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Project-Team Odyssée

Computer and biological vision

Sophia Antipolis - Méditerranée

Theme : Computational Medicine and Neurosciences

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2. Overall Objectives

2.1. Presentation

ODYSSÉE has been created in 2002. Until late 2008, ODYSSÉE focused on computational neuroscience and some of its applications to try to unveil the principles that govern the functioning of neurons and assemblies thereof, to understand the relations between the anatomy of the human brain and its functions and to bridge the gap between biological and computational vision. The research activity has been conducted in the following four main areas:

1. Modeling and simulating single and assemblies of neurons.
2. Measuring and modeling the human brain anatomical connectivity using Diffusion Magnetic Resonance Imaging (D-MRI).
3. Measuring and modeling the functioning of the human brain through its electrical activity using Magneto- and Electroencephalography (M/EEG).
4. Computational and biological vision.

Research within Axes 1 and 4 is now the main focus of the project-team NEUROMATCHCOMP while Research directions 2 and 3 have been the main focus of ODYSSÉE in 2009. Details about directions 1 and 4 are available in the NEUROMATCHCOMP scientific activity report.

The main objective of our research 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 CNS Imaging and in order to have an impact on this field, our research focusses mainly on the Anatomical and Functional Computational Imaging of the CNS with a particular emphasis on signal and image recording from Diffusion Magnetic Resonance Imaging (D-MRI), 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 make research on new models and computational tools to analyse CNS signals and imaging data with the goal of pushing forward the state-of-the-art to help address pressing and challenging clinical and neuroscience questions. This is our main objective within this research. This will help to better understand the architecture and function of the CNS and allow the development of biomarkers to better understand the progression of certain types of neurodegenerative diseases. Such an understanding will also help improving BCI systems with the above 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 will be 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.
- Building of a dense network of collaborations with national as well as international neuroimaging laboratories through which we will access equipment and data and with whom we will jointly contribute to solve common crucial problems of interest.
- Development of software packages that will be used in a first stage by our national and international collaborators and then made available to other partners.

2.2. Highlights

As of January 1st, 2009, the project-team NEUROMATHCOMP was created. Olivier Faugeras became the head of this new EPI and stepped down from being the head of ODYSSÉE while Rachid Deriche took over this responsibility.ODYSSÉE has been evaluated October, 7th to 9th. This process has occured during the evaluation of INRIA Computational Medicine and Neurosciences theme.

ODYSSÉE has been successful in obtaining the following new grants: ANR CO-ADAPT, ANR NUCLEIPARK, ADT Immersive BCI and Equipe Associée CD-MRI.

Three PhD students have successfully defended their thesis in 2009: J. Piovano [11], M. Péchaud [12] and A. Gramfort [10].

3. Scientific Foundations

3.1. Computational Diffusion MRI

DT-MRI Diffusion Tensor Magnetic Resonance Imaging is an MRI technique that allows one measuring in-vivo and in a non-invasise way the restricted diffusion of water molecule in a biological tissue. A tensor describes the 3D shape of diffusion.

HARDI High Angular Resolution Diffusion Imaging allows apparent diffusion coefficients to be measured along a large number of directions, poses no assumptions on the underlying diffusion process and is capable of detecting the presence of multiple diffusion directions within a single voxel.

QBI Q-Ball Imaging is a HARDI method that measures apparent diffusion coefficients along many directions distributed almost isotropically on the surface of a sphere.

ODF The Orientation Distribution Function describes the probability distribution for a water molecule to displace in a given direction.

Because the relationship between brain structure and brain function is fundamental to neuroscience, developing techniques that allow recovering the anatomical connectivity in the in vivo brain is of utmost importance and a major goal to achieve if one wants to understand how the brain works and acquire a better understanding of its mechanisms.

How to get information about the CNS anatomy, in particular, about cerebral and spinal cord white matter? Anatomical MRI permits to distinguish and classify grey matter, white matter and cerebrospinal fluid. However, with this contrast, white matter retains a homogeneous aspect, preventing any observation of neural fibers and thus of neuronal connectivity. Cerebral and spinal dissection used to be the only means of accessing the neural architecture [51], [56], [72]. Then, anatomists started using chemical markers for neuronography [67], [68]. More recently, neural fiber tractography based on local injection of chemical markers and subsequent observation of the induced propagation yielded high-quality connectivity mapping for the cat and monkey cerebral cortices [74], [68].

Diffusion Magnetic Resonance Imaging (D-MRI) is 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 [60], Merboldt et al [62] 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 D-MRI stems from its ability to accurately describe the geometry of the underlying microstructure and to probe the structure of the biological tissue at much smaller scales than the imaging resolution.

This drives our interest to develop new processing tools for DMRI. Because of the complexity of the data, this imaging modality raises a large amount of mathematical and computational challenges. We have therefore started by developing new 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 [9], [8] and [7]).

However, due to the limited current resolution of diffusion-weighted (DW) MRI, one third to two thirds of imaging voxels in the human brain white matter contain fiber crossing bundles. Therefore, it's also of utmost importance to tackle the problem of recovering fiber crossing and develop techniques that go beyond the limitations of diffusion tensor imaging (DTI). We are contributing towards these objectives and recent work deals with the development of local reconstruction methods, segmentation and tractography algorithms able to infer multiple fiber crossing from diffusion data. To do so, high angular resolution diffusion imaging (HARDI) is used to measure diffusion images along several directions. Q-ball imaging (QBI) is a recent such HARDI technique that reconstructs the diffusion orientation distribution function (ODF), a spherical function whose maxima are aligned with the underlying fiber directions at every voxel. QBI and the diffusion ODF play a central role in our work focused on the development of a robust and linear spherical harmonic estimation of the HARDI signal and on 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. They are at the core of our probabilistic and deterministic tractography algorithms devised to best exploit the full distribution of the fiber ODF (see [2], [3] and [4], [5]).

Overall, we are now able to show local reconstruction, segmentation and tracking results on complex fiber regions with known fiber crossing on simulated HARDI data, both on a biological phantom and on multiple human brain datasets. Most current DTI based methods neglect these complex fibers, which might lead to wrong interpretations of the brain anatomy and functioning.

In order to acquire a better understanding of the brain mechanisms and to improve the diagnosis of neurological disorders, we are also interested in the application of our tools to some neuroscience problems tackled within the framework of our collaborations with the Center for Magnetic Resonance Research of the University of Minnesota (Minneapolis), the STBB group leaded by P. Basser at NICHD (NIH, Bethesda), the centre IRMf of the hospital la Timone (Marseille), the Centre for Neuro Imaging Research (CENIR - Pitié-Salpêtrière - Paris), InserM U678 Faculté de Médecine Pierre et Marie Curie - Site Pitié-Salpétrière, the Max Planck Institute for Human Cognitive and Brain Sciences (Leipzig, Germany) and the Montreal Neurological Institute (McGill - Montréal, Canada).

3.2. Electrical and Magnetic Functional Brain Imaging

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 measures of the magnetic field generated by the electrophysiological activity of the brain have been done in 1968 at MIT by D. Cohen. Nowadays, EEG is relatively inexpensive and used routinely 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 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 hundreds of simultaneous 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). Contrarily to fMRI, which "only" measures an haemodynamic response linked to the metabolic demand, MEG and EEG also 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 hundreds of 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 Odyssée 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], [64] and means to calibrate them [71] 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 is currently being set up at Odyssée.

4. Software

4.1. Software for Diffusion MRI

Participants: Maxime Descoteaux [NeuroSpin, IFR 49 CEA Saclay and since July 2009 at Sherbrooke University, Quebec], Christophe Lenglet [CMRR, University of Minnesota], Demian Wassermann, Aurobrata Ghosh, Rachid Deriche.

The algorithms developed within the ODYSSÉE Project team and related to the Diffusion Tensor and Q-Ball imaging are all available upon request from the INRIA source forge (https://gforge.inria.fr) as an extension to the Brainvisa (http://brainvisa.info) software platform for visualization and analysis of multi-modality brain data. One can use all the estimation and visualization tools developed at ODYSSE, ranging from estimation, regularization, segmentation to Q-ball estimation, fiber ODF estimation and tractography algorithms.

Users of our software tools are from IRISA, VISAGES, Rennes (Barillot et al), from INSERM, Paris and Université de Montreal (H. Benali, J.C. Cohen-Adad et al), from Salpêtrière Hospital, Paris (S. Lehéricy, C.Delmaire, et al), from Toulouse (Landreau et al), from Eindhoven Technical University, CalTech in USA and other national and international sites.

The current software library comprising 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 languages, TCL and Python. Within the new software library, new visualization tools for Q-Ball images represented by spherical harmonic decomposition were developed.

This work allowed integration with the interactive medical imaging platforms MedINRIA and 3D Slicer QBallSlicer.

4.2. OpenMEEG

Participants: Maureen Clerc [correspondent], Alexandre Gramfort, Emmanuel Olivi, Théo Papadopoulo.

OpenMEEG provides state-of-the art software for processing EEG and MEG data. It incorporates a newly proposed, symmetric BEM for the forward problem, and a distributed source inverse problem, with three different types of regularizations, two of which are original, based on norms of the surface gradient of the source distribution. OpenMEEG is a free, open software written in C++, and can be accessed either through a command line interface or through a user-friendly interface. In 2009, OpenMEEG has been integrated into FieldTrip, a Matlab-environment package for EEG and MEG processing. http://www-sop.inria.fr/odyssee/software/OpenMEEG/

4.3. FindSources3D

Participants: Maureen Clerc, Juliette Leblond [correspondent].

FindSources3D is dedicated to the resolution of inverse problems of source detection and localization. It deals with pointwise measurements of the electric potential on a scalp modeled as a sphere, and considers a head model made of spherical layers with constant conductivities. It allows to approximately locate pointwise dipolar sources, in the brain from EEG measurements taken by electrodes on the scalp, or from numerical data. It uses the RARL2 software developped by APICS for the rational approximation step in plane sections. The data transmission preliminary step ("cortical mapping") is solved using the OpenMEEG symmetric BEM (see above). FindSources3D was developped in Matlab within the APICS team-project, in joint collaboration with Odyssée and Ecole des Mines.

4.4. EMBAL

Participants: Maureen Clerc, Alexandre Gramfort, Théo Papadopoulo.

EMBAL, initiated by Alexandre Gramfort during his PhD [10], is a Matlab library for solving the inverse problem involved in neuronal source localization using MEG and EEG. It includes MUSIC source localization, distributed inverse problems with ℓ_1, ℓ_2, Total Variation, spatio-temporal, and graph-cut based optimization.

5. New Results

5.1. Computational Diffusion MRI

This sub-theme is dedicated to describe the various contributions performed within the framework of Computational Diffusion MRI. We start by a work reviewing our contributions to Computational Diffusion MRI and continue by a description of our recent contributions connected to optimal D-MRI acquisition schemes. We then describe our main achievements on D-MRI modelling and algorithms and conclude with contributions related to brain and spinal cord applications.

5.1.1. Mathematical Methods for Diffusion MRI Processing

Participants: Rachid Deriche, Christophe Lenglet [CMRR, University of Minnesota], Maxime Descoteaux, Demian Wassermann, Peter Savadjiev [School of Computer Science, McGill University, Montreal Canada], Jennifer S. W. Campbell [School of Computer Science/McConnell Brain Imaging Center, McGill University, Montreal Canada], G. Bruce Pike [McConnell Brain Imaging Center, McGill University, Montreal Canada], Kaleem Siddiqi [School of Computer Science, McGill University, Montreal Canada], Alfred Anwander [Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany], Gloria Haro [Universitat Politecnica de Catalunya, Barcelona, Spain], Guillermo Sapiro [Department of Electrical and Computer Engineering, University of Minnesota, Minneapolis MN USA], Paul Thompson [LONI, University of California, Los Angeles CA, USA].

This work was partially supported by the ARC Diffusion MRI, the NSF/INRIA and the INRIA/FQRNT frameworks.

In [23], we review recent mathematical models and computational methods for the processing of diffusion Magnetic Resonance Images, including state-of-the-art reconstruction of diffusion models, cerebral white matter connectivity analysis, and segmentation techniques. We focus on Diffusion Tensor Images (DTI) and Q-Ball Images (QBI).

5.1.2. Optimal real-time Q-ball imaging using regularized Kalman filtering with incremental orientation sets

Participants: Rachid Deriche, Maxime Descoteaux [NeuroSpin, IFR 49 CEA Saclay and since July 2009 at Sherbrooke University, Quebec], Jeff Calder.

This work was partly supported by the INRIA ARC Diffusion MRI Program, the INRIA Internship Program, the Odyssée-EADS Grant Number 2118 and the Association France Parkinson for the NucleiPark project.

The acquisition and analysis of Diffusion MRI data is very challenging due to its complexity. Recently, an exciting new Kalman filtering framework has been proposed for DTI and QBI reconstructions in real-time during the repetition time (TR) of the acquisition sequence. In this work, we first revisit and thoroughly analyze this approach and show that it is actually sub-optimal and not recursively minimizing the intended criterion due to the Laplace–Beltrami regularization term. We therefore propose a new approach that implements the QBI reconstruction algorithm in real-time using a fast and robust Laplace–Beltrami regularization without sacrificing the optimality of the Kalman filter. We demonstrate that our method solves the correct minimization problem at each iteration and recursively provides the optimal QBI solution. We validate with real QBI data that our proposed real-time method is equivalent in terms of QBI estimation accuracy to the standard offline processing techniques and outperforms the existing solution. Last, we propose a fast algorithm to recursively compute gradient orientation sets whose partial subsets are almost uniform and show that it can also be applied to the problem of efficiently ordering an existing point-set of any size. This work enables a clinician to start an acquisition with just the minimum number of gradient directions and an initial estimate of the orientation distribution functions (ODF) and then the next gradient directions and ODF estimates can be recursively and optimally determined, allowing the acquisition to be stopped as soon as desired or at any iteration with the optimal ODF estimates. This opens new and interesting opportunities for real-time feedback for clinicians during an acquisition and also for researchers investigating into optimal diffusion orientation sets and real-time fiber tracking and connectivity mapping. This work has been published in [17], [33], [34].

5.1.3. Online orientation distribution function reconstruction in constant solid angle and its application to motion detection in high angular resolution diffusion imaging

Participants: Rachid Deriche, Emmanuel Caruyer, Iman Aganj [Department of Electrical and Computer Engineering, University of Minnesota], Christophe Lenglet [Department of Electrical and Computer Engineering, University of Minnesota], Guillermo Sapiro [Department of Electrical and Computer Engineering, University of Minnesota].

This work was partly supported by the CD-MRI Associated Team.

The diffusion orientation distribution function (ODF) can be reconstructed from q-ball imaging (QBI) to map the complex intravoxel structure of water diffusion. As acquisition time is particularly large for high angular resolution diffusion imaging (HARDI), fast estimation algorithms have recently been proposed, as an on-line feedback on the reconstruction accuracy. Thus the acquisition could be stopped or continued on demand. We adapt these real-time algorithms to the mathematically correct definition of ODF in constant solid angle (CSA), and develop a motion detection algorithm upon this reconstruction. Results of improved fiber crossing detection by CSA ODF are shown, and motion detection was implemented and tested in vivo.

This work has been published in [46].

5.1.4. Adaptive Design of Sampling Directions in Diffusion Tensor MRI and Validation on Human Brain Images

Participants: Rachid Deriche, Emmanuel Caruyer.

This work was partly supported by the CD-MRI Associated Team.

Diffusion tensor reconstruction is made possible through the acquisition of several diffusion weighted images, each corresponding to a given sampling direction in the Q-space. We address the question of sampling efficiency, and show that in case where we have some prior knowledge on the diffusion characteristics, we may be able to adapt the sampling directions for better reconstruction of the diffusion tensor. The prior is a tensor distribution function, estimated over a given region of interest, possibly on several subjects. We formulate an energy related to error on tensor reconstruction, and calculate analytical gradient expression for efficient minimization. We validate our approach on a set of 5199 tensors taken within the corpus callosum of the human brain, and show improvement by an order of 10% on the MSE of the reconstructed tensor.

This work has been published in [28].

5.1.5. NEX or no NEX? A high angular resolution diffusion imaging study

Participants: Rachid Deriche, Maxime Descoteaux [NeuroSpin, IFR 49 CEA Saclay and since July 2009 at Sherbrooke University, Quebec], Nicolas Wiest-Daessle [INRIA, Rennes], Christian Barillot [INRIA, Rennes], Sylvain Prima [INRIA, Rennes], Cyril Poupon [NeuroSpin, IFR 49 CEA Saclay].

This work was partly supported by the INRIA ARC Diffusion MRI Program, the INRIA Internship Program, the Odyssée-EADS Grant Number 2118 and the Association France Parkinson for the NucleiPark project.

To remove noise artifacts and enhance SNR, diffusion-weighted (DW) measurements are often repeated multiple times (NEX) along each gradient direction (typically, from 2 to 4 measurements) and each DW image is averaged. This averaging considerably increases acquisition time . It is also not clear what effects it produces on the reconstructed diffusion profiles such as the orientation distribution function (ODF) or fiber density orientation (FOD) function also called fiber ODF (fODF). In magnitude MRI, noise is Rician-distributed and is often conveniently approximated as Gaussian in high SNR regions. In the context of diffusion tensor imaging (DTI), recent attempts have been made to account for the Rician noise to regularize the DW data, to estimate the diffusion tensor, or to perform both tasks simultaneously. However, among the existing methods to estimate or to regularize ODF reconstructions from high angular resolution diffusion imaging (HARDI), the Rician noise bias has just started to be addressed but the impact on the reconstructed HARDI profiles such as the ODF and fODF have not been validated yet on real data. In particular, it is important to make sure that angular resolution of HARDI is not lost when removing Rician noise. In this work, the DW images are filtered with a specific Rician-based, structure-preserving, Non-Local Means method (NLMr), which recently showed to outperform other state-of-the-art methods to denoise DTI at low b-values. The filtering is applied on the raw DW images before estimating the HARDI profiles such as the ODF and the fODF. We show that multiple DW measurements and averaging can be avoided because NLMr filtering of the individual DW images can remove the Rician noise bias while preserving angular resolution. The method also produces better quality generalized fractional anisotropy (GFA) maps and more coherent ODF fields.

This work has been published in [36]

5.1.6. Deterministic and Probabilistic Tractography Based on Complex Fiber Orientation Distributions

Participants: Rachid Deriche, Maxime Descoteaux [NeuroSpin, IFR 49 CEA Saclay and since July 2009 at Sherbrooke University, Quebec], Alfred Anwander [Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany], Thomas Knoesche [Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany].

This work was partially supported by the CRSNG Canada graduate scholarship, PAI Procope and the Odyssée-EADS Grant Number 2118.

An integral concept for tractography is proposed to describe crossing and splitting fibre bundles based on the fibre orientation distribution function (ODF) estimated from high angular resolution diffusion imaging (HARDI). We show that in order to perform accurate probabilistic tractography, one needs to use a fibre ODF estimation and not the diffusion ODF. We use a new fibre ODF estimation obtained from a sharpening deconvolution transform (SDT) of the diffusion ODF reconstructed from q-ball imaging (QBI). This SDT provides new insight into the relationship between the HARDI signal, the diffusion ODF, and the fibre ODF. We demonstrate that the SDT agrees with classical spherical deconvolution and improves the angular resolution of QBI. Another important contribution of this work is the development of new deterministic and probabilistic tractography algorithms using the full multidirectional information obtained through fibre ODF. An extensive comparison study is performed on human brain datasets comparing our new deterministic and probabilistic tracking algorithms in complex fibre crossing regions. Finally, as an application of our new probabilistic tracking, we quantify the reconstruction of transcallosal fibres intersecting with the corona radiata and the superior longitudinal fasciculus in a group of 8 subjects. Most current DTI-based methods neglect these fibres, which might lead to incorrect interpretations of brain functions.

This work has been published in [19].

5.1.7. High Angular Resolution Diffusion MRI Segmentation Using Region-Based Statistical Surface Evolution

Participants: Rachid Deriche, Maxime Descoteaux [NeuroSpin, IFR 49 CEA Saclay and since July 2009 at Sherbrooke University, Quebec].

This work was partially supported by the CRSNG Canada graduate scholarship, PAI Procope and the Odyssée-EADS Grant Number 2118.

We develop a new method to segment high angular resolution diffusion imaging (HARDI) data. We first estimate the orientation distribution function (ODF) using a fast and robust spherical harmonic (SH) method. Then, we use a region-based statistical surface evolution on this image of ODFs to efficiently find coherent white matter fiber bundles. We show that our method is appropriate to propagate through regions of fiber crossings and show that our results outperform state-of-the-art diffusion tensor (DT) imaging segmentation methods, inherently limited by the DT model. Results obtained on synthetic data, on a biological phantom, on real datasets and on all 13 subjects of a public NMR database show that our method is reproducible, automatic and brings a strong added value to diffusion MRI segmentation.

This work has been published in [18].

5.1.8. Diffusion propagator imaging: using Laplace's equation and multiple shell acquisitions to reconstruct the diffusion propagator.

Participants: Rachid Deriche, Maxime Descoteaux [NeuroSpin, IFR 49 CEA Saclay and since July 2009 at Sherbrooke University, Quebec], Denis Le-Bihan [NeuroSpin, IFR 49 CEA Saclay], Jean-François Mangin [NeuroSpin, IFR 49 CEA Saclay], Cyril Poupon [NeuroSpin, IFR 49 CEA Saclay].

This work was partly supported by the INRIA ARC Diffusion MRI Program, the Odyssée-EADS Grant Number 2118 and the Association France Parkinson for the NucleiPark project.

Many recent single-shell high angular resolution diffusion imaging reconstruction techniques have been introduced to reconstruct orientation distribution functions (ODF) that only capture angular information contained in the diffusion process of water molecules. By also considering the radial part of the diffusion signal, the reconstruction of the ensemble average diffusion propagator (EAP) of water molecules can provide much richer information about complex tissue microstructure than the ODF. In this work, we present diffusion propagator imaging (DPI), a novel technique to reconstruct the EAP from multiple shell acquisitions. The DPI solution is analytical and linear as based upon the Laplace equation modeling of the diffusion signal. DPI is validated with ex vivo phantoms and also illustrated on an in vivo human brain dataset. DPI is shown to reconstruct EAP from only two b-value shells and approximately 100 diffusion measurements.

This work has been published in [35].

5.1.9. A Riemannian Framework for Orientation Distribution Function Computing.

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

We propose a state of the art Riemannian framework for Orientation Distribution Function (ODF) computing based on Information Geometry and sparse representation of orthonormal bases. In this Riemannian framework, the exponential map, logarithmic map and geodesic have closed forms and the weighted Frechet mean exists uniquely on this manifold. We also propose a novel scalar measurement, named Geometric Anisotropy (GA), which is the Riemannian geodesic distance between the ODF and the isotropic ODF. The Renyi entropy H1 2 of the ODF can be computed from the GA. Moreover, we propose an Affine-Euclidean framework and a Log-Euclidean framework so that we can work in an Euclidean space. As an application, Lagrange interpolation on ODF field is proposed based upon the weighted Frechet mean. We validate our methods on synthetic and real data experiments. Compared with existing Riemannian frameworks on ODF, our framework is model-free. The estimation of the parameters, i.e. Riemannian coordinates, is robust and linear. Moreover it should be noted that our theoretical results can be used for any probability density function (PDF) under an orthonormal basis representation.

This work has been published in [29].

5.1.10. A polynomial based approach to extract the maxima of an antipodally symmetric spherical function and its application to extract fiber directions from the Orientation Distribution Function in Diffusion MRI

Participants: Rachid Deriche, Maxime Descoteaux [NeuroSpin, IFR 49 CEA Saclay and since July 2009 at Sherbrooke University, Quebec], Aurobrata Ghosh, Elias Tsigaridas [Galaad Project Team, INRIA Sophia Antipolis, Méditerranée], Bernard Mourrain [Galaad Project Team, INRIA Sophia Antipolis, Méditerranée], Pierre Comon [I3S, Nice University/CNRS].

This work was partially supported by the ARC Diffusion MRI and the ANR-06-BLAN-0074 "Decotes" contracts.

We extract the geometric characteristics from an antipodally symmetric spherical function (ASSF), which 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. All three bases span the same vector space and are bijective when the rank of the SH series equals the order of the ST and equals the degree of the HP. We show, therefore, how it is possible to extract the maxima and minima of an ASSF by computing the stationary points of a constrained HP. In Diffusion MRI, the Orientation Distribution Function (ODF), represents a state of the art reconstruction method whose maxima are aligned with the dominant fiber bundles. Therefore, it is important to be able to correctly estimate these maxima to detect the fiber directions. The ODF is an ASSF. To illustrate the potential of our method, we take up the example of the ODF, and extract its maxima to detect the fiber directions. Thanks to our method we are able to extract the maxima without limiting our search to a discrete set of values on the sphere, but by searching the maxima of a continuous function. Our method is also general, not dependent on the ODF, and the framework we present can be applied to any ASSF described in one of the three bases. This work has been published in [54] while

the work published in [38] presents its experimental validation on synthetic, phantom, and real data, and its comparaison to an existing discrete *mesh-search* approach. It is shown how this approach naturally overcomes the inherent shortcomings of the discrete search. Finally, although, the approach is demonstrated on the ODF, it can be equally applied to any spherical function.

5.1.11. Ternay Quartic Approach for Positive 4th Order Diffusion Tensors Revisited

Participants: Rachid Deriche, Aurobrata Ghosh, Maher Moakher [ENIT, Tunis].

In Diffusion Magnetic Resonance Imaging (D-MRI), the 2nd order diffusion tensor has given rise to a widely used tool – Diffusion Tensor Imaging (DTI). However, it is known that DTI is limited to a single prominent diffusion direction and is inaccurate in regions of complex fiber structures such as crossings. Various other approaches have been introduced to recover such complex tissue micro-geometries, one of which is Higher Order Cartesian Tensors. Estimating a positive diffusion function has also been emphasised mathematically, since diffusion is a physical quantity. Recently, there have been efforts to estimate 4th order diffusion tensors from Diffusion Weighted Images (DWIs), which are capable of describing crossing configurations with the added property of a positive diffusion function. We take up one such, the Ternary Quartic approach, and reformulate the estimation equation to facilitate the estimation of the non-negative 4th order diffusion tensor. With our modified approach we test on synthetic, phantom and real data and confirm previous results.

This work has been published in [37].

5.1.12. Unsupervised White Matter Fiber Clustering and Tract Probability Map Generation: Applications of a Gaussian Process framework for white matter fibers

Participants: Rachid Deriche, Demian Wassermann, Luc Bloy [Section of Biomedical Image Analysis Department of Radiology University of Pennsylvania], Efstathios Kanterakis [Section of Biomedical Image Analysis Department of Radiology University of Pennsylvania], Ragini Verma [Section of Biomedical Image Analysis Department of Radiology University of Pennsylvania].

With the increasing importance of fiber tracking in diffusion tensor images for clinical needs, there has been a growing demand for an objective mathematical framework to perform quantitative analysis of white matter fiber bundles incorporating their underlying physical significance. This work presents such a novel mathematical framework that facilitates mathematical operations between tracts using an inner product based on Gaussian processes, between fibers which span a metric space. This metric facilitates combination of fiber tracts, rendering operations like tract membership to a bundle or bundle similarity simple. Based on this framework, we have designed an automated unsupervised atlas-based clustering method that does not require manual initialization nor an a priori knowledge of the number of clusters. Quantitative analysis can now be performed on the clustered tract volumes across subjects thereby avoiding the need for point parametrization of these fibers, or the use of medial or envelope representations as in previous work. Experiments on synthetic data are provided and the applicability of the unsupervised clustering framework is also demonstrated on a 21 subject dataset.

This work has been published in [47], [41], [42].

5.1.13. Evaluation of q-ball metrics for assessing the integrity of the injured spinal cord

Participants: Rachid Deriche, Demian Wassermann, Aurobrata Ghosh, Julien Cohen-Adad [Athinoula A. Martinos Center for Biomedical Imaging, MGH, Harvard Medical School], Hugues Leblond [Laboratoire d'Imagerie Fonctionnelle, INSERM U678, Faculté de Médecine, Univ Paris 6 / Hôpital Pitié-Salpêtrière], Habib Benali [Laboratoire d'Imagerie Fonctionnelle, INSERM U678, Faculté de Médecine, Univ Paris 6 / Hôpital Pitié-Salpêtrière], Serge Rossignol [Groupe de recherche sur le Système Nerveux Central, Département de Physiologie, Université de Montréal].

This work was partially supported by the ARC Diffusion MRI.

Assessment of spinal cord integrity following injury is crucial for evaluating the potential for functional rehabilitation. Previous studies showed the benefits of diffusion tensor imaging (DTI) for the non-invasive characterization of the healthy and injured spinal cord. However, biases related to the incapability of DTI to represent complex diffusion profiles suggested the use of less constraining techniques. Recently, we demonstrated that q-ball imaging (QBI) is capable of partly solving fiber crossing information in the intact spinal cord. In this study, we extended the application of QBI in a model of cat partial spinal cord injury and we compared various QBI quantitative metrics to the ones used in DTI. We also proposed an original QBI-based metric to quantify the homogeneity of diffusion directions.

This work has been published in [31].

5.1.14. Comparison of DTI and Q-Ball imaging metrics in a cat model of spinal cord injury

Participants: Rachid Deriche, Aurobrata Ghosh, Maxime Descoteaux [NeuroSpin, IFR 49 CEA Saclay and since July 2009 at Sherbrooke University, Quebec], Julien Cohen-Adad [Athinoula A. Martinos Center for Biomedical Imaging, MGH, Harvard Medical School], Hugues Leblond [Laboratoire d'Imagerie Fonctionnelle, INSERM U678, Faculté de Médecine, Univ Paris 6 / Hôpital Pitié-Salpêtrière], Habib Benali [Laboratoire d'Imagerie Fonctionnelle, INSERM U678, Faculté de Médecine, Univ Paris 6 / Hôpital Pitié-Salpêtrière], Serge Rossignol [Groupe de recherche sur le Système Nerveux Central, Département de Physiologie, Université de Montréal].

This work was partially supported by the ARC Diffusion MRI.

Following spinal cord injury, functional outcome is highly dependent on the presence of spared tracts. Therefore, it is crucial to be able to assess white matter integrity in the spinal cord non invasively. Diffusion tensor imaging (DTI) is a means to quantify water diffusion properties, providing various markers of white matter abnormality. However, DTI is limited in complex diffusion profiles and other reconstruction methods such as q-ball imaging (QBI) were shown to be more appropriate in the spinal cord. It was recently shown that metrics derived from higher order tensors may provide useful information in an ex vivo rat model of spinal cord injury. In this study, we investigate what would be the most sensitive marker using an in vivo cat model of partial spinal cord injury, based on DTI and QBI metrics.

This work has been published in [30].

5.1.15. Diffusion Abnormalities in the Primary Sensorimotor Pathways in Writer's Cramp

Participants: Rachid Deriche, Maxime Descoteaux [NeuroSpin, IFR 49 CEA Saclay and since July 2009 at Sherbrooke University, Quebec], Demian Wassermann, Christophe Lenglet [CMRR, University of Minnesota], Christine Delmaire [CENIR, CHUPS, Paris], Marie Vidailhet [UPMC, Paris 6, INSERM U679], Stéphane Lehéricy [CENIR, CHUPS, Paris].

This work was partially supported by the ARC Diffusion MRI.

Writer's cramp is a task-specific form of primary dystonia that occurs in patients having a long history of repetitive, stereotyped, overlearned writing movements before the onset of dystonia. Structural imaging studies have shown the involvement of the sensorimotor circuit in dystonia. Early morphological imaging studies in stroke patients reported that dystonia was observed after damage in several subcortical areas including the basal ganglia, the thalamus, and less often the cerebellum, suggesting a role of the basal ganglia in dystonia. A common hypothesis to explain to pathophysiology of dystonia is that defects in the basal ganglia and particularly the indirect pathway result in impaired suppression of unwanted excessive muscle activity that is observed in dystonia. Subsequently, progress in image analysis methods, such as voxel-based statistical comparisons in grey matter density, allowed the detection of structural changes in primary dystonia. Changes in grey matter density were reported in writer's cramp in the basal ganglia, as well as the sensorimotor cortex, the thalamus, and the cerebellum. Using similar imaging approaches, grey matter changes were detected in other forms of primary dystonia. These observations suggest that writer's cramp may be associated not only with the dysfunction of the basal ganglia but also of several brain structures interconnected within the sensorimotor network. In white matter, water diffusion is directionally dependent, predominantly along the direction of axons. This property can be quantified using various objective measures, the most popular being

fractional anisotropy (FA). FA which can be computed using region-of- interest measurements or tractography or voxel-wise measurements, and quantifies diffusion anisotropy within a voxel. From DTI images, axonal orientation within each voxel can be estimated based on its alignment with the direction of fast diffusion. Then, by subsequently relating the predominant diffusion orientation among neighboring voxels, three dimensional pathways macroscopically representing axonal bundles can be obtained by the technique called tractograpy. Using DTI, changes in FA were reported in the subcortical white matter of the sensorimotor cortex in DYT1 carriers. Therefore, diffusion abnormalities may involve fibers connecting the sensorimotor cortex with subcortical structures. In this work, we combined voxel-wise cross-subject statistics and tractography to test this hypothesis and evaluate white matter pathology in writer's cramp disease patients.

This work has been published in [15].

5.1.16. Straightening the Spinal Cord using Fiber Tractography

Participants: Rachid Deriche, Demian Wassermann, Julien Cohen-Adad [Athinoula A. Martinos Center for Biomedical Imaging, MGH, Harvard Medical School], Stephane Lehéricy [Laboratoire d'Imagerie Fonctionnelle, INSERM U678, Faculté de Médecine, Univ Paris 6 / Hôpital Pitié-Salpêtrière], Habib Benali [Laboratoire d'Imagerie Fonctionnelle, INSERM U678, Faculté de Médecine, Univ Paris 6 / Hôpital Pitié-Salpêtrière], Serge Rossignol [Groupe de recherche sur le Système Nerveux Central, Département de Physiologie, Université de Montréal].

Spinal Cord MRI (SC-MRI) is a challenging research field with numerous important clinical and basic research applications. Some of the SC-MRI applications strongly need to deal with a well straightened spinal cord either for appropriate methodological developments, for better visualization or diagnostic purposes. In this work, we develop an efficient and automatic method to straighten the spinal cord image and fibres. Diffusion Tensor MRI is first used to recover by tractography the bundles of fibres related to the spinal cord. An efficient Gaussian process framework is then used to automatically recover in a robust way the most representative fibre which is used to interpolate and straighten the spinal cord image and fibres. Our method is successfully tested on real images of one cat with partial spinal cord injury and two healthy volunteers. This capability to reliably reconstruct straightened animal and human spinal cord opens new opportunities for SC-MRI applications. This work is under submission.

5.2. Brain functional imaging using MEG/EEG

The work depicted in this sub-theme concerns various aspects related to the problem of estimating the sources in the brain corresponding to some given activity. Besides the forward and inverse EEG/MEG problems (see sections 5.2.1 and 5.2.3) which are directly connected to this problem, there are a number of additional problems such as finding the events of interest in the recorded signal (section 5.2.2). Some of the tools described in this sub-theme are distributed in the opensource library OpenMEEG (see section 4.2).

5.2.1. Inverse problems of MEG and EEG

Participants: Maureen Clerc, Alexandre Gramfort, Kaushik Majumdar, Théo Papadopoulo, Juliette Leblond [APICS project-team], Jean-Paul Marmorat [APICS project-team], Meriem Zghal [APICS project-team].

This work was partially supported by the Fondation d'Entreprise EADS and by the ANR ViMAGINE grant.

Investigating on brain activity with EEG or MEG measurements requires the solution of ill-posed inverse problems, whose solution implies regularization. Source models for EEG and MEG can be either distributed dipoles or isolated dipoles. In distributed models, the relationship between sources and measurements is linear, but the problem is undercontrained because thousands of putative positions for the cortical activity must be handled at the same time. In isolated dipole models, on the contrary, there are less unknowns than measurements, but the relationship between sources and measurements is more complex.

Their work on rational approximation has allowed researchers from the APICS project-team to propose an original method for source localization, when the sources are modeled as isolated dipoles. The force of the method is to provide a good and stable estimation of the number of sources and of their positions and moments. It requires the knowledge of the potential on the inner skull surface, provided by a Cortical Mapping method developed at Odyssée [49]. Cortical Mapping and rational approximation techniques are now being combined, leading to a dipolar source localization directly from scalp electrode measurements [48].

We are involved in an ANR grant on Multimodal Neuroimaging of Rapid Brain Processes in the Human Visual System (ViMAGINE). An initial step in the exploration of the Human Visual System has been to perform retinotopy, i.e. determine the subject-dependent mapping linking positions in the visual field to the positions of the associated activity in the low-level visual cortex [50]. Since brain activity is not static, but varies in time, the regularization of the inverse problem should take time into account. A new approach has been proposed to track cortical activity with spatio-temporal constraints, and its implementation uses graph-cuts for computational efficiency [55], [10]. This spatio-temporal regularization is a post-processing which is applied to a minimum-norm inverse problem. Another kind of minimum-norm processing takes into account a statistical measure of phase-synchronization between sources [25].

The regularization of the M/EEG inverse problem involves the choice of a norm. In addition to spatio-temporal regularization, we have also studied regularization that incorporates different experimental conditions. For this a mixed L2-L1-L2 norm has been proposed, with the sparsity-inducing L1 norm applied across conditions [39], [44].

5.2.2. Single trial analysis of brain signals

Participants: Maureen Clerc, Théo Papadopoulo, Jean Le Pavec, Joan Fruitet, Alexandre Gramfort, Christian Bénar [INSERM U751], Bruno Torrésani [LATP, CMI, Université de Provence].

This work was partially supported by the Fondation d'Entreprise EADS and by the ANR ViMAGINE grant.

Extracting information from multi-trial MEG or EEG recordings is challenging because of the very low signal-to-noise ratio (SNR), and because of the inherent variability of brain responses. The problem of low SNR is commonly tackled by averaging multiple repetitions of the recordings, also called trials, but the variability of response across trials leads to biased results and limits interpretability.

In the signal processing literature, there is a growing interest in sparse representations, using the matching pursuit algorithm, which iteratively subtracts from the signal its projection on atoms selected from a dictionary. So far, most approaches have assumed a stable pattern across channels or trials, even though cross-trial variability is often observed in brain signals. We have adapted Matching Pursuit for brain signals with cross-trial variability in all their characteristics (time, frequency, number of oscillations). The originality of our approach is to select each atom using a voting technique that is robust to variability, and to subtract it by adapting the parameters to each trial. Because it is designed to handle inter-trial variability using a voting technique, the method is called Consensus Matching Pursuit (CMP) [14].

We have also explored a data-driven way of decoding the variability of neural responses, which makes use of graph representations. Our approach has several advantages compared to other existing methods: first, it avoids the a priori definition of a model for the waveform of the neural response, second, it does not make use of the average data for parameter estimation, third, it does not suffer from initialisation problems by providing solutions that are global optimum of cost functions, and last, it is fast. We proceed in two steps. First, a manifold learning algorithm based on a graph Laplacian offers an efficient way of ordering trials with respect to the response variability, under the condition that this variability itself depends on a single parameter. Second, the estimation of the variability is formulated as a combinatorial optimization that can be solved very efficiently using graph cuts. We have applied this method to the problem of latency estimation, on P300 oddball experiments [22].

We are starting to explore the use of EEG for Brain Computer Interfaces, more specifically, the classification of signals corresponding to different mental states, voluntarily produced by a subject [73]. We have observed that the classification performance strongly depends on the type of mental tasks performed by the subject [61].

We are currently investigating whether or not the use of Inverse Problems can enhance the discriminability of mental tasks measured by EEG [43].

5.2.3. Forward models for MEG and EEG

Participants: Maureen Clerc, Emmanuel Olivi, Théo Papadopoulo, Jérôme Piovano, Sylvain Vallaghé, Jean-Michel Badier [INSERM U751].

This work was partially supported by the Fondation d'Entreprise EADS.

Most methods for the inverse source problem in electroencephalography (EEG) and magnetoencephalography (MEG) use a lead field as an input. The lead field is the function which relates any source in the brain to its measurements at the sensors. Its computation requires solving a forward problem.

The inverse source localization problem of EEG and MEG strongly depends on the quality of the forward solution. The information required to specify the forward problem are the geometrical and physiological description of the head, in terms of its electrical conductivity.

Appropriate computational methods are compulsory for solving the M/EEG forward problem: either by surface-based Boundary Element Methods (BEM) or volume-based Finite Element or Finite Difference Methods. Until recently, the state of the art in BEM consisted in using a double-layer formulation [53], with an accuracy improvement provided by the isolated Skull Approach [57]. We have proposed a new, symmetric BEM [59] which improves over the state of the art in terms of accuracy. This has been implemented within OpenMEEG. Finite Element Methods (FEM) are also being studied for M/EEG because of their ability to account for anisotropic media. The cumbersome meshing procedure associated to the FEM should be alleviated after our recent development of the Implicit Mesh FEM [63]. It is quite tempting to combine the Boundary Element Method and FEM in an hybrid model that would exploit each model for its strengths (Symmetric BEM for its accuracy for tissues having an isotropic homogeneous conductivity, FEM for its ability to deal with anisotropy) to provide even better forward problems. This work would clearly benefit from a better comparison of the strengths/drawbacks of the available methods; this coupling has started in the PhD of Emmanuel Olivi.

We have proposed a global sensitivity analysis of conductivity, which provides new information about EEG forward models. It identifies the main input parameters which need model refinement, and gives directions on how to calibrate these models [26].

For complex geometries, there is no analytical formula of the lead field. The common approach is to numerically compute the value of the lead field for a finite number of point sources (dipoles). There are several drawbacks: the model of the source space is fixed (a set of dipoles) and the computation can be expensive for as much as 10000 dipoles. The common idea to bypass these problems is to compute the lead field from a sensor point of view. We use the adjoint method to derive general EEG and MEG sensor-based lead field equations. Within a simple framework, we provide a complete review of the explicit lead field equations, and we are able to extend these equations to non-pointlike sensors [27].

Another problem with EEG and MEG forward modeling is the obtention of the complex geometry of the head. This is particularly true for the skull which is barely visible in standard T1 images. The local statistics based approach of segmentation [66], [65] has been adapted to segment the head using simultaneously T1- and T2-images. T1-images are best used to obtain the skin, grey matter and white matter interfaces, whereas T2-images enhance the contrast of CSF so that the inner interface of the skull (as well as blood vessels which are often segmented as grey/white matter material) are visible [11]. This approach leads to interfaces described by levelsets that can directly be used for the M/EEG forward method described in [64].

5.2.4. Forward models for functional electrical stimulation

Participants: Maureen Clerc, Jean-Louis Divoux [MXM], Sabir Jacquir [Université Bourgogne], David Guiraud [DEMAR], Jérémie Laforêt [DEMAR].

We are studying the 3D potential induced by functional electrical stimulation, with the aim to propose a numerical model of nerve-cuff electrode. This model will be used to study and predict interactions between nerve fibres and electrode during stimulation. Our recent contributions to this topic concern the numerical resolution of the problem: computing current densities and voltage within the nerve can eventually be used to determine whether an axon is fired or not depending on its position.

When contracting a muscle using NFES (Neural Functional Electrical Stimulation), the stimulus always activates the axons of greater diameter first. Also selective activation of given fascicle inside a nerve is not possible with classical cuff electrode as the recruitment is performed uniformly around the nerve. These limits lead to poorly selective muscle recruitment, inducing fatigue and possible pain. To overcome this, selective stimulation strategies can be used. We propose a toolchain to investigate, simulate and tune selective stimulation strategies. It consists of a conduction volume model to compute the electric field generated in the nerve by a cuff electrode surrounding it; an axon model to predict the effect of the field on the nerve fibre — the generation, propagation and possible block of action potentials; and an interface script that links the two models and generates the code of the input function for the nerve fibre model. We present some simulation results to illustrate the possibilities of the toolchain to simulate such strategies. Ongoing experimental validations are also discussed. They will enable us to tune the model and may lead to further improvements [40].

5.2.5. Unified generative source models

Participants: Maureen Clerc, Théo Papadopoulo, Nicole Voges, Habib Benali [Laboratoire d'Imagerie Fonctionnelle, INSERM U678, Faculté de Médecine, Univ Paris 6 / Hôpital Pitié-Salpêtrière], Christian Bénar [INSERM U751, Faculté de Médecine, La Timone, Marseille], Olivier David [INSERM U594, Grenoble], Fabrice Wendling [INSERM U642, Rennes].

The models of source activities usually differ with various image modalities such as M/EEG, fMRI or optical imaging (OI). This is mostly due to the fact that these modalities deal with differing views of the functioning brain (different physical phenomena, different spatial or temporal scales). Various models cope with either the metabolic [52], [69] or the electrophysiologic [58] aspects of brain function. It is quite tempting to couple these two kinds of models into a unified neural-mass computational model that can explain a broad variety of measurements obtained with different image modalities. To be efficient, such a model should have a limited number of parameters while keeping its expressiveness, and be computationally tractable. This is currently starting to be investigated within the context of an INRIA-INSERM collaboration, and of Nicole Voges's postdoc (begun in June 2009).

6. Contracts and Grants with Industry

6.1. Fondation d'Entreprise EADS: A multi-scale investigation of the operating brain with an eye on visual perception.

Participants: Maureen Clerc, Rachid Deriche, Olivier Faugeras, Pierre Kornprobst, Théo Papadopoulo.

This project deals with the problem of better measuring, modeling and simulating the set of representations that are used and the flow of processing that is performed in the human brain to achieve efficient visual perception. This is indeed a challenge because despite all the knowledge that has been accumulated on the functioning of the brain over the last years, many very basic questions still remain open, e.g.: What is the "information" conveyed by neuronal electrical and chemical activity? How is the information encoded in this activity? How is the information distributed among brain areas? In particular, what are the respective roles of feedforward and feedback connections between brain areas? Can we infer any "computational" paradigms from the observation of the functioning of the brain and the computer simulation of parts of this functioning? Most of these questions arise from the fact that it has proven to be extremely difficult to connect 1) the small scale knowledge of the functioning of one neuron or a small population of neurons (chemical/electrical models) to 2) the large scale (in space and/or in time) knowledge (spatial organisation, main connections, spatial

and temporal activations,...) provided by brain imagery observations (functional Magnetic Resonance Images (fMRI), MagnetoEncephalography (MEG), ElectroEncephalography (EEG), Diffusion Magnetic Resonance Images (DMRI), optical imaging). Similarly, the large scale knowledge of the brain activations has turned out to be difficult to relate to 3) the mathematical and computational principles underlying their (somewhat) equivalent computer implementations (when they exist). As an example, what we know about the processing of visual motion in humans has hardly ever been compared with the field of motion analysis in computer vision. But certainly the abilities of the best computer programs in terms of the analysis of 2D and 3D motions of objects in video sequences of images are way behind the state of the art of most mammalian brains. The intent of this project is double. First, we want to build some connections between these three levels of description, particularly for the low-level vision areas of the brain and the feedback loops between these areas. Second, we want to show that this increase of knowledge can be put to good use from the technological standpoint and opens the door to new ways of interacting with the machines our societies build. The project covers some of the parts of the current research program of the Odyssée laboratory which are not covered by other grants.

7. Other Grants and Activities

7.1. National Actions

7.1.1. CD-MRI Associated Team

Participants: Rachid Deriche, Emmanuel Caruyer, Demian Wassermann, Aurobrata Ghosh.

Duration: January 2009 to December 2012

Our research group together with the group of Peter Basser (Laboratory of Integrative & Medical Biophysics, NICHD, NIH, Bethesda NIH) and the groups of Guillermo Sapiro (Department of Electrical and Computer Engineering, University of Minnesota) and Kamil Ugurbil (CMRR, Center dor Magnetic Resonance Research, University of Minnesota) have been developing increasingly strong ties over the past several years. This associated team, started since Januray 2009, helps us combining our great expertise, as well our strong scientific synergy and our respective computing and experimental facilities, to help resolve some of the most difficult problems and mathematical challenges in Diffusion MRI.

Through an extensive exchange program involving junior as well senior scientists from all the partners, our Associate Team is pursuing and intensifying our past collaborative work on this subject. We start to develop new mathematical models and computational tools to unleash the full power and multivariate information content of diffusion MRI and advance the state-of-the-art in Computational Diffusion MRI. One of our objective is to write joint publications in international conferences and journals dedicated to promoting advances in computational methods for Diffusion MRI analysis and use of diffusion MRI in clinical and neuroscience (web site http://www-sop.inria.fr/teams/odyssee/ext/AssociateTeamOdyNIHMin).

7.1.2. ANR ViMAGINE

Participants: Maureen Clerc, Rachid Deriche, Olivier Faugeras, Alexandre Gramfort, Emmanuel Olivi, Théo Papadopoulo.

The partners of this project are Odyssée, the LENA (CHU Pitié-Salpétrière), and the Pariétal project-team at INRIA Futurs and Neurospin-Saclay. It has been accepted in summer 2008 and is funded for four years.

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, Alexandre Gramfort, Emmanuel Olivi, Théo Papadopoulo.

Duration: September 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 team and the "laboratoire d'Analyse Topologie et Probabilités UMR6632/CNRS of Aix en Provence

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 sensorymotor 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.

7.1.4. ANR NucleiPark

Participants: Rachid Deriche, Emmanuel Caruyer, Demian Wassermann, Aurobrata Ghosh.

Duration: September 2009 to December 2012

This project is about High field MR imaging (7T and 3T) of the brainstem, the deep nuclei and their connections in the parkinsonian symdromes 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. Lehéricy).

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. ADT Immersive BCI

Participants: Théo Papadopoulo, Maureen Clerc, Nicolas Servant, Joan Fruitet.

Duration: December 2009 to December 2011

The goal of this technical project, funded by INRIA for 2 years (starting in 2009), is to facilitate the use of EEG within a new immersive environment at INRIA Sophia Antipolis Méditerranée, in order to make it possible to perform BCI or cognitive experiments within this environment. Using a BCI within an immersive environment will open up new possibilities for scientific research, both in BCI and in Virtual Reality. All development linked to this project will take place within an integrative software platform. This development will include electrode localization and real-time EEG processing with feedback to the user.

7.2. Actions Funded by the EC

7.2.1. FACETS: Fast Analog Computing with Emergent Transient States

Participant: Théo Papadopoulo.

FACETS is an integrated project within the biologically inspired information systems branch of IST-FET. The FACETS project aims at addressing, with a concerted action of neuroscientists, computer scientists, engineers and physicists, the unsolved question of how the brain computes. It combines a substantial fraction of the European groups working in the field into a consortium of 13 groups from Austria, France, Germany, Hungary, Sweden, Switzerland and the UK. About 80 scientists will join their efforts over a period of 4 years, starting in September 2005. A project of this dimension has rarely been carried out in the context of brain-science related work in Europe, in particular with such a strong interdisciplinary component (web site: http://facets.kip.uni-heidelberg.de/).

8. Dissemination

8.1. Diffusion and Community Services

Maureen Clerc is a member of two local (Sophia Antipolis) committees: CUMIR and Commission d'Animation Scientifique. She has been since 2008 a member of the Program Committee of RFIA 2010, and of the EADS PhD Award Committee. She gave an invited talk at a Workshop on "Dictionaries of Atoms" at the Centre de Recherches Mathématiques of Montréal in September 2009, and at the CRAN in Nancy in September 2009. She organized, together with J-F Gerbeau and M. Fernandez a CEA-EDF-INRIA School on "Electrophysiological Modeling of the Heart and Brain", held at INRIA Rocquencourt in November 2009. She is the coordinator of the ANR DEFIS grant "CoAdapt".

Rachid Deriche is Project committee vice-chairman at INRIA Sophia Antipolis - Méditerranée and member of the Direction of the Sophia Antipolis Research Center (DGSA). Rachid Deriche is Adj. Director at the Doctoral School EDSTIC (http://edstic.i3s.unice.fr/index.html) and member of the Scientific Council of the ITMO ITS (Institut des Technologies pour la Santé). He has co-organised MICCAI 2009 Diffusion MRI Tutorial: *Technology Trends and unsolved problems" (20/09/2009-ICL)* [with D. Alexander, UCL; C.F.Westin, Harvard Med. School-Boston and R.Verma, U.Penn].

Rachid Deriche is Associate Editor of SIAM Journal on Imaging Sciences (SIIMS), editorial board member at Springer for the book series entitled Computational Imaging and Vision, editorial board member of International Journal of Computer Vision (IJCV). He served as Area-Chair for RFIA 2010 and currently serves as Co-Chair for Track VI: Bioinformatics and Biomedical Applications for the 20th International Conference on Pattern Recognition 2010. R. Deriche has also 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 also served as president, reviewer and examiner in the jury committee of a number of PhD thesis (C. Frindel(INSA), J.M.Peyrat (INRIA), G.Operto (LSIS),F. Huguet (Université J. Fourier), M. Pechaud (ENPC), A. Qazi (DIKU, University of Copenhagen)).

Rachid Deriche gave an invited talk at MICCAI 2009 entitled *Diffusion MRI Tutorial: Technology Trends and unsolved problems* at Imperial College London (GB).

Théo Papadopoulo served as a referee for the international conferences ICCV 2009, CVPR 2010 and for the national conference RFIA 2010. He has also been area chair for the national conference GRETSI 2009. Since July 2007, he is the task leader of the WP8 work package of the European project FACETS 7.2.1. He is also the coordinator of the ADT "Immersive BCI". He also served as a jury member for the INRIA Chair at University of Nice-Sophia Antipolis.

8.2. Teaching

- Maureen Clerc and Théo Papadopoulo teach "Inverse problems for brain functional imaging" (20H) at ENS Cachan and at the Master for Computational Biology at University of Nice Sophia Antipolis.
- Maureen Clerc is in charge of a module at Ecole des Ponts: Fourier Analysis and Applications.
- Théo Papadopoulo teaches "Computer Vision" at the Polytechnic Engineering School of the University of Nice-Sophia Antipolis (24H).
- Rachid Deriche teaches "Variational approches and Geometrical Flows for Brain Anatomical Imaging" (24H) at the Master for Computational Biology at University of Nice Sophia Antipolis.
- Rachid Deriche is in charge of the module "PDE's and Geometric Flows in Computer Vision and Image Processing" in the Master MPRI *Master Parisien de Recherche en Informatique* - University of Paris 7, ENS and Ecole Polytechnique and teaches - (15H).
- Rachid Deriche teaches "Advanced Image Processing and Computer Vision" at Telecom & Management Sud Paris School (ex INT - Evry) - (12H).

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