal geometry without taking specific hypotheses of the WM structure. This hinders the tracing of fascicles through certain WM areas with complex organization such as branching, crossing, merging, and bottlenecks that are indistinguishable using the orientation-only part of the DWI signal. Microstructure measuring techniques, such as AxCaliber, require the direction of the axons within the probed tissue before the acquisition as well as the tissue to be highly organized. Our contributions are twofold. First, we extend the theoretical DWI models proposed by Callaghan et al. to characterize the distribution of axonal calibers within the probed tissue taking advantage of the MAP-MRI model. Second, we develop a simultaneous tractography and axonal caliber distribution algorithm based on the hypothesis that axonal caliber distribution varies smoothly along a WM fascicle. To validate our model we test it on in-silico phantoms and on the HCP dataset

This work has been published in [23]

6.3.2. *Studying white matter tractography reproducibility through connectivity matrices*

Participants: Gabriel Girard [Athena, Inria Sophia-A-M & SCIL Lab., Sherbrooke University], Kevin Whittingstall [SCIL Lab., Sherbrooke University], Maxime Descoteaux [SCIL Lab., Sherbrooke University], Rachid Deriche.

Diffusion-weighted imaging is often used as a starting point for in vivo white matter (WM) connectivity to reconstruct potential WM pathways between brain areas. In this study, we investigate the reproducibility of the connectivity matrix, resulting from different tractography parameters. We vary the number of streamlines used to construct the matrix in cortical to cortical connectivity and analyze its effects. We also compare the effect of probabilistic and deterministic local streamline tractography algorithms, seeding both from the WM and from WM-grey matter interface.

This work has been published in [31]

6.3.3. *Structural connectivity reproducibility through multiple acquisitions*

Participants: Gabriel Girard [Athena, Inria Sophia-A-M & SCIL Lab., Sherbrooke University], Kevin Whittingstall [SCIL Lab., Sherbrooke University], Maxime Descoteaux [SCIL Lab., Sherbrooke University], Rachid Deriche.

dMRI is often used to reconstruct white matter pathways between brain areas for in vivo brain connectivity. In this study, we investigate the reproducibility and the specificity of connectivity matrices in cortico-cortical connectivity using probabilistic and deterministic streamline tractography, seeding from both the white matter and the white matter-grey matter interface.

This work has been published in [30]

6.4. Computational Diffusion MRI

6.4.1. *Robust and efficient linear registration of white-matter fascicles in the space of streamlines*

Participants: Eleftherios Garyfallidis [SCIL Lab., Sherbrooke University], Omar Cepeda [SCIL Lab., Sherbrooke University], Demian Wassermann, Maxime Descoteaux [SCIL Lab., Sherbrooke University].

The neuroscientific community is very much interested in analyzing specific white matter bundles like the arcuate fasciculus, the corticospinal tract, or the recently discovered Aslant tract to study sex differences, lateralization and many other connectivity applications. For this reason, experts spend time manually segmenting these fascicles and bundles using streamlines obtained from diffusion MRI tractography. However, to date, there are very few computational tools available to register these fascicles directly so that they can be analyzed and their differences quantified across populations. In this work, we introduce a novel, robust and efficient framework to align bundles of streamlines directly in the space of streamlines. We call this framework Streamline-based Linear Registration. We first show that this method can be used successfully to align individual bundles as well as whole brain streamlines. Additionally, if used as a piecewise linear registration across many bundles, we show that our novel method systematically provides higher overlap (Jaccard indices) than state-of-the-art nonlinear image-based registration in the white matter. We also show how our novel method can be used to create bundle-specific atlases in a straightforward manner and we give an example of a probabilistic atlas construction of the optic radiation. In summary, Streamline-based Linear Registration provides a solid registration framework for creating new methods to study the white matter and perform group-level tractometry analysis.

This work has been published in [14]

6.4.2. *Cortical surface parcellation via dMRI using mutual nearest neighbor condition*

Participants: Brahim Belaoucha, Maureen Clerc, Théodore Papadopoulo.

In this work, we present a method that aims at parcellating the cortical surface from individual anatomy. The parcellation is obtained using the mutual nearest neighbor criteria to obtain regions that have similar fiber distribution. The later is obtained by applying a probabilistic tractography on the diffusion MRI (dMRI), a non-invasive modality allowing the access to the structural information of the cortical surface. The proposed algorithm is compared to some of the atlases that can be found in the literature. We show that these atlases have lower similarity of fibers distributions than the proposed algorithm.

This work has been accepted at the conference ISBI 2016.

6.5. Clinical and Neurocognitive Applications of Diffusion MRI

6.5.1. *Plasticity of left perisylvian white-matter tracts is associated with individual differences in math learning brain structure and function*

Participants: Dietsje Jolles [Stanford University & Leiden University], Demian Wassermann, Ritika Chokhani [Stanford University], Jennifer Richardson [Stanford University], Caitlin Tenison [Stanford University], Roland Bammer [Stanford University], Lynn Fuchs [Vanderbilt University], Kaustubh Supekar [Stanford University], Vinod Menon [Stanford University].

Plasticity of white matter tracts is thought to be essential for cognitive development and academic skill acquisition in children. However, a dearth of high-quality diffusion tensor imaging (DTI) data measuring longitudinal changes with learning, as well as methodological difficulties in multi-time point tract identification have limited our ability to investigate plasticity of specific white matter tracts. Here, we examine learning-related changes of white matter tracts innervating inferior parietal, prefrontal and temporal regions following an intense two-month math tutoring program. DTI data were acquired from 18 third grade children, both before and after tutoring. A novel fiber tracking algorithm based on a White Matter Query Language (WMQL) was used to identify three sections of the superior longitudinal fasciculus (SLF) linking frontal and parietal (SLF-FP), parietal and temporal (SLF-PT) and frontal and temporal (SLF-FT) cortices, from which we created child-specific probabilistic maps. The SLF-FP, SLF-FT, and SLF-PT tracts identified with the WMQL method were highly reliable across the two time points and showed close correspondence to tracts previously described in adults. Notably, individual differences in behavioral gains after two months of tutoring were specifically correlated with plasticity in the left SLF-FT tract. Our results extend previous findings of individual differences in white matter integrity, and provide important new insights into white matter plasticity related to math learning in childhood. More generally, our quantitative approach will be useful for future studies examining longitudinal changes in white matter integrity associated with cognitive skill development.

This work has been published in [16]

6.5.2. *Prefrontal cortex white matter tracts in prodromal Huntington disease*

Participants: Joy T. Matsui [Iowa University], Jatin G. Vaidya [Iowa University], Demian Wassermann [Iowa University], Regina Eunyoung Kim [Iowa University], Vincent A. Magnotta [Iowa University], Hans J. Johnson [Iowa University], Jane S. Paulsen [Iowa University], Predict-Hd Investigators And Coordinators Of The Huntington Study Group [NIH].

Huntington disease (HD) is most widely known for its selective degeneration of striatal neurons but there is also growing evidence for white matter (WM) deterioration. The primary objective of this research was to conduct a large-scale analysis using multi-site diffusion-weighted imaging (DWI) tractography data to quantify diffusivity properties along major prefrontal cortex WM tracts in prodromal HD. Fifteen international sites participating in the PREDICT-HD study collected imaging and neuropsychological data on gene-positive HD subjects without a clinical diagnosis (i.e. prodromal) and gene-negative control subjects. The anatomical prefrontal WM tracts of the corpus callosum (PFCC), anterior thalamic radiations (ATR), inferior fronto-occipital fasciculi (IFO), and uncinate fasciculi (UNC) were identified using streamline tractography of DWI. Within each of these tracts, tensor scalars for fractional anisotropy, mean diffusivity, radial diffusivity, and axial diffusivity coefficients were calculated. We divided prodromal HD subjects into three CAG-age product (CAP) groups having Low, Medium, or High probabilities of onset indexed by genetic exposure. We observed

significant differences in WM properties for each of the four anatomical tracts for the High CAP group in comparison to controls. Additionally, the Medium CAP group presented differences in the ATR and IFO in comparison to controls. Furthermore, WM alterations in the PFCC, ATR, and IFO showed robust associations with neuropsychological measures of executive functioning. These results suggest that long-range tracts essential for cross-region information transfer show early vulnerability in HD and may explain cognitive problems often present in the prodromal stage.

This work has been published in [17]

6.6. Perfusion MRI

6.6.1. *Perfusion MRI deconvolution with delay estimation and non-negativity constraints*

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

Perfusion MRI deconvolution aims to recover the time-dependent residual amount of indicator (residue function) from the measured arterial and tissue concentration time-curves. The deconvolution is complicated by the presence of a time lag between the measured concentrations. Moreover the residue function must be non-negative and its shape may become non-monotonic due to dispersion phenomena. We introduce Modified Exponential Bases (MEB) to perform deconvolution. The MEB generalizes the previously proposed exponential approximation (EA) by taking into account the time lag and introducing non-negativity constraints for the recovered residue function also in the case of non-monotonic dispersed shapes, thus overcoming the limitation due to the non-increasing assumption of the EA. The deconvolution problem is solved linearly. Quantitative comparisons with the widespread block-circulant Singular Value Decomposition show favorable results in recovering the residue function.

This work has been published in [34]

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

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

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

This work has been accepted at the conference ISBI 2016.

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

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

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

This work has been submitted to the conference ISMRM 2016.

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

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

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

This work has been submitted to the conference ISMRM 2016.

6.7. MEG, EEG and cochlear modeling

6.7.1. MEM-diffusion MRI framework to solve MEEG inverse problem

Participants: Brahim Belaoucha, Jean-Marc Lina, Maureen Clerc, Théodore Papadopoulos.

In this work, we present a framework to fuse information coming from diffusion magnetic resonance imaging (dMRI) with Magnetoencephalography (MEG)/ Electroencephalography (EEG) measurements to reconstruct the activation on the cortical surface. The MEG/EEG inverse-problem is solved by the Maximum Entropy on the Mean (MEM) principle and by assuming that the sources inside each cortical region follow Normal distribution. These regions are obtained using dMRI and assumed to be functionally independent. The source reconstruction framework presented in this work is tested using synthetic and real data. The activated regions for the real data is consistent with the literature about the face recognition and processing network.

This work was published in the proceedings of the conference EUSIPCO 2015 [22].

6.7.2. MEG/EEG reconstruction in the reduced source space

Participants: Brahim Belaoucha, Théodore Papadopoulos.

Obtaining the brain activity with the distributed source model from MEG or EEG measurements is ill-posed problem due to the high number of unknowns compared to the number of measurements. The idea of this work is to reduce the solution space size from the number of sources to a smaller space. Assuming that sources inside each functional region have equal activation allows us to reduce the number of columns in the leadfield matrix from the number of nodes S required to model the cortex to a number of regions K , which is much smaller. These regions are obtained from a dMRI parcellation-based region growing algorithm. A region is assumed to contain sources that have similar fibers distribution. To obtain a sparse solution, we assume that only a few regions are active simultaneously. BIC1 is used to obtain the optimal number of regions (K_p) that explains the MEG/EEG data.

We compared the results of the proposed method to the ones from Minimum Norm Estimate (MNE) and LASSO. The first gives a smooth solution and the second gives a sparse solution. To test the accuracy of the reconstruction, we activated simultaneously from two to five regions in both hemispheres with synthetic low SNR signals (10 dB). Our approach could detect the right number of activated regions and provided more accurate reconstructions compared to MNE and LASSO.

Our approach assumes that few regions are active simultaneously which allows us to reduce the space to a few unknowns. It can be seen as an approximation to the l_0 norm. Even though assuming a constant activation in each functional region is a hard constraint, it allows us to reduce the space size from S to K . The obtained solution can be used to detect extended sources (e.g epileptic activity) or as an initialization step to other approaches to obtain more detailed solutions in the active regions.

This work was presented at the conference BaCI 2015 [24].

6.7.3. Realistic simulation of electric potential distributions of different stimulation modes in an implanted cochlea

Participants: Kai Dang, Maureen Clerc, Clair Vandersteen [Institut Universitaire de la Face et du Cou, Nice], Nicolas Guevara [Institut Universitaire de la Face et du Cou, Nice], Dan Gnansia [Oticon Medical/Neurelec].

Simulation of the intracochlear potentials is an important approach to study the activation of auditory nerve fibers under electrical stimulations. However, it is still unclear to which extent the simulation results are affected by precision in reproducing the exact cochlear geometry. In this study, we address to this question by comparing the actual electric potential measured from implanted human specimen with the simulation outputs from two different parametric 3D cochlear models. One of the models is created from the default values while the other is adapted to the micro-CT scan data of the implanted cochlea.

This work was presented at the Association of Research in Otolaryngology 38th MidWinter Meeting, Feb 2015, Baltimore, United States [38].

We also made an in situ validation of electrical models: Cochlear implants have been proved to be an effective treatment for patients with sensorineural hearing loss. Among all the approaches that have been developed to design better cochlear implants, 3D model-based simulation stands out due to its detailed description of the electric field which helps reveal the electrophysiological phenomena inside the cochlea. With the advances in the cochlear implant manufacturing technology, the requirement on simulation accuracy increases. Improving the simulation accuracy relies on two aspects: 1) a better geometrical description of the cochlea that is able to distinguish the subtle differences across patients; 2) a comprehensive and reliable validation of the created 3D model. In this paper, targeting at high precision simulation, we propose a parametric cochlea model which uses micro-CT images to adapt to different cochlea geometries, then demonstrate its validation process with multi-channel stimulation data measured from a implanted cochlea. Comparisons between the simulation and validation data show a good match under a variety of stimulation configurations. The results suggest that the electric field distribution is affected by the geometric characteristics of each individual cochlea. These differences can be correctly reflected by simulations based on a 3D model tuned with personalized data.

This work was presented at the 7th International IEEE EMBS Conference on Neural Engineering, Apr 2015, Montpellier, France [25].

6.7.4. Influence of skull modelling on conductivity estimation for EEG source analysis

Participants: Christos Papageorgakis, Maureen Clerc, Benjamin Lanfer [BESA GmbH].

The skull conductivity strongly influences the accuracy of EEG source localization methods. As the conductivity of the skull has strong inter-individual variability, conductivity estimation techniques are required. Typically, conductivity estimation is performed on data from a single event-related stimulation paradigm, which can be explained by one dipole source. A conductivity value for the skull can be estimated as the value for which the single dipole source provides the best goodness of fit to the data. This conductivity value is then used to analyse the actual data of interest. It is known that the optimal local skull conductivity when modelling the skull as one compartment depends on the amount of spongiosa present locally. The research question arising is: Is conductivity estimation based on data from a single paradigm meaningful without accounting for the internal skull structure ?

This work was presented at the conference BaCI 2015 [33], and is submitted for journal publication.

6.7.5. Dictionary learning for M/EEG multidimensional data

Participants: Christos Papageorgakis, Sebastian Hitziger, Théodore Papadopoulo.

Signals obtained from magneto- or electroencephalography (M/EEG) are very noisy and inherently multi-dimensional, i.e. provide a vector of measurements at each single time instant. To cope with noise, researchers traditionally acquire measurements over multiple repetitions (trials) and average them to classify various patterns of activity. This is not optimal because of trial-to-trial variability (waveform variation, jitters). The jitter-adaptive dictionary learning method (JADL) has been developed to better handle for this variability (with a particular emphasis on jitters). JADL is a data-driven method that learns a dictionary (prototype pieces) from a set of signals, but is currently limited to a single channel, which restricts its capacity to work with very noisy data such as M/EEG. We propose an extension to the jitter-adaptive dictionary learning method, that is able to handle multidimensional measurements such as M/EEG.

This work was presented at the conference BaCI 2015 [32].

6.8. Brain Computer Interfaces

6.8.1. *Decoding covert shifts of attention induced by ambiguous visuospatial cues*

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

Simple and unambiguous visual cues (e.g., an arrow) can be used to trigger covert shifts of visual attention away from the center of gaze. The processing of visual stimuli is enhanced at the attended location. Covert shifts of attention modulate the power of cerebral oscillations in the alpha band over parietal and occipital regions. These modulations are sufficiently robust to be decoded on a single trial basis from electroencephalography (EEG) signals. It is often assumed that covert attention shifts are under voluntary control, and that they also occur in more natural and complex environments, but there is no direct evidence to support this assumption. We address this important issue by using random-dot stimuli to cue one of two opposite locations, where a visual target is presented. We contrast two conditions, one in which the random-dot motion is predictive of the target location, and the other, in which it provides ambiguous information. Behavioral results show attention shifts in anticipation of the visual target, in both conditions. In addition, using the common spatial patterns (CSPs) algorithm, we extract EEG power features in the alpha-band (around 10 Hz) that best discriminate the attended location in single trials. We obtain a significant decoding accuracy in 7/10 subjects using a cross-validation procedure applied in the predictive condition. Interestingly, similar accuracy (significant in 5/10 subjects) is obtained when the CSPs trained in the predictive condition are tested in the ambiguous condition. In agreement with this result, we find that the CSPs show very similar topographies in both conditions. These results shed a new light on the behavioral and EEG correlates of visuospatial attention in complex visual environments. This study demonstrates that alpha-power features could be used in brain computer interfaces to decode covert attention shifts in an environment containing ambiguous spatial information.

This work was published in *Frontiers in Human Neurosciences* [20].

6.8.2. *Online extraction and single trial analysis of regions contributing to erroneous feedback detection*

Participants: Eoin Thomas, Matthew Dyson, Laurence Casini, Boris Burle.

Understanding how the brain processes errors is an essential and active field of neuroscience. Real time extraction and analysis of error signals provide an innovative method of assessing how individuals perceive ongoing interactions without recourse to overt behaviour. This area of research is critical in modern Brain-Computer Interface (BCI) design, but may also open fruitful perspectives in cognitive neuroscience research. In this context, we sought to determine whether we can extract discriminatory error-related activity in the source space, online, and on a trial by trial basis from electroencephalography data recorded during motor imagery. Using a data driven approach, based on interpretable inverse solution algorithms, we assessed the extent to which automatically extracted error-related activity was physiologically and functionally interpretable according to performance monitoring literature. The applicability of inverse solution based methods for automatically extracting error signals, in the presence of noise generated by motor imagery, was validated by simulation.

Representative regions of interest, outlining the primary generators contributing to classification, were found to correspond closely to networks involved in error detection and performance monitoring. We observed discriminative activity in non-frontal areas, demonstrating that areas outside of the medial frontal cortex can contribute to the classification of error feedback activity.

This work was published in NeuroImage [13].

7. Bilateral Contracts and Grants with Industry

7.1. Bilateral Grants with Industry

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

8. Partnerships and Cooperations

8.1. National Initiatives

8.1.1. ANR

8.1.1.1. ANR MRSEI LEMONS

Participants: Maureen Clerc, Théodore Papadopoulo.

Duration: *October 2015 to April 2017* The ANR MRSEI LEMONS aims to consolidate a European Network by organizing meetings and visits, in order to submit a proposal for a MSCA-ITN. The European consortium is led by Inria (coordinator Maureen Clerc).

8.1.1.2. ANR MOSIFAH

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

Duration: *October 2013 to September 2017*

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

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

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

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

8.1.1.3. ANR VIBRATIONS

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

Duration: February 2014 to January 2018

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

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

The project follows a three-fold strategy:

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

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

8.1.2. ADT

8.1.2.1. ADT BOLIS

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

Duration: December 2014 to December 2016

ADT BOLIS aims to:

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

8.1.2.2. ADT OpenViBE-X

Participants: Théodore Papadopoulo, Maureen Clerc, Nathanaël Foy.

Duration: October 2014 to October 2016

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

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

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

8.2. European Initiatives

8.2.1. FP7 & H2020 Projects

8.2.1.1. ChildBrain ETN

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

Program: European Training Network

Project acronym: ChildBrain

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

Duration: March 2015 to March 2019

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

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

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

8.3. International Initiatives

8.3.1. Inria International Partners

8.3.1.1. Informal International Partners

- SCIL Laboratory, Sherbrooke University, CA (Maxime Descoteaux)
- CMRR, University of Minnesota, USA (Christophe Lenglet)
- Verona University, It (Gloria Menegaz)
- Department of CISE, the University of Florida, Gainesville, USA (Baba C. Vemuri)
- Centre for Medical Image Computing (CMIC), Dept. Computer Science, UCL, UK (D. Alexander)
- SBIA, University of Pennsylvania Medical School, USA (R. Verma).
- University Houari Boumediene (USTHB, Algiers) (L. Boumghar) and University of Boumerdes, (D. Cherifi), Algeria.
- BESA company on EEG/MEG source localisation.
- CRM, Centre de Recherche Mathématiques, Montréal, Canada.

8.4. International Research Visitors

8.4.1. Visits of International Scientists

- Maxime Descoteaux (Sherbrooke University, CA) visited ATHENA from March 13 to April 3, 2015
- Gabriel Girard (Sherbrooke University, CA) visited ATHENA from March 13 to April 3, 2015
- Mauro Zuccheli (Verona University, It) visited ATHENA from March 23 to 27, 2015
- Dalila Cherifi (Boumerdes University, Algiers) visited ATHENA from April 24 to 27, 2015
- Mouloud Kachouane (USTHB, Algiers) visited ATHENA from November 2015 to October 2016.

8.4.1.1. Internships

Guillermo Alejandro Gallardo Diez

Date: June 2015 - August 2015

Institution: Universidad de Buenos Aires (Argentina)

Etienne Guerlais

Date: October 2015 - February 2016

Institution: Ecole d'ingénieurs informatique CESI, eXia

Jelena Mladenovic

Date: April 2015 - September 2015

Institution: Université de Nice-Sophia Antipolis

Siobhan Powell

Date: May 2015 - Jul 2015

Institution: Queens Univeristy, Ontario (Canada)

9. Dissemination

9.1. Promoting Scientific Activities

9.1.1. Scientific events organisation

9.1.1.1. General chair, scientific chair

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

9.1.2. Scientific events selection

9.1.2.1. Member of the conference program committees

- R. Deriche is member of the conference Programme Committee (PC) of the International Symposium on Biomedical Imaging (ISBI), member of the PC of MICCAI 2015 Workshop on Computational Diffusion MRI and member of the PC of MFCA 2015 5th MICCAI workshop on Mathematical Foundations of Computational Anatomy.
- D. Wassermann is member of the conference Program Committee (PC) of Medical Image Computing and Computed Assisted Intervention (MICCAI 2015), and Information Processing in Medical Imaging (IPMI 2015).

- M. Clerc is a member of the Program Committee of BaCI 2015, and a member of the Scientific Committee of the Sophia Antipolis Colloquium.
- T. Papadopoulo is member of the PC of GRETSI 2015 and of MICCAI 2015 Workshop on Computational Diffusion MRI.

9.1.2.2. Reviewer

- R. Deriche serves several international conferences (Isbi, MICCAI, ISMRM..) and international workshops (CD-MRI Miccai, MFCA Miccai..)
- D. Wassermann serves several international conferences (ISBI, MICCAI, IPMI, ...) and international workshops (CD-MRI Miccai, ..)
- T. Papadopoulo served the international conferences: (ICIP, ISBI, EUSIPCO, NER, VISAPP).

9.1.3. Journal

9.1.3.1. Member of the editorial boards

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

9.1.3.2. Reviewer - Reviewing activities

- R. Deriche serves several international journals (NeuroImage, IEEE Transactions on Medical Imaging, Magnetic Resonance in Medicine, Journal of Mathematical Imaging and Vision, Medical Image Analysis Journal,...).
- D. Wassermann serves several international journals (NeuroImage, IEEE Transactions on Medical Imaging, Human Brain Mapping, Medical Image Analysis Journal,...).
- T. Papadopoulo serves several international journals (IEEE Transactions on Biomedical Engineering, Frontiers Neuroscience, Transactions on Neural Systems & Rehabilitation Engineering, International Journal on Computer Vision,...).

9.1.4. Invited talks

- R. Deriche gave an invited talk at USTHB on September 20th, 2015.
- D. Wassermann gave the following invited talks:
 - MedicSS Summer School, London, UK, 2015: Gaussian Processes: Sound Bases for Stochasticity in Medical Imaging
 - Microbiology Department, University of Buenos Aires, Argentina, 2015: Diffusion MRI-based microscopy, applications to Neuroscience
 - ICM, Paris, France 2015: Automated in vivo dissection and microstructure-based tractography analyses of cerebral white matter structures
 - Universidad de Valladolid, Valladolid, Spain 2015: Automated in vivo dissection and microstructure-based tractography analyses of cerebral white matter structures
 - UCL, London, UK 2015: Automated in vivo dissection and microstructure-based tractography analyses of cerebral white matter structures
- M. Clerc gave the following invited talks:
 - TedX Cannes conference, March 2015.
 - Connected Health, Monaco, June 2015.
 - Keynote at EUSIPCO 2015 Conference, Nice, September 2015.

- Invited talk at BaCI conference, Utrecht, September 2015.
- ENS Lyon Colloquium, October 2015.
- Horizon Maths (IBM Bois Colombes), December 2015.

9.1.5. Leadership within the scientific community

The Inria Project-Lab **BCI-LIFT** was created in 2015, to foster the work of 8 Inria teams and 2 more teams outside Inria on Brain Computer Interfaces Learning, Interaction, Feedback and Training. It is coordinated by Maureen Clerc.

BCI-LIFT was responsible for setting up a **Brain Computer Interface Challenge** which attracted 260 participants. The results of the Challenge were presented at the IEEE EMBS Conference on Neural Engineering in Montpellier, April 2015.

9.1.6. Scientific expertise

- 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,...).
- D. Wassermann serves as a reviewer for the following scientific funding institutions: French ANR, Dutch Organisation for Scientific Research, Argentine Agencia Nacional de Promocion Cientifica y Tecnologica.

9.1.7. Research administration

- R. Deriche is Chair of the 2015 and 2016 Inria Sophia Antipolis recruitment committees
- R. Deriche is member of 4 Scientific Councils: University of Nice Sophia Antipolis, ITMO ITS (Institut des Technologies pour la Santé), Olea Medical Company (<http://www.olea-medical.com/>) and the GIS UNS-ENSL-CNRS-Inria.
- R. Deriche is member of the Administration Council of AFRIF (Association Française pour la Reconnaissance et l'Interprétation des Formes) and member of the Academic Council of UCA (Nice Côte d'Azur University)
- M. Clerc is Déléguée Scientifique Adjointe for the Inria Sophia Antipolis Research Center.
- M. Clerc is a member of the Evaluation Committee of Inria.
- M. Clerc is a member of the Commission Scientifique Interne of Inria.
- M. Clerc is a deputy member of the Administration Council of Université Côte d'Azur.
- M. Clerc was a member of the ENS Rennes Professor recruitment committee in 2015.
- M. Clerc was a member of the University of Nice, JAD laboratory Professor recruitment committee in 2015.
- T. Papadopoulo is a member of the Inria committee for software development.

9.2. Teaching - Supervision - Juries

9.2.1. Teaching

- Master: R. Deriche, Variational approaches and Geometrical Flows for Computational Brain Imaging, 36 ETD, M2 "Computational Biology and Biomedicine", University of Nice Sophia Antipolis, France.
- Master: R. Deriche, Advanced Image Processing Techniques, 12 ETD, M1 International CBB & Ubinet, University of Nice Sophia Antipolis, France.
- Master: R. Deriche, Computational Image Processing, Analysis and Artificial Vision, 18 ETD, Institut Telecom / Telecom SudParis, Evry, France.

- Master: T. Papadopoulo, *3D Computer Vision*, 12 ETD, M1 International Ubinet, University of Nice Sophia Antipolis, France.
- Master: T. Papadopoulo, *Inverse Problems in Brain Functional Imaging*, 36 ETD, M2 "Computational Biology and Biomedicine", University of Nice Sophia Antipolis, France.
- Master: T. Papadopoulo, *Inverse problems for brain functional imaging*, 24 ETD, M2, Mathématiques, Vision et Apprentissage, ENS Cachan, France.

9.2.2. Supervision

- PhD defended April 14, 2015: Sebastian Hitziger, "MEEG signal processing", started Nov. 2011, Supervisors: Théodore Papadopoulo & Maureen Clerc.
- PhD in progress: Rutger Fick, "Microstructure Recovery via dMRI", started Oct. 2013, Université Nice Sophia Antipolis. Supervisor: Rachid Deriche.
- PhD in progress: Kai Dang, "Modeling and characterizing electrical conductivity for cochlear implantation", started Dec. 2013, Université Nice Sophia Antipolis. Supervisor: Maureen Clerc.
- PhD in progress: Gabriel Girard, "fMRI & dMRI", started Sept. 2012, Supervisors: Rachid Deriche & Maxime Descoteaux (University of Sherbrooke, CA).
- PhD in progress: Mouloud Kachouane, "Invariants and biomarqueurs in dMRI", started Oct. 2012, Supervisors: Rachid Deriche & L. Boumghar (USTHB, Algiers).
- PhD in progress: Thinhinane Megherbi, "HARDI & High Order Tensors", started Sept. 2011, Supervisors: Rachid Deriche & L. Boumghar (USTHB, Algiers)
- PhD in progress: Marco Pizzolato, "Diffusion & Perfusion MRI: From bench to bedside" started Dec. 2013, Université Nice Sophia Antipolis. Supervisor: Rachid Deriche.
- PhD in progress: Brahim Belaoucha, "Using diffusion MR information to reconstruct networks of brain activations from MEG and EEG measurements", Université Nice Sophia Antipolis, started Oct. 2013, Supervisor: Theo Papadopoulo.
- PhD in progress: Guillermo Gallardo Diez, "Connectivity-Based Brain Parcellation", started Nov. 2015, Université Nice Sophia Antipolis. Supervisors: D. Wassermann/ R. Deriche
- PhD in progress: Nathalie Gayraud, "Structured Dictionary Learning", University Nice Sophia Antipolis, started November 2015, supervisor: Maureen Clerc.
- Master: Guillermo Gallardo Diez, "Connectivity-Based Brain Parcellation", Supervised by D. Wassermann.

9.2.3. Juries

- R. Deriche participated in the PhD jury of Jianfei Yang (Delft University, Eindhoven, Sept. 2015).
- M. Clerc participated in the PhD jury of Juliette Spinnato (Aix-Marseille Université, July 2015).
- M. Clerc participated in the PhD jury of Ronan Hamon (ENS Lyon, Oct. 2015).
- M. Clerc participated in the PhD jury of Alexandre Fouchard (CEA LETI, Nov. 2015).
- D. Wassermann participated in the PhD jury of Ariel Hernan Curiale (Universidad de Valladolid, Spain, June 2015).

9.3. Popularization

Maureen Clerc gave a conference at the TedX Cannes event in March 2015 (Youtube video link: <https://youtu.be/z5AO-603AmE>).

10. Bibliography

Major publications by the team in recent years

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