
Activity Report 2012

# Project-Team ATHENA

## Computational Imaging of the Central Nervous System

RESEARCH CENTER
**Sophia Antipolis - Méditerranée**

THEME
**Computational Medicine and Neuro-sciences**

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# Project-Team ATHENA

**Keywords:** Computational Neurosciences, Medical Images, Image Processing, Signal Processing, Inverse Problem, Brain Computer Interface

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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) is an application of EEG that has been proposed as a means to translate in real-time the electrical activity of the brain in commands to control devices. While BCI had been advocated as a means to communicate and help restore mobility or autonomy for very severe cases of disabled patients, it is more realistically a tool for a new interactive probing and training of 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. Scientific Foundations

## 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 [64] and Taylor et al [70]. 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. The great success of dMRI comes from its ability to accurately describe the geometry of the underlying microstructure and probe the structure of the biological tissue at scales much smaller than the imaging resolution.

The diffusion of water molecules is Brownian in an isotropic medium and under normal unhindered conditions, but in fibrous structure such as white matter, the diffusion is very often directionally biased or anisotropic and water molecules tend to diffuse along fibers. For example, a molecule inside the axon of a neuron has a low probability to cross a myelin membrane. Therefore the molecule will move principally along the axis of the neural fiber. Conversely if we know that molecules locally diffuse principally in one direction, we can make the assumption that this corresponds to a set of fibers.

**Diffusion Tensor Imaging**

Shortly after the first acquisitions of diffusion-weighted images (DWI) were made in vivo [65], [66], Basser et al [45], [44] proposed the rigorous formalism of the second order Diffusion Tensor Imaging model (DTI). DTI describes the three-dimensional (3D) nature of anisotropy in tissues by assuming that the average diffusion of water molecules follows a Gaussian distribution. It encapsulates the diffusion properties of water molecules in biological tissues (inside a typical 1-3 $mm^3$ sized voxel) as an effective self-diffusion tensor given by a $3 \times 3$ symmetric positive definite tensor $\mathbf{D}$ [45], [44]. Diffusion tensor imaging (DTI) thus produces a three-dimensional image containing, at each voxel, the estimated tensor $\mathbf{D}$. This requires the acquisition of at least six Diffusion Weighted Images (DWI) $S_k$ in several non-coplanar encoding directions as well as an unweighted image $S_0$. Because of the signal attenuation, the image noise will affect the measurements and it is therefore important to take into account the nature and the strength of this noise in all the pre-processing steps. From the diffusion tensor $\mathbf{D}$, a neural fiber direction can be inferred from the tensor's main eigenvector while various diffusion anisotropy measures, such as the Fractional Anisotropy (FA), can be computed using the associated eigenvalues to quantify anisotropy, thus describing the inequality of diffusion values among particular directions.

DTI has now proved to be extremely useful to study the normal and pathological human brain [60], [51]. It has led to many applications in clinical diagnosis of neurological diseases and disorder, neurosciences applications in assessing connectivity of different brain regions, and more recently, therapeutic applications, primarily in neurosurgical planning. An important and very successful application of diffusion MRI has been brain ischemia, following the discovery that water diffusion drops immediately after the onset of an ischemic event, when brain cells undergo swelling through cytotoxic edema.

The increasing clinical importance of diffusion imaging has drived our interest to develop new processing tools for Diffusion MRI. Because of the complexity of the data, this imaging modality raises a large amount of mathematical and computational challenges. We have therefore started to develop 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], [8] and [61]).

**High Angular Resolution Diffusion Imaging**

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. This is an important limitation, since resolution of DTI acquisition is between $1\text{mm}^3$ and $3\text{mm}^3$ while the physical diameter of fibers can be between $1\mu$m and 30 $\mu m$ [68], [46]. Research groups currently agree that there is complex fiber architecture in most fiber regions of the brain [67]. In fact, it is currently thought that between one third to two thirds of imaging voxels in the human brain white matter contain multiple fiber bundle crossings [47]. This has led to the development of various High Angular Resolution Diffusion Imaging (HARDI) techniques [72] such as Q-Ball Imaging (QBI) or Diffusion Spectrum Imaging (DSI) [73], [74], [76] to explore more precisely the microstructure of biological tissues.

HARDI samples q-space along as many directions as possible in order to reconstruct estimates of the true diffusion probability density function (PDF) – also referred as the Ensemble Average Propagator (EAP) – of water molecules. This true diffusion PDF is model-free and can recover the diffusion of water molecules in any underlying fiber population. HARDI depends on the number of measurements $N$ and the gradient strength ($b$-value), which will directly affect acquisition time and signal to noise ratio in the signal.

Typically, there are two strategies used in HARDI: 1) sampling of the whole q-space 3D Cartesian grid and estimation of the EAP by inverse Fourier transformation or 2) single shell spherical sampling and estimation of fiber distributions from the diffusion/fiber ODF (QBI), Persistent Angular Structure [58] or Diffusion Orientation Transform [79]. In the first case, a large number of q-space points are taken over the discrete grid ($N > 200$) and the inverse Fourier transform of the measured Diffusion Weighted Imaging (DWI) signal is taken to obtain an estimate of the diffusion PDF. This is Diffusion Spectrum Imaging (DSI) [76], [73], [74]. The method requires very strong imaging gradients ($500 \leq b \leq 20000$ s/mm$^2$) and a long time for acquisition (15-60 minutes) depending on the number of sampling directions. To infer fiber directions of the diffusion PDF at every voxel, people take an isosurface of the diffusion PDF for a certain radius. Alternatively, they can use the second strategy known as Q-Ball imaging (QBI) i.e just a single shell HARDI acquisition to compute the diffusion orientation distribution function (ODF). With QBI, model-free mathematical approaches can be developed to reconstruct the angular profile of the diffusion displacement probability density function (PDF) of water molecules such as the ODF function which is fundamental in tractography due to the fact that it contains the full angular information of the diffusion PDF and has its maxima aligned with the underlying fiber directions at every voxel.

QBI and the diffusion ODF 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 available. Those contributions are fundamental and have already started to impact on the Diffusion MRI, HARDI and Q-Ball Imaging community [50]. They are at the core of our probabilistic and deterministic tractography algorithms devised to best exploit the full distribution of the fiber ODF (see [48], [3] and [49],[4]).

**High Order Tensors**

Other 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 [77], [80] or 4th order Tensor Model [43]. For more details, we refer the reader to our recent article in [53] where we review HOT models and to our article in [7], 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.

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. 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 [2], these imaging modalities raise a large amount of mathematical and computational challenges at the core of the research we develop at ATHENA [56].

**Improving dMRI Acquisitions and Modeling**

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 developped 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 [2]. 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. We have also 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 [10], [11]. 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 [10], [11].

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 [55]

## 3.2. MEG and EEG

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

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

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

- First, as acquisition is continuous and is run at a rate up to 1kHz, the amount of data generated by each experiment is huge. Data selection and reduction (finding relevant time blocks or frequency bands) and pre-processing (removing artifacts, enhancing the signal to noise ratio, ...) are largely done manually at present. Making a better and more systematic use of the measurements is an important step to optimally exploit the M/EEG data [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 [6], [9] and means to calibrate them [75] 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

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.

**Clinical domain: Diagnosis of neurological disorder**

- *Parkinson's and Alzheimer's diseases* are among the most important CNS diseases. Six million patients (among which 850.000 in France) are suffering from Alzheimer's, making it the most important neurodegenerative disease in Europe. Over 85 years of age, 1 woman in 4 and 1 man in 5 are affected in Europe. In France, the number of Alzheimer's patients is expected to reach at least 2 million in 2025 and will probably double in 2050, with the increasing age of the population. Parkinson's disease is the second most important neurodegenerative disease. There are six and a half

million patients in the world and roughly 150.000 patients in France, among which $10\%$ are under 40 and $50\%$ over 58. Together with our partners from NeuroSpin (Saclay), Inserm U678 and CENIR (CHUPS, Paris), we are involved in the ANR project NucleiPark which is about high field MRI of the braintem, the deep nuclei and their connections in the Parkinsonian syndromes.

- *Spinal Cord Injury* (SCI) has a significant impact on the quality of life since it can lead to motor deficits (paralysis) and sensory deficits. In the world, about 2.5 million people live with SCI (http://www.campaignforcure.org). To date, there is no consensus for full rehabilitative cure in SCI, although many therapeutic approaches have shown benefits [69], [71]. It is thus of great importance to develop tools that will improve the characterization of spinal lesions as well as the integrity of remaining spinal tracts to eventually establish better prognosis after spinal injury. We have already started to be active in this domain with our collaborators at Inserm U678 (H. Benali) and CRSN/Faculté de médecine Université de Montréal (Pr. S. Rossignol).

## 4.2. Applications of M/EEG

Applications of EEG and MEG cover:

- **Clinical domain:** diagnosis of neurological disorders such as
  - 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.
- **Brain Computer Interfaces** look at allowing a direct control of the world using brain signal such as EEG signals. Those can be considered both as an application of EEG processing techniques and as a tool for fundamental and applied research as it opens the way for more dynamical and active brain cognitive protocols.

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 collaboration with the La Timone hospital in Marseille. M/EEG are also used in **cognitive research**, and we collaborate with the *Laboratory for Neurobiology of Cognition* in order to develop methods that suit their needs for sophisticated data analysis.

# 5. Software

## 5.1. OpenMEEG

**Participants:** Théodore Papadopoulo, Maureen Clerc, Alexandre Gramfort [Telecom ParisTech].

OpenMEEG provides state-of-the art tools for low-frequency bio-electromagnetism, notably solving forward problems related to EEG and MEG [5]. It implements the symmetric BEM which provides excellent accuracy and versatility OpenMEEG is a free open software written in C++. It can be accessed either through a command line interface or through Python/Matlab interfaces.

OpenMEEG is multiplatform (Linux, MacOS, Windows) and it is distributed under the French opensource license CeCILL-B. See also the web page http://www-sop.inria.fr/athena/software/OpenMEEG/.

## 5.2. Diffusion MRI

**Participants:** Aurobrata Ghosh, Rachid Deriche.

The algorithms previously developed within the ODYSSÉE Project team and related to the Diffusion Tensor and Q-Ball imaging are available upon request from the Inria source forge (https://gforge.inria.fr). One can use all the estimation and visualization tools developed, ranging from estimation, regularization, segmentation to Q-ball estimation, fiber ODF estimation and tractography algorithms. New visualization tools for Q-Ball images represented by spherical harmonic decomposition have also been developed.

The software library comprises geometric and variational methods devised to estimate, regularize, segment and perform tractography in DT (Diffusion Tensor) and HARDI (High Angular Resolution) MRI images. The library is multi-platform (Linux, Windows and OS X) ans is embedded into two open-source high level languages, TCL and Python.

## 5.3. medInria

**Participants:** Jaime Garcia Guevara, Théodore Papadopoulo.

The Athena team is involved along with the research teams Asclepios, Parietal and Visages in the development of medInris a free software platform dedicated to medical data visualization and processing.

It aims at providing to clinicians and researchers state-of-the-art algorithms developed at Inria and elsewhere (for the future), through an intuitive user interface. medInria offers from standard to cutting-edge processing functionalities for medical images such as 2D/3D/4D image visualization, image registration, diffusion MR processing and tractography.

Athena contribution so far consists in various improvements on the core application as well as several plugins which will be available in the next version: advanced dMRI visualization and processing (integration of the Diffusion MRI library depicted in the previous section), M/EEG signal visualisation (by integrating code from the software AnyWave developed at by Bruno Colombet and J.-M. Badier Inserm UMR 1106 and Aix-Marseille University).

See also the web page http://med.inria.fr.

- Version: 2.0.1
- Keywords: Medical Image Processing and Visualization
- License: Proprietary Licence (soon open source for the core application)
- Multiplatform: Windows - Linux - MacOSX
- Programming language: C++

# 6. New Results

## 6.1. Computational Diffusion MRI

### *6.1.1. Improving dMRI Signal and Acquisitions*

*6.1.1.1. Diffusion MRI Signal Reconstruction with Continuity Constraint and Optimal Regularization*

**Participants:** Emmanuel Caruyer, Rachid Deriche.

In diffusion MRI, the reconstruction of the full Ensemble Average Propagator (EAP) provides new insights in the diffusion process and the underlying microstructure. The reconstruction of the signal in the whole Q-space is still extremely challenging however. It requires very long acquisition protocols, and robust reconstruction to cope with the very low SNR at large b-values. Several reconstruction methods were proposed recently, among which the Spherical Polar Fourier (SPF) expansion, a promising basis for signal reconstruction. Yet the reconstruction in SPF is still subject to noise and discontinuity of the reconstruction. In this work, we present a method for the reconstruction of the diffusion attenuation in the whole Q-space, with a special focus on continuity and optimal regularization. We derive a modified Spherical Polar Fourier (mSPF) basis, orthonormal and compatible with SPF, for the reconstruction of a signal with continuity constraint. We also derive the expression of a Laplace regularization operator in the basis, together with a method based on generalized cross validation for the optimal choice of the parameter. Our method results in a noticeable dimension reduction as compared with SPF. Tested on synthetic and real data, the reconstruction with this method is more robust to noise and better preserves fiber directions and crossings.

This work has been published in [13]

*6.1.1.2. A Computational Framework for Experimental Design in Diffusion MRI*

**Participants:** Emmanuel Caruyer, Rachid Deriche.

In this work, we develop a computational framework for optimal design of experiment in parametric signal reconstruction. We apply this to the optimal design of one dimensional Q-space, Q-ball imaging and multiple Q-shell experimental design. We present how to construct sampling scheme leading to minimal condition number, and compare to state-of-the-art sampling methods. We show in particular a better noise performance of these scheme through Monte-Carlo simulations for the reconstruction of synthetic signal. This demonstrates the impact of this computational framework on acquisition in diffusion MRI.

This work has been published in [16]

*6.1.1.3. Parametric Dictionary Learning in Diffusion MRI*

**Participants:** Sylvain Merlet, Emmanuel Caruyer, Aurobrata Ghosh, Rachid Deriche.

*This work has been partly supported by the Association France Parkinson and the ANR NucleiPark project.*

In this work, we propose an approach to exploit the ability of compressive sensing to recover diffusion MRI signal and its characteristics from a limited number of samples. Our approach is threefold. First, we learn and design a parametric dictionary from a set of training diffusion data. This provides a highly sparse representation of the diffusion signal. The use of a parametric method presents several advantages: we design a continuous representation of the signal, from which we can analytically recover some features such as the ODF; besides, the dictionary we train is acquisition-independent. Next, we use this sparse representation to reconstruct the signal of interest, using cross-validation to assess the optimal regularization parameter for each signal reconstruction. The use of cross-validation is critical in the L1 minimization problem, as the choice of the parameter is sensitive to the noise level, the number of samples, and the data sparsity. Third, we use a polynomial approach to accurately extract ODF maxima. Finally, we motivate and describe the choice of experimental parameters for the HARDI contest.

This work has been published in [26].

*6.1.1.4. Diffusion and Multiple Orientations from 1.5 MR Systems with Limited Gradient Tables*

**Participants:** Sylvain Merlet, Rachid Deriche, Kevin Whittingstall [Radiology department, Université de Sherbrooke, Québec, Canada], Maxime Descoteaux [Sherbrooke Connectivity Imaging Laboratory, Computer Science Departement, Université de Sherbrooke, Québec, Canada].

*This work has been performed within the framework of the Brain Connectivities Associate Team.*

Diffusion MRI (dMRI) enables the quantification of water diffusion, influenced by the structure of biological tissues, from the acquisition of diffusion weighted magnetic resonance images (DW-MRI). While recent advances enable to recover complex fiber geometries using diffusion measurements along various sampling schemes of high order, some older MR systems work with limited gradient tables (ex: maximum of 6 or 12 directions). These systems are designed for Diffusion Tensor Imaging (DTI). Several hospitals and research institutes in the world are limited by these fixed DTI gradient sets. Therefore, groups that want to perform state-of-the-art tractography using high angular resolution diffusion imaging (HARDI) data are penalized and can only perform DTI tractography on their old system. The Gaussian assumption of the tensor model, in DTI, is an over simplification of the diffusion phenomenon of water molecules in the brain and thus cannot resolve crossing fibers. In this work, we show that new diffusion signal modeling and processing techniques enable to capture complex angular structure of the diffusion process even from a reduced gradient direction set arising from an older MR system.

This work has been published in [27].

*6.1.1.5. A Robust variational approach for simultaneous smoothing and estimation of DTI*

**Participants:** Rachid Deriche, Meizhu Liu [Department of CISE, University of Florida, Gainesville, USA], Baba C. Vemuri [Department of CISE, University of Florida, Gainesville, USA].

Estimating diffusion tensors is an essential step in many applications — such as diffusion tensor image (DTI) registration, segmentation and fiber tractography. Most of the methods proposed in the literature for this task are not simultaneously statistically robust and feature preserving techniques. In this work, we propose a novel and robust variational framework for simultaneous smoothing and estimation of diffusion tensors from diffusion MRI. Our variational principle makes use of a recently introduced total Kullback–Leibler (tKL) divergence for DTI regularization. tKL is a statistically robust dissimilarity measure for diffusion tensors, and regularization by using tKL ensures the symmetric positive definiteness of tensors automatically. Further, the regularization is weighted by a non-local factor adapted from the conventional non-local means filters. Finally, for the data fidelity, we use the nonlinear least-squares term derived from the Stejskal–Tanner model. We present experimental results depicting the positive performance of our method in comparison to competing methods on synthetic and real data examples.

This work has been accepted for publication in NeuroImage [63].

### *6.1.2. Modeling in Diffusion MRI*

*6.1.2.1. Fast and Analytical EAP Approximation from a 4th Order Tensor*

**Participants:** Aurobrata Ghosh, Rachid Deriche.

*This work has been partly supported by the Association France Parkinson and the ANR NucleiPark project.*

Generalized Diffusion Tensor Imaging (GDTI) was developed to model complex Apparent Diffusivity Coefficient (ADC) using Higher Order Tensors (HOT) and to overcome the inherent single-peak shortcoming of DTI. However, the geometry of a complex ADC profile doesn't correspond to the underlying structure of fibers. This tissue geometry can be inferred from the shape of the Ensemble Average Propagator (EAP). Though interesting methods for estimating a positive ADC using 4th order diffusion tensors were developed, GDTI in general was overtaken by other approaches, e.g. the Orientation Distribution Function (ODF), since it is considerably difficult to recuperate the EAP from a HOT model of the ADC in GDTI. In this work, we present a novel closed-form approximation of the EAP using Hermite polynomials from a modified HOT model of the original GDTI-ADC. Since the solution is analytical, it is fast, differentiable, and the approximation converges well to the true EAP. This method also makes the effort of computing a positive ADC worthwhile, since now both the ADC and the EAP can be used and have closed forms. We demonstrate our approach with 4th order tensors on synthetic data and in vivo human data.

This work has been accepted for publication in the International Journal of Biomedical Imaging [54].

*6.1.2.2. A Polynomial Approach for Extracting the Extrema of a Spherical Function and its Application in Diffusion MRI*

**Participants:** Aurobrata Ghosh, Elias Tsigaridas [PolSys Project-Team, Inria, Paris Rocquencourt, France], Bernard Mourrain [Galaad Project-Team, Inria, Sophia Antipolis, Méditerranée, France], Rachid Deriche.

*This work has been partially supported by the ANR project NucleiPark and the France-Parkinson Association.*

Antipodally symmetric spherical functions play a pivotal role in diffusion MRI in representing sub-voxel-resolution microstructural information of the underlying tissue. This information is described by the geometry of the spherical function. In this work, we propose a method to automatically compute all the extrema of a spherical function. We then classify the extrema as maxima, minima and saddle-points to identify the maxima. We take advantage of the fact that a spherical function can be described equivalently in the spherical harmonic (SH) basis, in the symmetric tensor (ST) basis constrained to the sphere, and in the homogeneous polynomial (HP) basis constrained to the sphere. We extract the extrema of the spherical function by computing the stationary points of its constrained HP representation. Instead of using traditional optimization approaches, which are inherently local and require exhaustive search or re-initializations to locate multiple extrema, we use a novel polynomial system solver which analytically brackets all the extrema and refines them numerically, thus missing none and achieving high precision. To illustrate our approach we consider the Orientation Distribution Function (ODF). In diffusion MRI, the ODF is a spherical function which represents a state-of-the-art reconstruction algorithm whose maxima are aligned with the dominant fiber bundles. It is, therefore, vital to correctly compute these maxima to detect the fiber bundle directions. To demonstrate the po- tential

of the proposed polynomial approach we compute the extrema of the ODF to extract all its maxima. This polynomial approach is, however, not dependent on the ODF and the framework presented in this work can be applied to any spherical function described in either the SH basis, ST basis or the HP basis.

This work has been submitted to Medical Image Analysis and has been accepted for a publication to appear early 2013 [57].

*6.1.2.3. 4th Order Symmetric Tensors and Positive ADC Modelling*
**Participants:** Aurobrata Ghosh, Rachid Deriche.

High Order Cartesian Tensors (HOTs) were introduced in Generalized DTI (GDTI) to overcome the limitations of DTI. HOTs can model the apparent diffusion coefficient (ADC) with greater accuracy than DTI in regions with fiber heterogeneity. Although GDTI HOTs were designed to model positive diffusion, the straightforward least square (LS) estimation of HOTs doesn't guarantee positivity. In this work, we address the problem of estimating 4th order tensors with positive diffusion profiles. Two known methods exist that broach this problem, namely a Riemannian approach based on the algebra of 4th order tensors, and a polynomial approach based on Hilbert's theorem on non-negative ternary quartics. In this work, we review the technicalities of these two approaches, compare them theoretically to show their pros and cons, and compare them against the Euclidean LS estimation on synthetic, phantom and real data to motivate the relevance of the positive diffusion profile constraint.

This work is under submission.

*6.1.2.4. Higher-Order Tensors in Diffusion Imaging: A Survey*
**Participants:** Thomas Schultz [MPI for Intelligent Systems, Tubingen, Germany], Andrea Fuster [Eindhoven University of Technology, The Netherlands], Aurobrata Ghosh, Luc Florack [Eindhoven University of Technology, The Netherlands], Rachid Deriche, Lek-Heng Lim [University of Chicago, USA].

Diffusion imaging is a noninvasive tool for probing the microstructure of fibrous nerve and muscle tissue. Higher-order tensors provide a powerful mathematical language to model and analyze the large and complex data that is generated by its modern variants such as High Angular Resolution Diffusion Imaging (HARDI) or Diffusional Kurtosis Imaging. This survey gives a careful introduction to the foundations of higher-order tensor algebra, and explains how some concepts from linear algebra generalize to the higher-order case. From the application side, it reviews a variety of distinct higher-order tensor models that arise in the context of diffusion imaging, such as higher-order diffusion tensors, q-ball or fiber Orientation Distribution Functions (ODFs), and fourth-order covariance and kurtosis tensors. By bridging the gap between mathematical foundations and application, it provides an introduction that is suitable for practitioners and applied mathematicians alike, and propels the field by stimulating further exchange between the two.

This work has been submitted and is under review.

*6.1.2.5. Nonnegative Definite EAP and ODF Estimation via a Unified Multi-Shell HARDI Reconstruction*
**Participants:** Rachid Deriche, Jian Cheng [ATHENA and LIAMA, China], Tianzi Jiang [LIAMA, China].

*This work has been partly supported by the Association France Parkinson and the ANR NucleiPark project.*

In High Angular Resolution Diffusion Imaging (HARDI), Orientation Distribution Function (ODF) and Ensemble Average Propagator (EAP) are two important Probability Density Functions (PDFs) which reflect the water diffusion and fiber orientations. Spherical Polar Fourier Imaging (SPFI) is a recent model-free multi-shell HARDI method which estimates both EAP and ODF from the diffusion signals with multiple b values. As physical PDFs, ODFs and EAPs are nonnegative definite respectively in their domains $S2$ and $R3$. However, existing ODF / EAP estimation methods like SPFI seldom consider this natural constraint. Although some works considered the nonnegative constraint on the given discrete samples of ODF / EAP, the estimated ODF/EAP is not guaranteed to be nonnegative definite in the whole continuous domain. The Riemannian framework for ODFs and EAPs has been proposed via the square root parameterization based on pre-estimated ODFs and EAPs by other methods like SPFI. However, there is no work on how to estimate the square root of ODF/EAP called as the wavefuntion directly from diffusion signals. In this work, based on the Riemannian framework for ODFs / EAPs and Spherical Polar Fourier (SPF) basis representation, we propose

a unified model-free multi-shell HARDI method, named as Square Root Parameterized Estimation (SRPE), to simultaneously estimate both the wavefunction of EAPs and the nonnegative definite ODFs and EAPs from diffusion signals. The experiments on synthetic data and real data showed SRPE is more robust to noise and has better EAP reconstruction than SPFI, especially for EAP profiles at large radius.

This work has been published in [11] and [18].

*6.1.2.6. An Intrinsic Diffeomorphism Invariant Riemannian Framework for Probability Density Function Computing in diffusion MRI*

**Participants:** Rachid Deriche, Jian Cheng [ATHENA and LIAMA, China], Aurobrata Ghosh, Tianzi Jiang [LIAMA, China].

*This work has been partly supported by the Association France Parkinson and the ANR NucleiPark project.*

In High Angular Resolution Imaging (HARDI),Ensemble Average Propagator (EAP) and Orientation Distribution Function (ODF) are two important Probability Density Functions (PDFs), which describe the diffusion probability respectively in 3D space and along directions. Fisher information metric has been successfully applied in Diffusion Tensor Imaging (DTI) on tensor estimation, filtering, registration, statistical analysis, etc. However, to our knowledge, existing works in HARDI mainly focus on ODF/EAP estimation, not on ODF and EAP data processing. In this work, we propose a general state-of-the-art Riemannian framework as a mathematical tool to process such PDF data, by representing the square root of the PDF, called *wavefunction* based on quantum mechanics, as a linear combination of some orthonormal basis functions. The proposed Riemannian framework is showed to be a natural extension of previous Riemannian framework for tensors. We deduced the Riemannian metric for the PDF family via orthonormal basis representation, and proved the statistical manifold to be a convex subset of a high dimensional sphere. In this framework, the exponential map, logarithmic map and geodesic have closed forms, and the weighted Riemannian mean and median uniquely exist. Moreover, we generalized the Log-Euclidean framework and the Geodesic Anisotropy (GA) form tensors to ODFs/EAPs. The theoretical results can be applied to any general PDF data under any orthonormal basis representation. Furthermore we analyzed theoretically the similarities and differences between the Riemannian frameworks for EAPs, ODFs and for tensors, and demonstrated the proposed Riemannian metric is diffeomorphism invariant, which is the natural extension of the previous affine-invariant metric for tensors. Some potential applications were proposed via the Riemannian operations on the ODF/EAP field, such as anisotropy description via GA, nonnegative definite ODF/EAP estimation, interpolation, filtering, Principal Geodesic Analysis (PGA) and atlas estimation. The Riemannian framework and its applications were validated in synthetic, phantom and real data. The experiments demonstrated that the Riemannian framework is very useful for ODF/EAP computing, although the results from Riemannian metric and Euclidean metric are similar for ODFs but much different for EAPs.

This work has been published in [11]. A longer version has been submitted and is under revision for the journal IEEE transaction on Medical Imaging.

*6.1.2.7. Ensemble Average Propagator Reconstruction via Compressed Sensing: Discrete or Continuous Bases ?*

**Participants:** Sylvain Merlet, Michael Paquette [Sherbrooke Connectivity Imaging Laboratory, Computer Science Departement, Université de Sherbrooke, Québec, Canada], Rachid Deriche, Maxime Descoteaux [Sherbrooke Connectivity Imaging Laboratory, Computer Science Departement, Université de Sherbrooke, Québec, Canada].

*This work has been partly supported within the framework of the Brain Connectivities Associate Team.*

In this work, we propose to compare the sparsity of two classes of representations for the EAP : The discrete representations, via the Haar, Daubechies-Cohen-Fauveau (DCF) 5-3, DCF 9-7 wavelets bases, and the continuous representations, via Spherical Polar Fourier (SPF) and 3D-SHORE bases.

This work has been published in [28].

*6.1.2.8. Parametric dictionary learning for modeling EAP and ODF in diffusion MRI*

**Participants:** Sylvain Merlet, Emmanuel Caruyer, Rachid Deriche.

In this work, we propose an original and efficient approach to exploit the ability of Compressed Sensing (CS) to recover Diffusion MRI (dMRI) signals from a limited number of samples while efficiently recovering important diffusion features such as the Ensemble Average Propagator (EAP) and the Orientation Distribution Function (ODF). Some attempts to sparsely represent the diffusion signal have already been performed. However and contrarly to what has been presented in CS dMRI, in this work we propose and advocate the use of a well adapted learned dictionary and show that it leads to a sparser signal estimation as well as to an efficient reconstruction of very important diffusion features. We first propose to learn and design a sparse and parametric dictionary from a set of training diffusion data. Then, we propose a framework to analytically estimate in closed form two important diffusion features : the EAP and the ODF. Various experiments on synthetic, phantom and human brain data have been carried out and promising results with reduced number of atoms have been obtained on diffusion signal reconstruction, thus illustrating the added value of our method over state-of-the-art SHORE and SPF based approaches.

This work has been published in [25].

*6.1.2.9. Constrained Diffusion Kurtosis Imaging Using Ternary Quartics and MLE*

**Participants:** Tristan Milne [Queen's University, Kingston, Ontario, Canada], Aurobrata Ghosh, Rachid Deriche.

*This work has been partly supported by the Inria International Internship Program.*

We present a ternary quartic based approach with an improved gradient based optimization scheme for diffusion kurtosis imaging to estimate constrained and physically realistic diffusion and kurtosis tensors. We account for the signal noise by considering a maximum likelihood estimation based on the Rician noise model. Diffusion kurtosis imaging (DKI) is a recent important improvement over the diffusion tensor imaging (DTI) model that quantifies the degree of non-Gaussian diffusion in a tissue using a 3D 4th order tensor. However, DKI estimation needs to consider three constraints to be physically relevant. By adopting the implicit ternary quartic parameterization which allows to elegantly impose a positivity constraint on the kurtosis tensor and by employing gradient based optimization schemes, we show dramatically improved performance in terms of estimation time and quality. We derive the mathematical framework and show results on extensive synthetic data experiments.

This work has been published in [30]. A longer version has been submitted and is under revision for the journal Magnetic Resonance in Medicine.

### *6.1.3. From DW-MRI to Fiber Pathways and Microstructures Recovery*

*6.1.3.1. From Diffusion MRI to Brain Connectomics*

**Participants:** Aurobrata Ghosh, Rachid Deriche.

Diffusion MRI (dMRI) is a unique modality of MRI which allows one to indirectly examine the microstructure and integrity of the cerebral white matter in vivo and non-invasively. Its success lies in its capacity to reconstruct the axonal connectivity of the neurons, albeit at a coarser resolution, without having to operate on the patient, which can cause radical alterations to the patient's cognition. Thus dMRI is beginning to assume a central role in studying and diagnosing important pathologies of the cerebral white matter, such as Alzheimer's and Parkinson's diseases, as well as in studying its physical structure in vivo. In this work, we present an overview of the mathematical tools that form the framework of dMRI – from modelling the MRI signal and measuring diffusion properties, to reconstructing the axonal connectivity of the cerebral white matter, i.e., from Diffusion Weighted Images (DWIs) to the human connectome.

This work will be published in [55].

*6.1.3.2. Biomarkers for HARDI : 2nd & 4th Order Tensor Invariants*

**Participants:** Rachid Deriche, Aurobrata Ghosh, Théodore Papadopoulo.

*This work has been partly supported by the Association France Parkinson and the ANR NucleiPark project.*

In this paper, we explore the theory of tensor invariants as a mathematical framework for computing new biomarkers for HARDI. We present and explain the integrity basis, basic invariants and principal invariants of 2nd & 4th order tensors to expand on a recently proposed paper on 4th order tensor invariants. We present the mathematical results and compute the basic and principal invariants on a controlled synthetic dataset and an in vivo human dataset. We show how the integrity bases of these two sets of invariants can form a promising framework for developing new biomarkers for HARDI.

This work has been published in [22].

*6.1.3.3. Generalized Invariants of a 4th order tensor: Building blocks for new biomarkers in dMRI*

**Participants:** Aurobrata Ghosh, Théodore Papadopoulo, Rachid Deriche.

*This work has been partly supported by the Association France Parkinson and the ANR NucleiPark project.*

This paper presents a general and complete (up to degree 4) set of invariants of 3D 4th order tensors with respect to SO3. The invariants to SO3 for the 2nd order diffusion tensor are well known and play a crucial role in deriving important biomarkers for DTI, e.g. MD, FA, RA, etc. But DTI is limited in regions with fiber heterogeneity and DTI biomarkers severely lack specificity. 4th order tensors are both a natural extension to DTI and also form an alternate basis to spherical harmonics for spherical functions. This paper presents a systematic method for computing the SO3 invariants of 3D 4th order tensors, derives relationships between the new (generalized) invariants and existing invariants and shows results on synthetic and real data. It also presents, hitherto unknown, new invariants for 4th order tensors. Analogously to DTI, these new invariants can perhaps form building blocks for new biomarkers.

This work has been published in [23].

*6.1.3.4. Tractography via the Ensemble Average Propagator in diffusion MRI*

**Participants:** Sylvain Merlet, Anne-Charlotte Philippe, Rachid Deriche, Maxime Descoteaux [Sherbrooke Connectivity Imaging Laboratory, Computer Science Departement, Université de Sherbrooke, Québec, Canada].

*This work has been partly supported within the framework of the Brain Connectivities Associate Team.*

It's well known that in diffusion MRI (dMRI), fibre crossing is an important problem for most existing diffusion tensor imaging (DTI) based tractography algorithms. To overcome these limitations, High Angular Resolution Diffusion Imaging (HARDI) based tractography has been proposed with a particular emphasis on the the Orientation Distribution Function (ODF). In this work, we advocate the use of the Ensemble Average Propagator (EAP) instead of the ODF for tractography in dMRI and propose an original and efficient EAP-based tractography algorithm that outperforms the classical ODF-based tractography, in particular, in the regions that contain complex fibre crossing configurations. Various experimental results including synthetic, phantom and real data illustrate the potential of the approach and clearly show that our method is especially efficient to handle regions where fiber bundles are crossing, and still well handle other fiber bundle configurations such as U-shape and kissing fibers.

This work has been published in [29].

*6.1.3.5. Using Radial NMR Profiles to Characterize Pore Size Distributions*

**Participants:** Rachid Deriche, John Treilhard [Queen's University, Ontario, Canada].

*This work has been partly supported by the Inria International Internship Program.*

Extracting information about axon diameter distributions in the brain is a challenging task which provides useful information for medical purposes; for example, the ability to characterize and monitor axon diameters would be useful in diagnosing and investigating diseases like amyotrophic lateral sclerosis (ALS) or autism. In [78], three families of operators are defined, whose action upon an NMR attenuation signal extracts the moments of the pore size distribution of the ensemble under consideration; also a numerical method is proposed to continuously reconstruct a discretely sampled attenuation profile using the eigenfunctions of the simple harmonic oscillator Hamiltonian – the SHORE basis. The work we have performed here extends this method to other bases that can offer a better description of attenuation signal behaviour – in particular,

we proposed the use of the radial Spherical Polar Fourier (SPF) basis. Testing is performed to contrast the efficacy of the radial SPF basis and SHORE basis in practical attenuation signal reconstruction. The robustness of the method to additive noise is tested and analyzed. We demonstrated that a low-order attenuation signal reconstruction outperforms a higher-order reconstruction in subsequent moment estimation under noisy conditions. We proposed the simulated annealing algorithm for basis function scale parameter estimation. Finally, analytic expressions are derived and presented for the action of the operators on the radial SPF basis (obviating the need for numerical integration, thus avoiding a spectrum of possible sources of error).

This work has been published [20].

*6.1.3.6. Elliptic Fourier Features of Brain White Matter Pathways*
**Participants:** Rachid Deriche, Ali Demir [Sabancy University, TU], Gozde Unal [Sabancy University, TU].

Magnetic resonance imaging provides diffusion weighted images (DMRI), which non-invasively reconstruct the brain white matter pathways. DMRI is used to study brain white matter diseases as well as aid surgical planning. As localization of different white matter pathways surrounding a pathology is crucial for surgical planning, automatic extraction and classification of different anatomical white matter pathways pre-operatively becomes an important computational tool. In this work, we propose a method for classification of brain white matter pathways based on 3D elliptic Fourier descriptors, which are extended from the 2D elliptic Fourier descriptors. We performed experiments and validation of the proposed method on a white matter atlas space and on real pathological cases.

This work has been published [41].

## 6.2. Multi-Imaging Modalities

### *6.2.1. Coupling functional and structural models*

*6.2.1.1. A nested cortex parcellation combining analysis of MEG forward problem and diffusion MRI tractography*
**Participants:** Anne-Charlotte Philippe, Maureen Clerc, Théodore Papadopoulo, Rachid Deriche.

Understanding the relationship between structure and function is a major challenge in neuroscience. Diffusion MRI (dMRI) in the only non-invasive modality allowing to have access to the neural structure. Magnetoencephalography (MEG) is another non-invasive modality that allows a direct access to the temporal succession of cognitive processes. Functional cortex parcellation being one of the most important ways to understanding structure-function relationship, we propose an innovative method merging MEG and dMRI to parcellate the cortex. The combination of MEG forward problem and connectivity information reveals cortical areas generating a similar magnetic field at sensors while having a similar connectivity. Results show suitable clusters that forecast interesting studies for inter- and intra- subjects comparisons of the cortex parcellations. The automatic nested cortex parcellation we propose could be a first step to analyse sources that are seeds of long or short range connectivity and to differentiate these connectivities in the white matter

This work has been published in [31].

*6.2.1.2. dMRI tractography of WM fibers to recover the anatomical connectivity supporting a MEG epileptic network*
**Participants:** Anne-Charlotte Philippe, Maureen Clerc, Théodore Papadopoulo, Rachid Deriche.

Cerebral organization is determined by segregated and integrated regions both functionally and anatomically. These cerebral networks are the foundations of the execution of major part of cognitive processes. Information about the structure of the white matter (WM) and the functionality of networks are both needed to understand these cerebral networks.

This work proposes an efficient method to inform a given functional network on its anatomical support: how many anatomical connections exist between functionally connected regions and what are their geometries . Diffusion MRI being the only non invasive method allowing to have access to the micro-structure of the WM, we used diffusion information to underline the degree of connectivity between functionally connected regions while taking advantage of WM fibers reconstruction to determine the way taken by the anatomical network supporting the functional network.

Due to the complex dynamical alteration of epilepsy, the study of large-scale functional connectivity is difficult. But diffusion imaging studies have shown alterations of the WM between epileptic zones and connected areas. This methodology allows to add qualitative (degree of connectivity) and geometrical (WM fibers reconstruction) information on the anatomical network supporting an epileptic network mostly determined by magneto-encephalography (MEG).

This work has been published in [35].

*6.2.1.3. Whole cortex parcellation combining analysis of MEG forward problem, structural connectivity and Brodmann's atlas*

**Participants:** Anne-Charlotte Philippe, Maureen Clerc, Théodore Papadopoulo, Rachid Deriche.

Functional cortex parcellation is one of the most important ways to understand the link between structure and function in the brain. Brodmann's atlas remains a fundamental pillar to understand this relationship because its areas are defined by similar cytoarchitecture and functional imaging notably had revealed that they correspond, entirely or in part, to functional areas. So, its integration to diffusion MRI (dMRI) data is pertinent, dMRI being the only non invasive and in-vivo imaging modality able to have access to a detailed geometric description of the anatomical connectivity between brain areas. In this work, we propose to define a new connectivity profile of cortical sources based on the Brodmann's atlas. After its registration to T1 and diffusion weighted images of the same subject, we reconstructed the brain surfaces and considered the cortical sources to be the vertices of the white matter/ grey matter boundary mesh. We performed a probabilistic tractography taking each cortical sources as seeds and the L Brodmann's areas as L targets. Thus, we obtained the connectivity profile of a cortical source: a vector v of size L where v (l) is the degree of connectivity of the source to the l th Brodmann's area. Then, we developped a cortical parcellation method jointly analyzing the MEG forward problem and the connectivity profiles based on Brodmann's atlas of cortical sources. We computed the leadfield matrix that relates the sources to the MEG sensors. We applied a k-means algorithm to the leadfield matrix to cluster sources having a close magnetic field to the MEG sensors. Then, in each leadfield-based cluster, we clustered sources via their connectivity profile based on Brodmann's atlas. This automatic parcellation is an efficient preprocessing to compute a MEG inverse problem on functional data informed by its structural connectivity.

This work has been published in [32].

*6.2.1.4. Study of the brain connectivity in an Immersive Space*

**Participants:** Anne-Charlotte Philippe, Jean-Christophe Lombardo [Dream Project-Team, Inria, Sophia Antipolis, Méditerranée, France].

Virtual reality is a powerful tool for scientific visualization. When the amount and complexity of the visualized data grows, standard visualization applications on desktop computers become inefficient. In this work, we present the use of a CAVE like VR facility in a neuroscientific context. The aim is to have a better understanding of the brain connectivity. Both anatomical and functional data are attached to a mesh representing the brain surface.

Specific tools developed for this study and the way we used them are presented in [36] emphasizing drawbacks and advantages of virtual reality in a scientific visualization context.

This work has been published in [36].

*6.2.1.5. Cortex parcellation via diffusion data as prior knowledge for the MEG inverse problem*

**Participants:** Anne-Charlotte Philippe, Maureen Clerc, Théodore Papadopoulo, Rachid Deriche.

In this work, we present a new approach to the recovery of dipole magnitudes in a distributed source mo-del for magnetoencephalographic (MEG) imaging. This method consists in introducing prior knowledge regarding the anatomical connectivity in the brain to this ill-posed inverse problem. Thus, we perform cortex parcellation via structural information coming from diffusion MRI (dMRI), the only non-invasive modality allowing to have access to the structure of the WM tissues. Then, we constrain, in the MEG inverse problem, sources in the same diffusion parcel to have close magnitude values. Results of our method on MEG simulations are presented and favorably compared with classical source reconstruction methods.

This work is currently under submission.

*6.2.1.6. Fractality in the neuron axonal topography of the human brain based on 3-D diffusion MRI*

**Participants:** Panayotis Katsaloulis [Institute of Physical Chemistry "Demokritos" (IPC),National Center for Scientific Research "Demokritos", Greece], Aurobrata Ghosh, Anne-Charlotte Philippe, Astero Provata [Institute of Physical Chemistry "Demokritos" (IPC),National Center for Scientific Research "Demokritos", Greece], Rachid Deriche.

In this work, we conduct a group study, with 18 subjects, to validate the computational robustness of the fractal dimension of the neuron axonal topography in the human brain that is derived from diffusion MRI (dMRI) acquisitions. We extend the work done in a previous paper by some of the current authors where the fractal dimension of the neuron axonal topography from dMRI data was computed from 2-D regions of interest. The fractal dimensions Df of the entire 3-D volume of the brain is here estimated via the Box Counting, the Correlation DImension and the Fractal Mass Dimension methods. 3-D neuron axon data are obtained using tractography algorithms on Diffusion Tensor Imaging of the brain. We find that all three calculations of Df give consistent results across subjects, namely, they demonstrate fractal characteristics in the short and medium length scales: different fractal exponents prevail at different length scales, an indication of multifractality. We surmise that this complexity stems as a collective property emerging when many local brain units performing different functional tasks and having different local topologies are recorded together.

This work has been published in [15].

## 6.3. Forward and Inverse Problems

### *6.3.1. Source localization using rational approximation on plane sections*

**Participants:** Maureen Clerc, Théodore Papadopoulo, Juliette Leblond [Apics Project-Team, Inria, Sophia Antipolis, Méditerranée, France], Jean-Paul Marmorat [CMA, Ecole des Mines Paristech, Sophia Antipolis, France].

In functional neuroimaging, a crucial problem is to localize active sources within the brain non-invasively, from knowledge of electromagnetic measurements outside the head. Identification of point sources from boundary measurements is an ill-posed inverse problem. In the case of electroencephalography (EEG), measurements are only available at electrode positions, the number of sources is not known in advance and the medium within the head is inhomogeneous. This work presents a new method for EEG source localization, based on rational approximation techniques in the complex plane. The method is used in the context of a nested sphere head model, in combination with a cortical mapping procedure. Results on simulated data prove the applicability of the method in the context of realistic measurement configurations.

This work has been published in the journal Inverse Problems [14].

### *6.3.2. The adjoint method of OpenMEEG for EEG and MEG with large source space*

**Participants:** Maureen Clerc, Théodore Papadopoulo, Alexandre Gramfort [Telecom Paristech], Emmanuel Olivi [Forner member of the Athena Project-Team].

In EEG or MEG, a lead field is the linear operator which associates unitary dipolar sources to the resulting set of sensor measurements. In practise, the source space often includes over 10 000 dipoles, which sometimes causes memory problems. The adjoint approach considers the forward problem from the viewpoint of sensors instead of sources: this drops down the number of linear systems to solve by two orders of magnitude. The adjoint approach is here proposed in the context of the Boundary Element Method, and its implementation is provided by the OpenMEEG library.

This work was presented at the BIOMAG conference [38].

### 6.3.3. Comparison of Boundary Element and Finite Element Approaches to the EEG Forward Problem

**Participants:** Maureen Clerc, Carsten Wolters [Institute for Biomagnetism and Biosignal Analysis, University of Münster], Johannes Vorwerk [Institute for Biomagnetism and Biosignal Analysis, University of Münster], Martin Burger [Institut für Numerische und Angewandte Mathematik, Fachbereich Mathematik und Informatik, Westfälische Wilhelms Universität (WWU) Münster], Jan de Munck [Vrije Universiteit Medical Centre (VUMC), The Netherlands].

The accurate simulation of the electric fields evoked by neural activity is crucial for solving the inverse problem of EEG. Nowadays, boundary element methods (BEM) are frequently applied to achieve this goal, usually relying on the simpli-fication of approximating the human head by three nested compartments with isotropic conductivities (skin, skull, brain). Here, including the highly-conducting cerebrospinal fluid (CSF) is a difficult task due to the complex geometrical structure of the CSF, demanding a high number of additional nodes for an accurate modeling and thus a strongly increased computational effort. Though, CSF conductivity is well-known and nearly not varying inter-individually and its significant influence on EEG forward simulation has been shown. The CSF can be included at negligible computational costs when applying finite element (FE) forward approaches. In this study we compare the accuracy and performance of state-of-the-art BE and FE approaches in both artificial and realistic three layer head models, showing that all approaches lead to high numerical accuracies. Furthermore, we demonstrate the significant influence of modeling the CSF compartment as disregarding this compartment leads to model errors that lie clearly above the observed numerical errors.

A book chapter on BEM and FEM models has been published in the Handbook for Neural Activity Measurement [40]. The comparison was presented at the BIOMAG conference [19].

### 6.3.4. Domain Decomposition to handle versatile conductivity models

**Participants:** Maureen Clerc, Théodore Papadopoulo, Emmanuel Olivi [Forner member of the Athena Project-Team].

Source localization from external data such EEG or MEG, requires a good understanding of the electromagnetic behavior of the patient head. Several models can been used, representing more or less complex geometrical shapes, and conductivity profiles. Different numerical methods allow to cope with different types of models: the Finite Element Method (FEM) can handle very general conductivity models, whereas the Boundary Element Method (BEM) is limited to piecewise constant conductivity. On the other hand, it is easier with BEM than with FEM to accurately represent sources in isotropic media. Thanks to domain decomposition, we propose to solve a EEG forward problem using BEM where the sources are (the brain) and FEM for other tissues (with notably inhomogeneities in the skull).

This work was presented at the BIOMAG conference [37].

## 6.4. Brain Computer Interfaces

### 6.4.1. Combining ERD and ERS features to create a system-paced BCI

**Participants:** Maureen Clerc, Théodore Papadopoulo, Joan Fruitet, Eoin Thomas.

An important factor in the usability of a brain computer interface (BCI) is the setup and calibration time required for the interface to function accurately. Recently, brain-switches based on the rebound following motor imagery of a single limb effector have been investigated as basic BCIs due to their good performance with limited electrodes, and brief training session requirements. Here, a BCI is proposed which expands the methodology of brain-switches to design an interface composed of multiple brain-buttons. The algorithm is designed as a system paced interface which can recognise 2 intentional-control tasks and a no-control state based on the activity during and following motor imagery in only 3 electroencephalogram channels. An online experiment was performed over 6 subjects to validate the algorithm, and the results show that a working BCI can be trained from a single calibration session and that the post motor imagery features are both informative and robust over multiple sessions.

This work, which was partially presented at the EMBS conference [33], is currently under revision for the Journal of Neuroscience Methods.

### *6.4.2. Bandit algorithms for faster task selection in BCI*

**Participants:** Maureen Clerc, Joan Fruitet, Alexandra Carpentier [Sequel Project-Team, Inria Lille, France], Rémi Munos [Sequel Project-Team, Inria Lille, France].

BCIs based on sensorimotor rhythms use a variety of motor tasks, such as imagining moving the right or left hand, the feet or the tongue. Finding the tasks that yield best performance, specifically to each user, is a time consuming preliminary phase to a BCI experiment. This study presents a new adaptive procedure to automatically select, online, the most promising motor task for an asynchronous brain-controlled button.
We develop for this purpose an adaptive *Upper Confidence Bound* algorithm based on the stochastic bandit theory, and design an EEG experiment to test our method. We compare (offline) the adaptive algorithm to a naive selection strategy which uses uniformly distributed samples from each task. We also run the adaptive algorithm online to fully validate the approach.
By not wasting time on inefficient tasks, and focusing on the most promising ones, this algorithm results in a faster task selection and a more efficient use of the BCI training session. More precisely, the offline analysis reveals that the use of this algorithm can reduce the time needed to select the most appropriate task by almost half without loss in precision, or alternatively, allow to investigate twice the number of tasks within a similar time span. Online tests confirm that the method leads to an optimal task selection.
This study is the first one to optimize the task selection phase by an adaptive procedure. By increasing the number of tasks that can be tested in a given time span, the proposed method could contribute to reducing "BCI illiteracy".

This work is the result of the collaboration between Sequel and Athena within the ANR CoAdapt. It has been published in NIPS [21] and is accepted in the Journal of Neural Engineering [52].

### *6.4.3. An analysis of performance evaluation for motor-imagery based BCI*

**Participants:** Maureen Clerc, Matthew Dyson [Laboratoire de Neurosciences Cognitives, Aix-Marseille Université, France], Eoin Thomas.

In recent years, numerous brain computer interfaces (BCIs) have been proposed which incorporate features such as adaptive classification, error detection and correction, fusion with auxiliary signals and shared control capabilities. Due to the added complexity of such algorithms, the evaluation strategy and metrics used for analysis must be carefully chosen to accurately represent the performance of the BCI. In this article, metrics are reviewed and contrasted using both simulated examples and experimental data. Furthermore, a review of the recent literature is presented to determine how BCIs are evaluated, in particular focusing on the correlation between how the data are used relative to the BCI subcomponent under investigation. From the analysis performed in this study, valuable guidelines are presented regarding the choice of metrics and evaluation strategy dependent upon any chosen BCI paradigm.

This work was supported by the ANR Co-Adapt and is currently under revision for the Journal of Neural Engineering.

# 7. Partnerships and Cooperations

## 7.1. National Initiatives

### *7.1.1. ANR*

### *7.1.2. ANR ViMAGINE*

**Participants:** Maureen Clerc, Rachid Deriche, Alexandre Gramfort [Parietal project-team, ENST since september 2012], Emmanuel Olivi [Forner member of the Athena Project-Team], Théodore Papadopoulo, Anne-Charlotte Philippe.

**Duration:** *July 2008 to July 2013*

The partners of this project are Athena, the LENA (CHU Pitié-Salpétrière), and the Parietal project-team at Inria Futurs and Neurospin-Saclay.

This project takes a new challenge on the non invasive exploration of the Human visual system in vivo. Beyond the basic mechanisms of visual perception – which have already been investigated at multiple scales and through a large variety of modalities – we are primarily interested in proposing and exploring innovative solutions to the investigation of dynamic neural activations and interactions at the systems level. Bridging the elements involved in this endeavour requires that we are capable of observing, modelling and predicting the interplay between the anatomical/functional architecture of the brain systems and some identified timing properties of neural processes. The overall framework in which this project will be conducted is a federation of partners who will be bringing complementary expertise to this multidisciplinary research. The collaborators include experts in (1) electromagnetic and magnetic resonance brain imaging methods, (2) computational models of neural systems and (3) the neuroscience of vision. A central asset of our group is the easy access to state-of-the-art imaging platforms (e.g. high-density MEG and EEG arrays; 3T and 7T MR scanners) that will ensure the acquisition of quality experimental data.

### *7.1.3. ANR CO-ADAPT*

**Participants:** Maureen Clerc, Dieter Devlaminck, Joan Fruitet, Sebastian Hitziger, Théodore Papadopoulo, Eoin Thomas, Romain Trachel.

**Duration:** *December 2009 to December 2013*

The partners of this projects are the INSERM U821 laboratory of Bron, the "laboratoire de Neurologie de la cognition" UMR6155 CNRS of Marseille, The Inria Lille Sequel project-team and the "Laboratoire d'Analyse Topologie et Probabilités UMR6632/CNRS of Université de Provence, Marseille.

Brain Computer Interfaces (BCI) provide a direct communication channel from the brain to a computer, bypassing traditional interfaces such as keyboard or mouse, and also providing a feedback to the user, through a sensory modality (visual, auditory or haptic). A target application of BCI is to restore mobility or autonomy to severely disabled patients, but more generally BCI opens up many new opportunities for better understanding the brain at work, for enhancing Human Computer Interaction, and for developing new therapies for mental illnesses.

In BCI, new modes of perception and interaction come into play, and a new user must learn to operate a BCI, as an infant learns to explore his/her sensorimotor system. Central to BCI operation are the notions of feedback and of reward, which we believe should hold a more central position in BCI research.

The goal of this project is to study the co-adaptation between a user and a BCI system in the course of training and operation. The quality of the interface will be judged according to several criteria (reliability, learning curve, error correction, bit rate). BCI will be considered under a joint perspective: the user's and the system's. From the user's brain activity, features must be extracted, and translated into commands to drive the BCI system. Feature extraction from data, and classification issues, are very active research topics in BCI. However, additional markers may also be extracted to modulate the system's behavior. It is for instance possible to monitor the brain's reaction to the BCI outcome, compared to the user's expectations. This type of information we refer to as meta-data because it is not directly related to the command, and it may be qualitative rather than quantitative. To our knowledge, there is so far no BCI system that integrates such meta-data from the user's brain. From the point of view of the system, it is important to devise adaptive learning strategies, because the brain activity is not stable in time. How to adapt the features in the course of BCI operation is a difficult and important topic of research. A Machine Learning method known as Reinforcement Learning (RL) may prove very relevant to address the above questions. Indeed, it is an adaptive learning method that explicitly incorporates a reward signal, which may be qualitative (hence allowing meta-data integration). The aim of CO-ADAPT is to propose new directions for BCI design, by modeling explicitly the co-adaptation taking place between the user and the system (web site http://coadapt.inria.fr).

### *7.1.4. ANR NucleiPark*

**Participants:** Rachid Deriche, Aurobrata Ghosh, Anne-Charlotte Philippe, Emmanuel Caruyer, Jian Cheng.

**Duration:** *September 2009 to June 2013*

This project is about High field MR imaging (7T and 3T) of the brainstem, the deep nuclei and their connections in the parkinsonian syndromes with applications to prognosis, pathophysiology and improvement of therapeutic strategies. It involves three partners: The NeuroSpin team including C. Poupon and D. Le Bihan, the Inria with our project as well as the VISAGES project-team and the UPMC (University Pierre and Marie Curie, Paris) including INSERM U678 (H. Benali) and the CENIR (S. Lehericy).

The goal of the project is to find new neuroimaging markers of deep brain nuclei in neurodegenerative diseases that can be used for the diagnosis of Parkinsonian syndromes at the early stage. In addition, the goal is the characterization of lesions of deep brain structures and the detection of biomarkers of neuronal lesions in PD that can be related to clinical signs, such as gait disorders. Biomarkers of Parkinsonian syndromes could be used to create a diagnostic tool of the pathology and to correlate the identified markers with clinical signs. We will perform tractography of small fibre bundles using our HARDI techniques and Diffusion markers (anisotropy, apparent diffusion coefficient, fibre density, curvature, average diameter) will be collected along the reconstructed bundles.

Complementary parts of these objectives directly related to the acquisitions protocols have been accepted within the framework of another proposal submitted by the same partners and accepted for grant for two years (2009 & 2010) by the *France-Parkinson Association*

### *7.1.5. ANR MULTIMODEL*

**Participants:** Théodore Papadopoulo, Maureen Clerc, Sebastian Hitziger.

**Duration:** *December 2010 to March 2014*

The general objectives of the MULTIMODEL project are twofold:

- Develop computational models at the level of neuronal systems that will help interpreting neuroimaging data in terms of excitation-, inhibition- and synchronization-related processes.
- Acquire multimodal datasets, obtained in rats and humans under physiological and epileptogenic conditions, which will be used to develop the biophysical models and to test their face validity and predictability.

Specifically, during this 3-year project, the following questions will be dealt with:

- How can models be integrated in order to link data from different modalities (electro/magneto-encephalography, optical imaging, functional MRI)?
- What is the influence of hidden parameters on the observed signals (e.g. ratio of excitation/inhibition and synchronization degree across regions)?
- To what extent can biophysical modelling bring valuable insights on physiological and pathological brain activity ?

We will operate at the level of population of cell, i.e. at a scale compatible with the resolution of neuroimaging tools (at the level of the mm). A novel model structure will be investigated. It will include astrocytes at this "mesoscopic" level and will operate in networks of connected regions. Moreover, models in physiological and pathological conditions will be compared, which will be a step towards a better understanding of mechanisms underlying epileptic condition.

The MULTIMODEL project stems from a conjoint INSERM-Inria scientific initiative launched in December 2008 and ended in 2010. It involves 5 partners (Inserm U751 in Marseille, U678 in Paris, U836 in Grenoble, U642 in Rennes and Inria Athena project-team).

### *7.1.6. ADT MedInria-NT*

**Participants:** Jaime Garcia Guevara, Loïc Cadour, Théodore Papadopoulo, Maureen Clerc, Rachid Deriche.

**Duration:** *December 2010 to December 2012, prolongated to december 2014*

The goal of this technical project, funded by Inria for 2 years, is to introduce some tools developed at ATHENA into the medInria platform. There are basically two such facilities:

- Integrate the tools developed for the statistical characterization of brain white matter fiber bundles.
- Develop an interface for M/EEG data within MedInria. This will focus on two main goals:
  - Create a facility to read and visualize M/EEG signals.
  - Integrate M/EEG forward problem tools.

### *7.1.7. ADT OpenViBe-NT*

**Participants:** Théodore Papadopoulo, Maureen Clerc, Loïc Mahé.

**Duration:** *October 2012 to December 2014*

OpenViBE is an opensource software which development started in 2005 with th egoal of offering an open research tool for BCI and for supporting disabled people. Since its release in 2009, this software has received a lot of success (+10.000 downloads). But since 2005, new use have appeared as well as some limitations. The current software thus lacks of some features that limit its use, deployement and perenity. The goal of this ADT is to solve these problems, to improve and to extend OpenViBe One main goal is to improve the usability and the attractivity of the software and to retain a large community of users so as to ensure its sustainability. This ADT will allow to support the research made in four Inria teams (ATHENA, HYBRID, NEUROSYS and POTIOC) on hot topics such as adaptive or hybrid BCIs.

## 7.2. International Initiatives

### *7.2.1. Inria Associate Teams*

#### *7.2.1.1. BRAINCONNECTIVITIES*

Title: Fusing anatomical and functional connectivity information using diffusion MRI, MEG and EEG.

Inria principal investigator: Théodore Papadopoulo

International Partners (Institution - Laboratory - Researcher):

University of Québec, School of Higher Technology (Canada) - PhysNum Group, Centre de recherches mathématiques, Montréal - Jean-Marc Lina

University of Sherbrooke (Canada) - Departement d'Informatique - Maxime Descoteaux

Duration: 2012 - 2014

See also: http://brainconnectivities.inria.fr/wordpress/

Currently brain connectivity is studied through two different lenses: 1) Anatomical connectivity aims at recovering the "wires" that connect the various brain cortical "units", 2) Functional connectivity studies when and how cortical regions are connected. Providing tools to fuse these two complementary views is the central goal of this project. Our effort will focus on three imaging modalities: diffusion MRI (dMRI), Electroencephalography (EEG) and Magnetoencephalography (MEG). dMRI (jointly with traditional MRI) provides a detailed anatomical view of the brain. It allows the recovery of the fiber structure of the white matter: these are the electrical connexions between distant cortical areas. But dMRI does not provide any clue on: 1) on the actual use of connexions during brain activity, 2) on the way information propagates along time for a given task. On the opposite, EEG and MEG (jointly named MEEG) provide (after source reconstruction) time courses of the activity of the cortical areas. It is possible to recover some connectivity information from these time courses, but these are purely signal based and do not take account of the anatomy so there are multiple solutions that are sometimes difficult to discriminate. Furthermore source reconstructions are regularized with purely mathematical a priori taking only partially account of the actual brain structures. The main goals of this project are to provide tools: 1) To acquire diffusion data more efficiently, 2) To use the information of dMRI to define better models and regularization schemes for spatio-temporal MEEG source reconstruction, 3) To use MEEG data to better understand the task-dependent spatio-temporal structure of connectivity patterns.

### *7.2.2. Participation In International Programs*

*7.2.2.1. STIC-Algérie*

Title: Computational Diffusion MRI.

Inria principal investigator: Rachid Deriche

International Partners: Université des Sciences et des Technologies Houari Boumedienne (F. Boumghar, USTHB - Algiers) - Université de Boumerdes (D. Cherifi).

## 7.3. International Research Visitors

### *7.3.1. Visits of International Scientists*

In the framework of the BrainConnectivities associate team:

- Pr. Linda Boumghar from USTHB (Université des Sciences et Technologies Hourai Boumedienne, Algiers) visited Athena from Jan. 30 to February 4th, 2012.
- Maxime Descoteaux and Michael Paquette (USherbrooke) visited Athena on Sept. 24th for a week.
- Gabriel Girard (USherbrooke) visited Inria from Sept. 24th to Oct. 26th.
- Jean-Christophe Houde and Maxime Chamberland (USherbrooke) visited Athena October 8-9th.
- Jean-Marc Lina and Younes Zerouali (CRM) visited Athena from Nov. 26 to Dec. 2 with the goal of starting integrating cortical patch information developed at Athena into the source localisation method developed at CRM.

In the framework of the STIC-Algérie program:

- Pr. Linda Boumghar from USTHB (Université des Sciences et Technologies Hourai Boumedienne, Algiers) visited Athena from Jan. 30 to February 4th, 2012.
- Thinhinane Megherbi and Sihem Zeggout from USTHB (Université des Sciences et Technologies Houari Boumedienne, Algiers) visited Athena from May 17 to June 21th, 2012.

### *7.3.2. Internships*

Tristan Milne (from May 2012 until Aug 2012)

Subject: Constrained Diffusion Kurtosis Imaging Using Ternary Quartics and MLE

Institution: Queen's University, Kingston, Ontario (Canada)

# 8. Dissemination

## 8.1. Scientific Animation

- R. Deriche is Adj. Director at the Doctoral School EDSTIC (http://edstic.i3s.unice.fr/index.html)
- 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 Concil of AFRIF (Association Française pour la Reconnaissance et l'Interprétation des Formes) and of GRETSI (Groupe d'Etudes du Traitement du Signal et des Images).
- R. Deriche is Associate Editor of SIAM Journal on Imaging Sciences (SIIMS) and editorial board member at Springer for the book series entitled Computational Imaging and Vision.
- R. Deriche visited Athènes Univerity from May 20 to 27, 2012. This visit was performed within the framework of the exchange between Inria and Dept. Informatics, National University of Athens - (http://en.uoa.gr/ et http://www.di.uoa.gr/en/).

- R. Deriche gave a seminar (http://itmb.di.uoa.gr/research/res_seminEng.html) and a series of lectures on "Computational Brain Imaging" at University of Athens (http://en.uoa.gr) within the framework of the Master "Information Technologies in Medicine and Biology".
- R. Deriche gave an invited lecture at the "Biomedical Image Analysis Summer School" held in Paris from July 8 to 13, 2012.
- R. Deriche gave an invited talk at the Asilomar Conference on Signals, Systems, and Computers held November 4-7th, 2012.
- R. Deriche has served for many years as area-chair and/or as program committee member for International Conferences as ICCV, MICCAI, ECCV, CVPR, ISBI and national conferences as AFRIF-AFIA RFIA and serves several international journals and conferences (NeuroImage, IEEE Transactions on Medical Imaging, Magnetic Resonance in Medicine, JMIV, Medical Image Analysis Journal, ISBI, ISMRM, HBM..).
- R. Deriche has co-organised MICCAI 2012 Tutorial on Brain Connectivity Networks: Biology, Imaging and Beyond.
- R. Deriche has organised the "Computational diffusion MR imaging" session of the BASP: international biomedical and astronomical signal processing (BASP) Frontiers to be held in Villars-sur-Ollon (Jan. 27, Feb.1, 2013).
- M. Clerc serves on several local committees at Inria Sophia Antipolis: Bureau du Comité des Projets, MASTIC (diffusion) and Colloquium.
- M. Clerc is associated editor of Biomedical Engineering OnLine.
- M. Clerc serves on an evaluation committee for the ANR: “SIMI 3 - Matériels et logiciels pour les systèmes et les communications”.
- M. Clerc was on the organizing committee of the 18th International Conference on Biomagnetism, held in Paris, August 2012 (Biomag 2012). She also organized the mini-symposium on “dMRI, MEG & EEG fusion” at Biomag 2012.
- M. Clerc is a reviewer for conferences and journals (Biomedical Engineering OnLine, Human Brain Mapping, NeuroImage, Inverse Problems, Physics in Medicine iand Biology, IEEE Transations on Computational Intelligence and AI in Games, Computational and Mathematical Methods in Medicine, Paladyn. Journal of Behavioral Robotics).
- M. Clerc was invited to give a talk in the workshop Mouv’ organized by DEFISENS “mission interdisciplinarité du CNRS”.
- T. Papadopoulo served as a referee for the international conferences MICCAI 2012 and ISBI 2013. He is also area chair for the national conference GRETSI 2013. He is also in the program committe of ICVS 2013. In 2012, he has been reviewer for the journals Physics in Medicine and Biology. Image and Vision Computing, International Journal of Computer Vision, Annals of Biomedical Engineering, Clinical EEG & Neuroscience and SIAM Journal on Imaging Sciences.
- T. Papadopoulo has reviewed several ANR proposal.
- 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).
- T. Papadopoulo is a member of the local (Sophia Antipolis) committees for software development (CDT) and for Sustainable development. He is also member of the piloting committee for the platform dtk.
- T. Papadopoulo is the Athena contact for the ADT MedInria-NT and the ANR MULTIMODEL.

## 8.2. Teaching - Supervision - Juries

### *8.2.1. Teaching*

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

Master: R. Deriche, *Computational Vision and Image Processing* 18 ETD, 3rd year Engineering School, Institut TELECOM / TELECOM SudParis, Evry, France.

Master: R. Deriche, *Computational Brain Imaging* 15 ETD, M2 "Information Technologies in Medicine and Biology", University of Athens, Greece (http://en.uoa.gr).

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

Master: T. Papadopoulo, *3D Computer Vision*, 36 ETD, M2, SSTIM/VIM/MAM5 option at Polytechnic Engineering School, 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.

Doctorat: M. Clerc *Inverse Problems in Brain Imaging*, 6 ETD, OIPE Doctoral Course, Ghent University, Belgium.

### *8.2.2. Supervision*

PhD: Joan Fruitet, Interfaces Cerveau-Machines basées sur l'imagination de mouvements brefs: vers des boutons contrôlés par la pensée, University of Nice Sophia Antipolis, July 4th, 2012.

PhD: Emmanuel Caruyer, Q-Space Diffusion MRI, Acquisition and Signal Processing, University of Nice Sophia Antipolis, July 18th, 2012.

PhD: Jian Cheng, Estimation and Processing of Ensemble Average Propagator and Its Features in Diffusion MRI, University of Nice Sophia Antipolis, May 30th, 2012.

PhD in progress: Sylvain Merlet, Compressed Sensing & dMRI, September 2010, Advisor: Rachid Deriche.

PhD in progress: Anne-Charlotte Philippe, MEEG & dMRI, September 2010, Advisors: Maureen Clerc & Rachid Deriche

PhD in progress: Sebastian Hitziger, MEEG signal processing, November 2011, Advisors: Théodore Papadopoulo & Maureen Clerc

PhD in progress: Romain Trachel, Real Time analysis of Visual Attention, October 2010, Advisors: Thomas Brochier & Maureen Clerc

PhD in progress: Gabriel Girard, fMRI & dMRI, September 2012, Advisors: Rachid Deriche & Maxime Descoteaux (University of Sherbrooke, CA).

PhD in progress: Thinhinane Megherbi, HARDI & High Order Tensors, September 2011, Advisors: Rachid Deriche & L. Boumghar (USTHB, Algiers)

### *8.2.3. Internships*

Diana Ibanescu, "Inverse source reconstruction combining different sources of information", Master CBB, , from April 2nd to September 30th (Théodore Papadopoulo).

Laura Serron, "Perturbation methods in PDE to model electric conductivity inhomogeneities", from June 18th to September 17th (Maureen Clerc).

J. Treilhard, "Constrained Diffusion Kurtosis Imaging Using Ternary Quartics and MLE", Queen's University, Kingston (CA), from May to August 2012.

### *8.2.4. Juries*

- Rachid Deriche served in the following PhD Juries as President, reviewer or member (Xavier Desquenses, Greyc Lab., Caen; Perrine Bertrand, University Paul Sabatier, Toulouse, Z. Ikri, Polytechnic School, Algiers; M.K Rajagopa, Telecom SudParis, Evry, Catherine Herold, UMPC & Télécom ParisTech, Paris).
- Maureen Clerc served in the following PhD Juries as reviewer: Emilie Villaron, LATP Aix-Marseille University; Sandra Rousseau, University Joseph Fourier, Grenoble; Alexandre Barachant, University Joseph Fourier, Grenoble) and was in the PhD advisory committee of Margaux Perrin (Lyon University).
- T. Papadopoulo served in the following Ph.D. committees as reviewer (S. Sockeel, ), or member (J. Cheng, University of Nice-Sophia Antipolis and Institute of Automation, China and J. Fruitet, University of Nice-Sophia Antipolis).

## 8.3. Popularization

Maureen Clerc gave an invited talk at the “Art Science Pensée” conference in Mouans Sartoux, September 2012.

Maureen Clerc organized and participated in an event at Lycée Masséna, Nice, to promote scientific careers, for the 40th anniversary of women’s admission to Ecole Polytechnique (September 2012).

# 9. Bibliography

## Major publications by the team in recent years

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[2] R. DERICHE, J. CALDER, M. DESCOTEAUX. *Optimal Real-Time Q-Ball Imaging Using Regularized Kalman Filtering with Incremental Orientation Sets.*, in "Medical Image Analysis", August 2009, vol. 13, n$^{o}$ 4, p. 564–579, http://dx.doi.org/10.1016/j.media.2009.05.008.

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[5] A. GRAMFORT, T. PAPADOPOULO, E. OLIVI, M. CLERC. *OpenMEEG: opensource software for quasistatic bioelectromagnetics*, in "BioMedical Engineering OnLine", September 2010, vol. 9, n$^{o}$ 45, http://hal.inria.fr/inria-00523624.

[6] J. KYBIC, M. CLERC, T. ABBOUD, O. FAUGERAS, R. KERIVEN, T. PAPADOPOULO. *A Common Formalism for the Integral Formulations of the Forward EEG Problem*, in "IEEE Transactions on Medical Imaging", January 2005, vol. 24, p. 12–28, ftp://ftp-sop.inria.fr/odyssee/Publications/2005/kybic-clerc-etal:05.pdf.

[7] C. LENGLET, J. S. W. CAMPBELL, M. DESCOTEAUX, G. HARO, P. SAVADJIEV, D. WASSERMANN, A. ANWANDER, R. DERICHE, G. B. PIKE, G. SAPIRO, K. SIDDIQI, P. THOMPSON. *Mathematical Methods for Diffusion MRI Processing*, in "NeuroImage", March 2009, vol. 45, n$^{o}$ 1, p. S111-S122., ftp://ftp-sop.inria.fr/odyssee/Publications/2009/lenglet-campbell-etal:09.pdf.

[8] C. LENGLET, M. ROUSSON, R. DERICHE, O. FAUGERAS. *Statistics on the Manifold of Multivariate Normal Distributions: Theory and Application to Diffusion Tensor MRI Processing*, in "Journal of Mathematical Imaging and Vision", October 2006, vol. 25, n$^{o}$ 3, p. 423-444, ftp://ftp-sop.inria.fr/odyssee/Publications/2006/lenglet-rousson-etal:06.pdf.

[9] S. VALLAGHÉ, T. PAPADOPOULO. *A Trilinear Immersed Finite Element Method for Solving the Electroencephalography Forward Problem*, in "SIAM Journal on Scientific Computing", 2010, vol. 32, n$^{o}$ 4, p. 2379–2394 [*DOI :* 10.1137/09075038X], http://link.aip.org/link/?SCE/32/2379/1.

## Publications of the year

### Doctoral Dissertations and Habilitation Theses

[10] E. CARUYER. *Q-Space diffusion MRI: Acquisition and signal processing*, University of Nice Sophia Antipolis, July 2012, http://hal.inria.fr/tel-00750144.

[11] J. CHENG. *Estimation and Processing of Ensemble Average Propagator and Its Features in Diffusion MRI*, University of Nice Sophia Antipolis, May 2012, http://hal.inria.fr/tel-00759048.

[12] J. FRUITET. *Interfaces Cerveau-Machines basées sur l'imagination de mouvements brefs : vers des boutons contrôlés par la pensée*, University of Nice Sophia Antipolis, 2012.

### Articles in International Peer-Reviewed Journals

[13] E. CARUYER, R. DERICHE. *Diffusion MRI Signal Reconstruction with Continuity Constraint and Optimal Regularization*, in "Medical Image Analysis", August 2012, vol. 16, n$^{o}$ 6, p. 1113-1120, http://dx.doi.org/10.1016/j.media.2012.06.011.

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