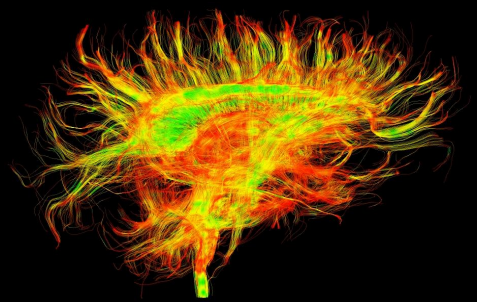
ATHENA Project Team

Computational Imaging of the Central Nervous System

Rachid DERICHE

INRIA Sophia Antipolis - Méditerranée Research Center



[February, 2012]

Roots & History

From 1988 to 2002 : Robotvis

- Computer Vision & Robotics : Theory and practice of machine visual perception.
- Realviz is created to generate 3D content and visual effects from photo imaging and 2D environments.

From 2002 to 2008 : Odyssée

- Computational Neuroscience.
- January 1st, 2009 : Creation of NeuroMathComp (O. Faugeras & al).

2009 : From Odyssée to Athena

- Measuring and modeling the functioning and the anatomical connectivities of the human brain.
- October 8th & 9th, 2009: Evaluation of Odyssée (O.Faugeras/R. Deriche).
- Computational Imaging of the Central Nervous System
- January 1st, 2010 : INRIA Team
- July 1st, 2010 : INRIA Project-Team

Team members

Permanent: 3 Research Scientists + 1 Administrative Assistant

- Maureen Clerc [ICPC, ENPC, Research Scientist - on 5 years assignment.]
- Rachid Deriche [DR1 INRIA, Research Director, Project-Team Leader.]
- Théo Papadopoulo [CR1 INRIA, Research Scientist.]
- *Administrative Assistant: Claire Senica.*

Non Permanent: 8 PhD's - 2 Post-Doc - 2 Junior Eng.

- Emmanuel Caruyer, ENS-Cachan Ph.D student, from October 1st, 2008
- Jian Cheng, Joint Program INRIA/LIAMA Ph.D student, from Sept. 1st, 2008
- Emmanuel Olivi, PACA/INRIA Ph.D student, from Oct. 1st, 2008
- Joan Fruitet, ENS-Ulm Ph.D student, from Sept. 1st, 2009
- Anne-Charlotte Philippe, PACA/INRIA Ph.D student, from Sept. 1st, 2010
- Sylvain Merlet, UNSA/INRIA Ph.D student, from Sept. 1st, 2010
- Romain Trachel, Ph.D. student, DGA/CNRS/INCM, from Oct. 1st, 2010
- Sebastian Hitziger, Ph.D. student, PACA/ANR Multimodel & CoAdapt, from Nov. 2nd, 2011
- Aurobrata Ghosh, PostDoc, ANR NucleiPark from May 1st, 2011
- Eoin Thomas, PostDoc, ANR CoAdapt from June 1st, 2011
- Jaime Garcia Guevara, Technical Assistant, ADT MedInria, from Jan. 17th 2011
- Dieter Devlaminck, Tech. Assistant, ANR CoAdapt, from Nov. 15th, 2011

Context/Motivations

Innovative methodological developments to better understand the Central Nervous System (CNS) and make true our dream to help people suffering from CNS diseases.

"...About 1/3 of the burden of all diseases in Europe is caused by brain diseases...In 28 European countries with a population of 466 million, 127 million were affected by at least one brain disorder" [1]

"...substantially increased funding for basic, clinical and public health research in order to identify better strategies for improved prevention and treatment for disorders of the brain as the core health challenge of the 21st century" [2]

- Very strong societal and economical need for improving the diagnosis and therapy of CNS diseases.
- CNS: Great advances in its exploration but still *Terra-Incognita*

Objective: Explore the CNS through computational imaging by putting the emphasis on better understanding its architecture and its functioning and on the relevance of neuroanatomy to the understanding of brain function.

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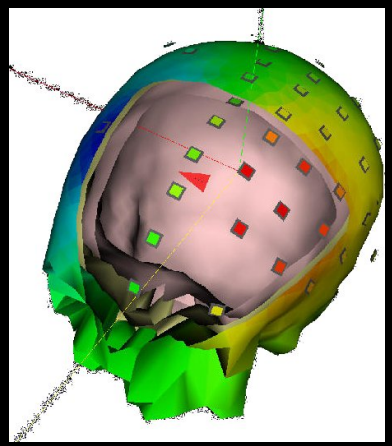
[1] Andlin-Sobocki eta, *Costs of disorders of the brain in Europe.* European Journal of Neurology, 12(1), 2005

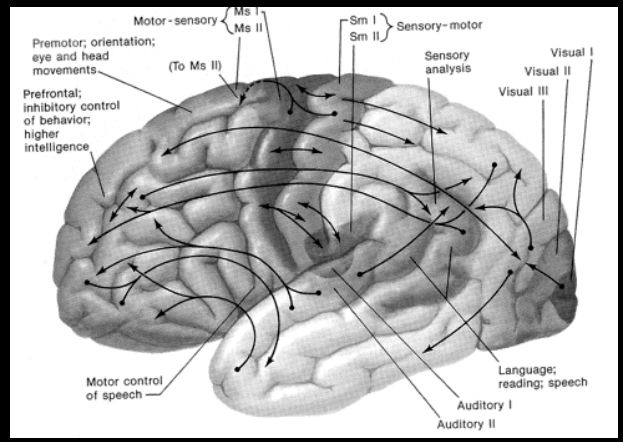
[2] H.U. Witchen & al ECNP/EBC Report 2011 - The size and burden of mental disorders and other disorders of the brain in Europe 2010. European Neuropsychopharmacology (2011) 21, 655–679

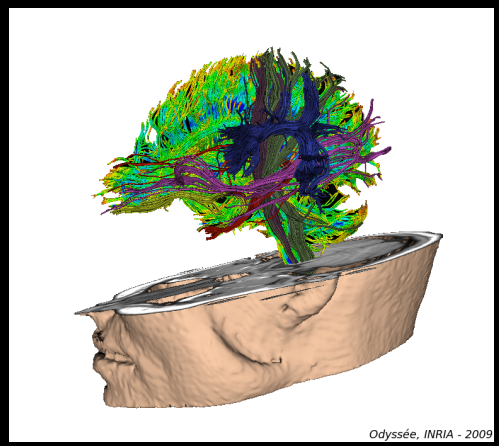
Computational Imaging of the CNS

Measuring and Modeling the CNS :

- *"Nothing defines the function of a neuron better than its connections".*[3]
- Develop mathematical tools and computational models for measuring and processing the CNS functional and anatomical connectivities.

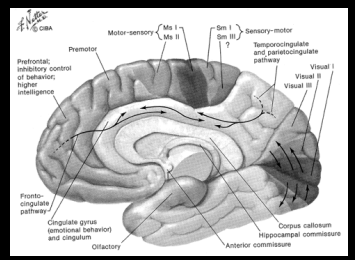






Applications :

- Building of a strong network of national and international collaborators.
- Clinical.
- Brain Computer Interface.



[3] Mesulam M-M. Imaging connectivity in the human cerebral cortex: the next frontier? Ann Neurol 2005

Imaging Modalities

In-vivo and non-invasive probing of CNS structure and function.

"Innovative methods are urgently needed if the study of human neuroanatomy is to advance beyond the rudimentary level. Most of the techniques used on monkeys cannot ethically be used on human"[4].

- Diffusion MRI (dMRI).
- Electro-Encephalography (EEG).
- Magneto-Encephalography (MEG).

MRI (CENIR, Pitié Salpêtrière, Paris)

MEG (La Timone, Marseille)

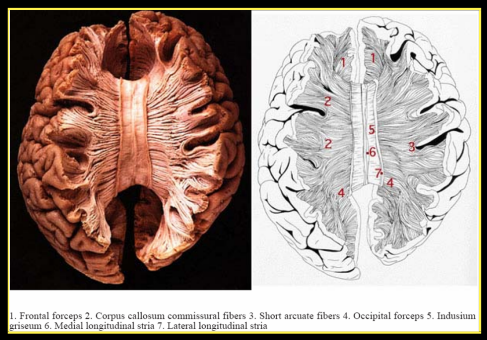
EEG (Inria, Sophia-Antipolis)

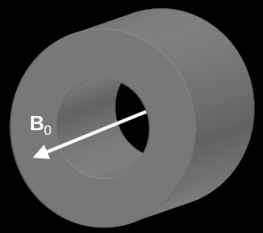
[4] Francis Crick & Edward Jones, *Backwardness of human neuroanatomy*, Nature 361, Jan. 1993

How to recover human CNS connections ?

For nonhuman primates, anatomists infer the connections indirectly from chemical tracers.

- MRI introduced by Paul C. Lauterbur and Peter Mansfield in 1973, jointly Nobel Prize in Physiology/Medicine - 2003.
- *Diffusion MRI* is a recent imaging modality that measures, *in vivo and non-invasively*, the random motion of water molecules in biological tissues.
- The random motion of water molecules allows *microstructure and anatomical connectivities* to be probed and imaged on a microscopic scale.
- Pioneering contributions introduced in the mid 1980s by Denis Le Bihan and others.





CD-MRI: Positioning

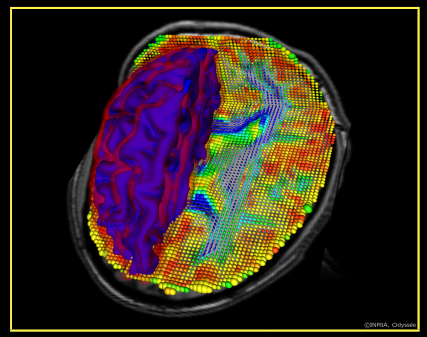
- Riemannian geometry, Variational and statistical methods on manifold, Level-sets, Gaussian processes, Manifold Learning..
- Development of pioneering studies in the area of CD-MRI and Diffusion Tensor MRI (DT-MRI) processing.
- Development of influential computational models for High Angular Resolution Diffusion Imaging (HARDI) processing.
- Innovative methodological developments and applications: DT-MRI and HARDI Estimation, Segmentation, Tractography and Fibers Clustering to recover the brain and spinal cord anatomical connectivities.
- Building of a strong network of national (CENIR, INSERM U678, NeuroSpin) and international (NIH-NICHD, CMRR, Montreal & Sherbrooke Univ., MPI) collaborators to provide us with real data (3T and 7T) and applications.

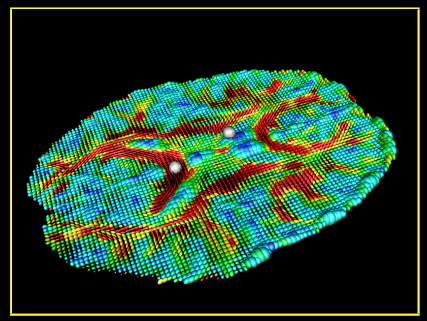
Computational DT-MRI: Main Achievements

Development of Geometric and Variational Methods for DT-MRI Processing

[Lenglet's PhD thesis 2006, AFRIF'2007 Award]

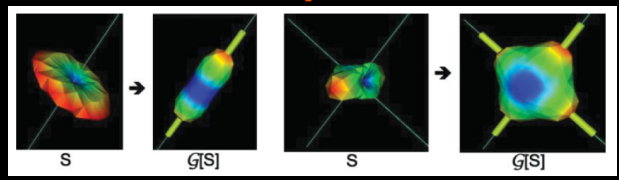
- Statistics on the Manifold of Multivariate Normal Distributions: Theory and Application to Diffusion Tensor MRI Processing [Lenglet & Deriche, Journal of Mathematical Imaging and Vision, 2006]
- DT-MRI Segmentation by Statistical Implicit Surface Evolution and Level-Sets [Lenglet, Rousson & R. Deriche. IEEE Transactions on Medical Imaging, 2006]
- Brain Connectivity Mapping using Riemannian Geometry and PDEs [Lenglet, Prados, Deriche & Faugeras, SIAM Journal on Imaging Sciences, 2009]
- Diffusion Abnormalities in the Primary Sensorimotor Pathways in Writer's Cramp [Delmaire & Wassermann & Deriche & Lehericy & al, Archives of Neurology, 2009]



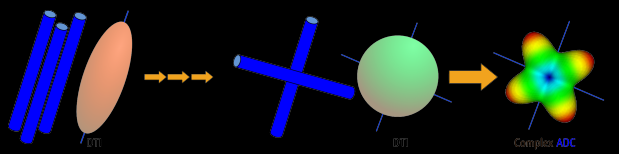


Computational HARDI: Main Achievements

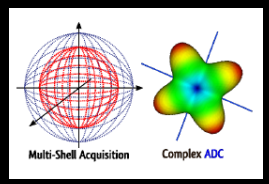
Obtain more accurate models for non-Gaussian diffusion processes to overcome the limitations of classical DT-MRI - [Descoteaux's PhD thesis 2008, ASTI'2009 Award]

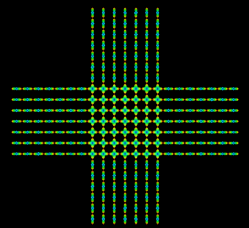


- High-order models for apparent diffusion coefficient estimation: Spherical harmonics, Laplace Beltrami regularization and Funk Radon [Descoteaux & Deriche: Magnetic Resonance in Medicine 2006]

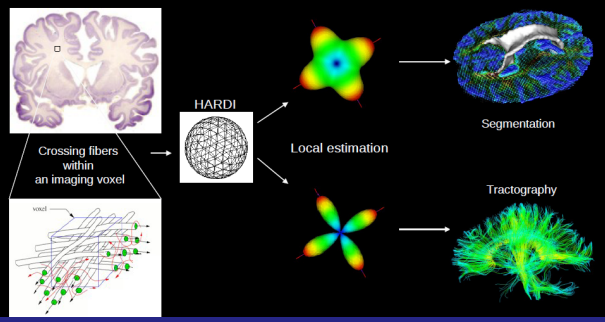


- Regularized, fast and robust analytical Q-Ball Imaging [Descoteaux and Deriche: Magnetic Resonance in Medicine 2007]





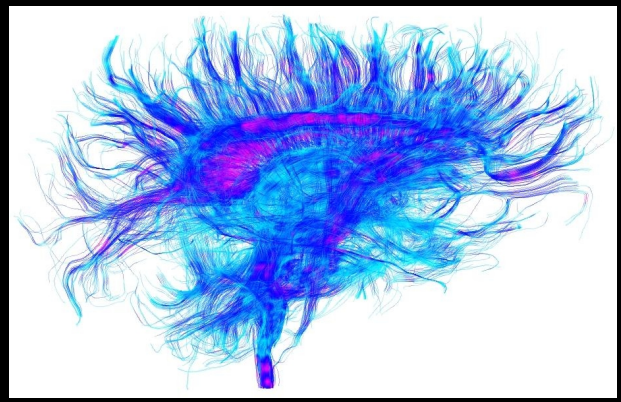
- HARDI images can be automatically segmented and deterministic and probabilistic Q-Ball tractography allow to reconstruct fibers and deal with complex fiber orientation distribution [Descoteaux and Deriche: Journal of Mathematical Imaging in Vision, 2008 & IEEE Transactions on Medical Imaging, 2009]



Objectives

- **Improving D-MRI Acquisitions:**
  - Live ODF Estimation
  - Priors & Rician noise
  - D-MRI Motion Detection and Correction
  - D-MRI Compressed Sensing
- **Modelling in Diffusion MRI:**
  - A Riemannian framework for ODF computing & Registration
  - High Order Tensors Models
  - PDF features Representation and Characterization
  - Multiple Shell Diffusion MRI
  - D-MRI Signal Modelling
- **CNS Anatomical Analysis:**
  - HARDI Segmentation and Tractography
  - Quantitative fibers clustering and beyond
  - Tissue Microstructures features recovery
  - Functional D-MRI

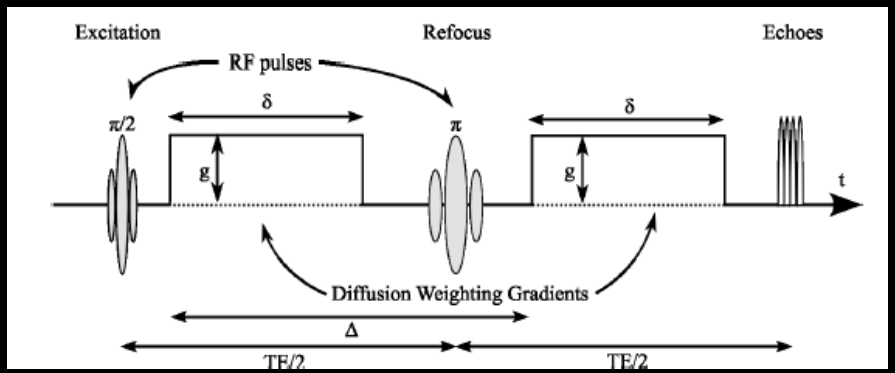
- **Applications:**
  - Parkinson's & Alzheimer's diseases
  - Writer's Cramp & Schizophrenia
  - Spinal Cord Injury
  - Traumatic Brain Injury

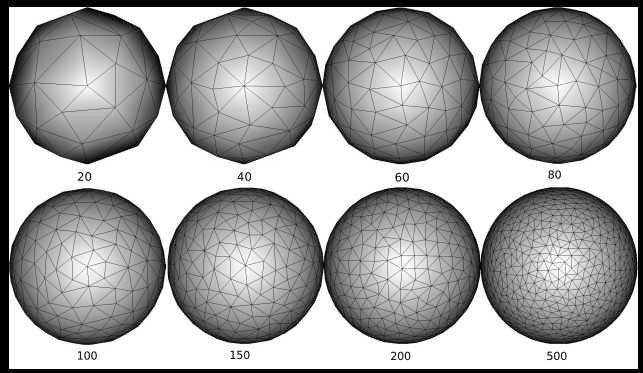


CD-MRI: Acquisitions

Improve acquisition schemes, scanning time and pre-processing of the CNS data.

- Optimal and real time in-vivo acquisition strategy.
- Advanced Diffusion MRI Preprocessing & Real Time Motion Detection & Correction.
- Diffusion MRI Compressed Sensing.



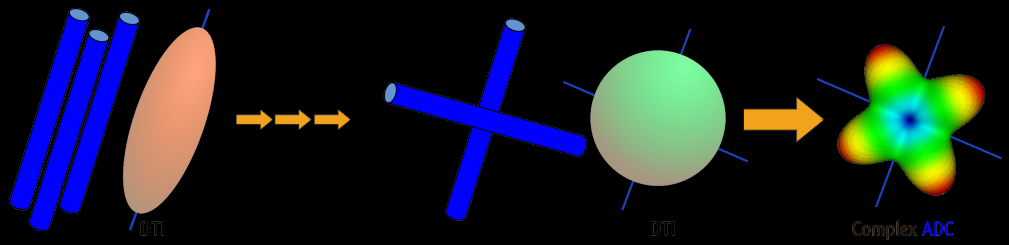


C. Poupon & D. Le Bihan (NeuroSpin, Saclay), P. Basser (NICHD, STBB, Bethesda), K. Ugurbil & G. Sapiro (Center for Magnetic Resonance Research - Univ. of Minnesota, Minneapolis).

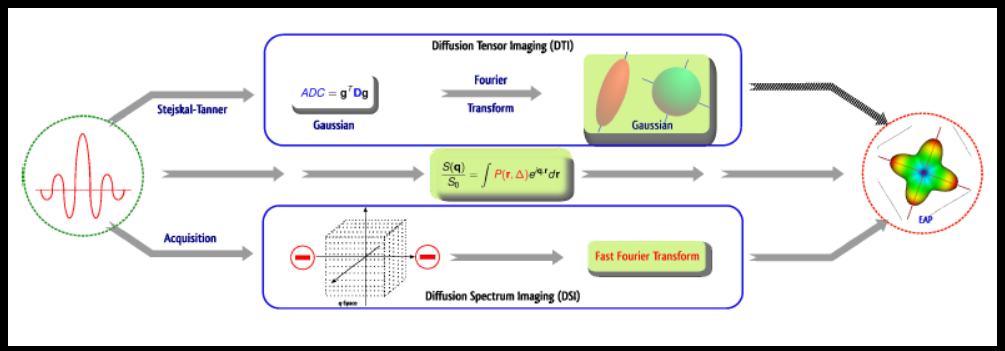
R. Deriche, J. Calder & M. Descoteaux - Optimal Real-Time Q-Ball Imaging using Regularized Kalman Filtering with Incremental Orientation Sets - Medical Image Analysis,Volume 13, Issue 4, August 2009, Pages 564-579.

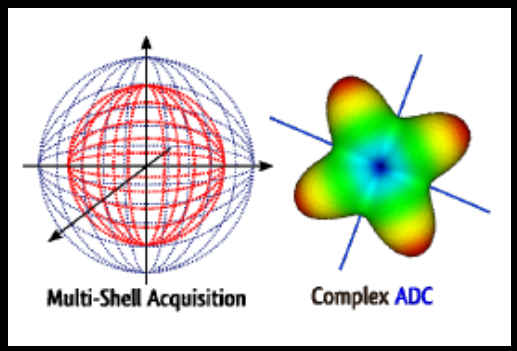
CD-MRI: Modelling

Appropriate tools and computational models for processing the CNS connectivity.



- Beyond the second order tensor model: High Order Tensors Models.





- Multiple Shell D-MRI & PDF features recovery.

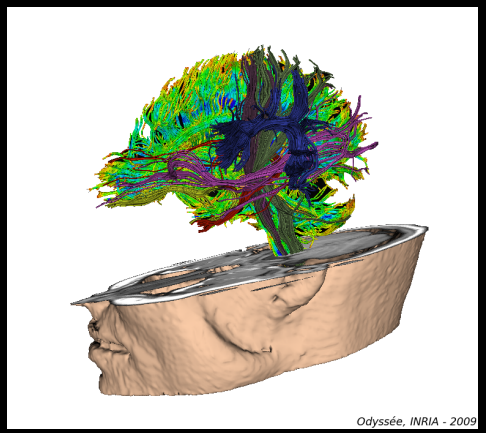
K. Siddiqi (McGill University, Montreal), M. Moakher (ENIT, Tunis), J. Tianzi (LIAMA, Beijing).

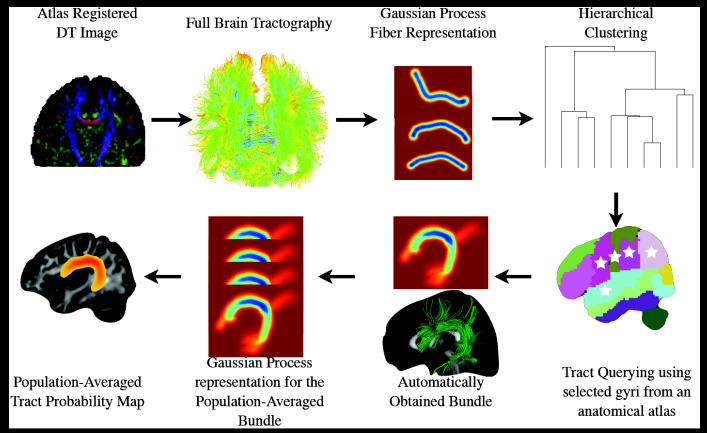
M. Descoteaux, R. Deriche, D. Le Bihan, J-F Mangin, C. Poupon - Multiple q-Shell Diffusion Propagator Imaging - Medical Image Analysis, Volume 15, Issue 4, August 2011, Pages 603-621

CD-MRI: CNS Anatomical Analysis

Recover, cluster and characterize the CNS anatomical connectivity.

- HARDI Segmentation, Tractography, Fibers clustering & beyond.
- Tissue Microstructures features recovery & Functional Diffusion MRI .



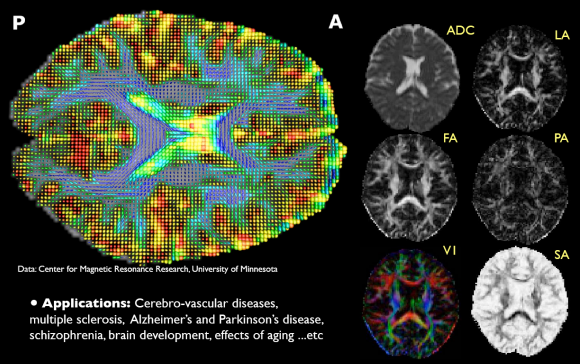


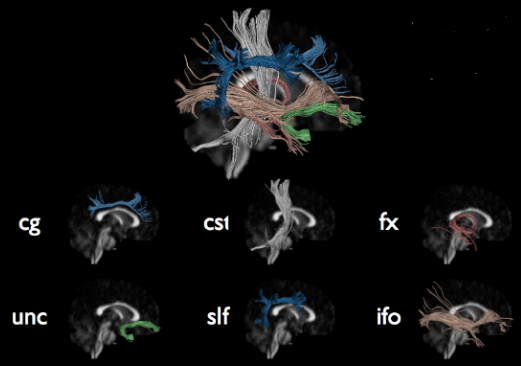
P. Basser (NIH, NICHD, STBB, Bethesda), A. Anwander (MPI, Leipzig).

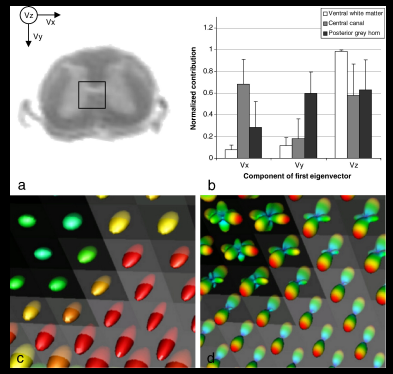
D. Wassermann, L. Bloy, E. Kanterakis, R. Verma, R. Deriche - Unsupervised White Matter Fiber Clustering and Tract Probability Map Generation: Applications of a Gaussian Process framework for white matter fibers - Neuroimage, Volume 51, Issue 1, 15 May 2010, Pages 228-241

CD-MRI: A Clinical tool to study White Matter

Better describe, characterize and quantify abnormalities within white matter.
Better neuroimaging markers for the diagnosis of CNS neurodegerative diseases.







- Parkinson's and Alzheimer's diseases.
- Other CNS disorder's diseases: Writer's Cramp, Schizophrenia..
- Spinal Cord Lesions.

VisAGeS, Asclepios, S. Lehericy (ICM, CENIR, CHUPS, Paris), H. Benali (INSERM U678, UPMC, Paris), S. Rossignol (Montreal Univ.), R. Verma (Univ. of Pennsylvania), P. Thomson (UCLA).

] C. Delmaire, R. Deriche, S. Lehéricy.& al - Diffusion Abnormalities in the Primary Sensorimotor Pathways in Writer's Cramp - Archives of Neurology, 66(4), 502-508, April 2009.

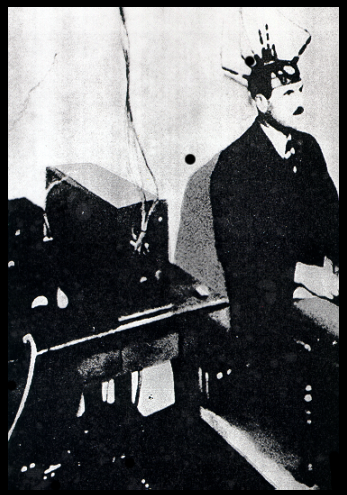
Principles

- Measurements of electric potentials (EEG, 1929) on the scalp and magnetic fields (MEG, 1972) outside the head.
- Computational reconstruction of the electrical activity in the cortex from spatio-temporal data.

⊕ Non-invasive method.

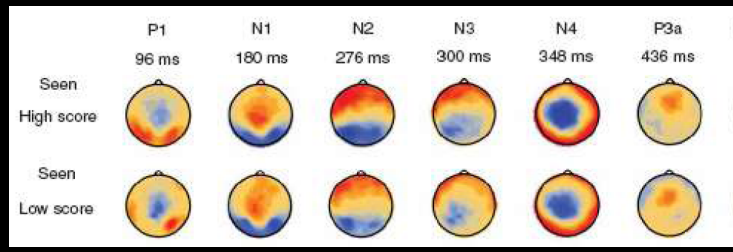
⊕ High temporal resolution (10^{-3} s).

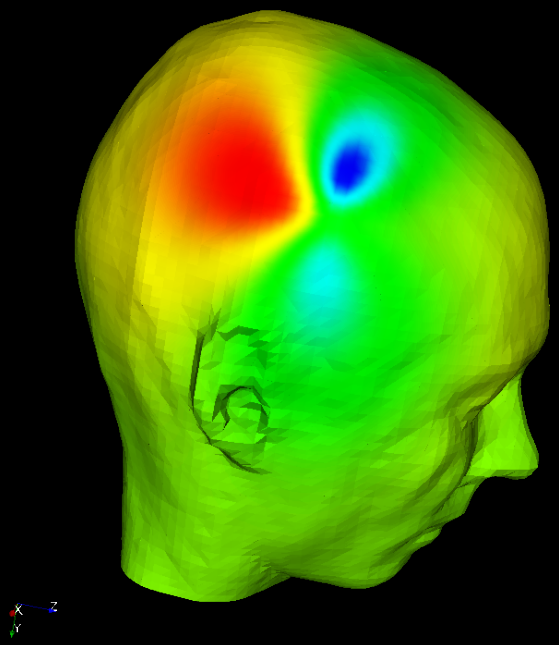
⊖ Small spatial resolution (EEG: 20 to 256 electrodes, MEG: up to 400 SQUIDS).



MEEG: Positioning

- **Signal processing:**
  - Detecting events.
  - Visualisation of activations.
- **Accurate forward/inverse models:**
  - Symmetric Boundary Element Method.
  - Implicit Mesh Finite Element Method.
  - Model calibration.
  - Focal/distributed sources.
- **MEEG in practice:**
  - EEG on site, MEG (La Timone).
  - Software development: OpenMEEG, FindSources3D, ...
  - Retinotopy.
  - Brain Computer Interface (BCI).

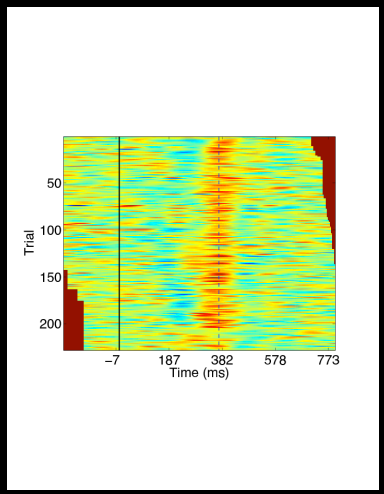


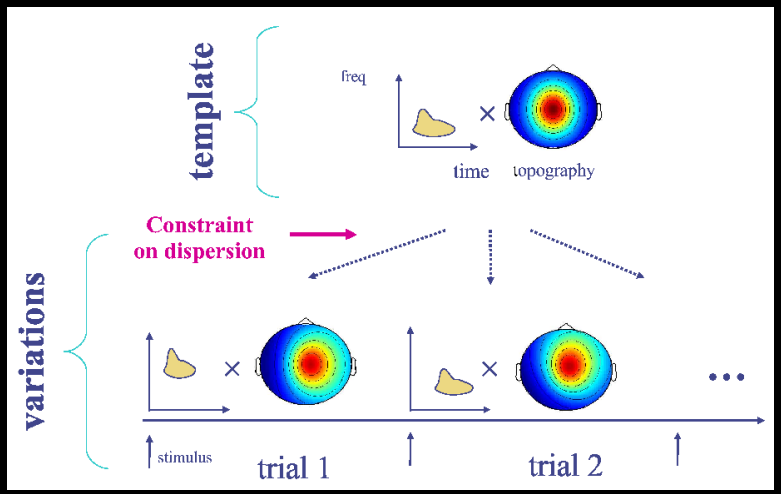


Detecting and extracting meaningful events

Extending Consensus Matching Pursuit

- Departing from mean across trials: cross-trial variability.
- Creating informed detectors for specific events.
- Multiple dimensions (subjects, conditions, trials, sessions, ...)





Ch. Bénar (INSERM U751), B. Torrésani (LATP), B. Burle (LNC).

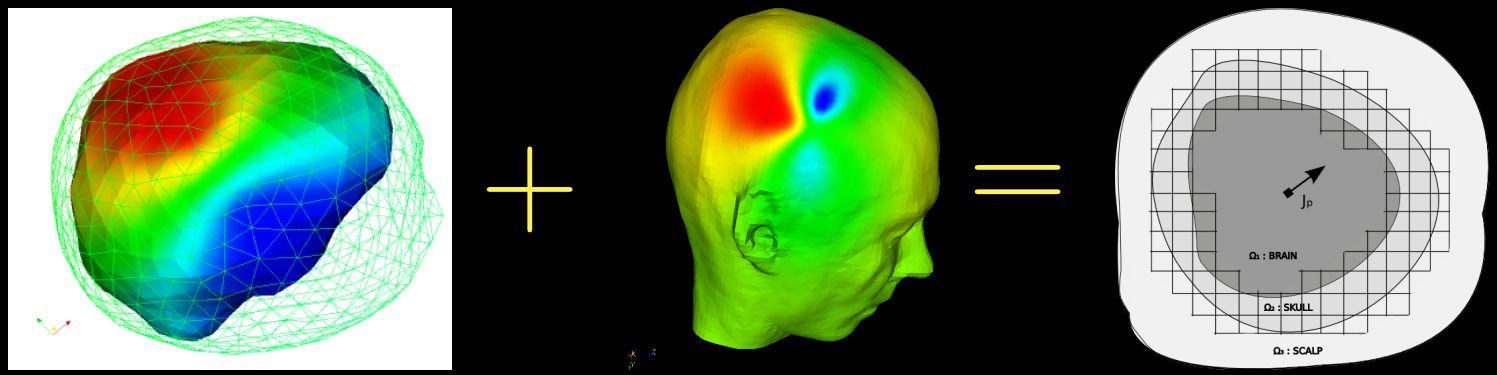
C. Bénar, T. Papadopoulo, B. Torrésani, M. Clerc. Consensus Matching Pursuit for Multi-Trial EEG Signal,

Journal of Neuroscience Methods, vol. 180, pp. 161-170, 2009.

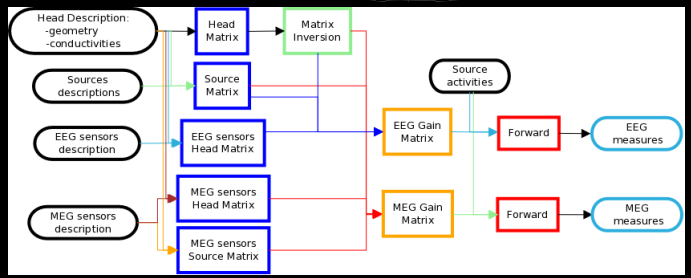
MEEG: Forward problems

Consolidation.

- Advanced forward models (BEM-FEM coupling, anisotropy).



- OpenMEEG.
- Implicit mesh.

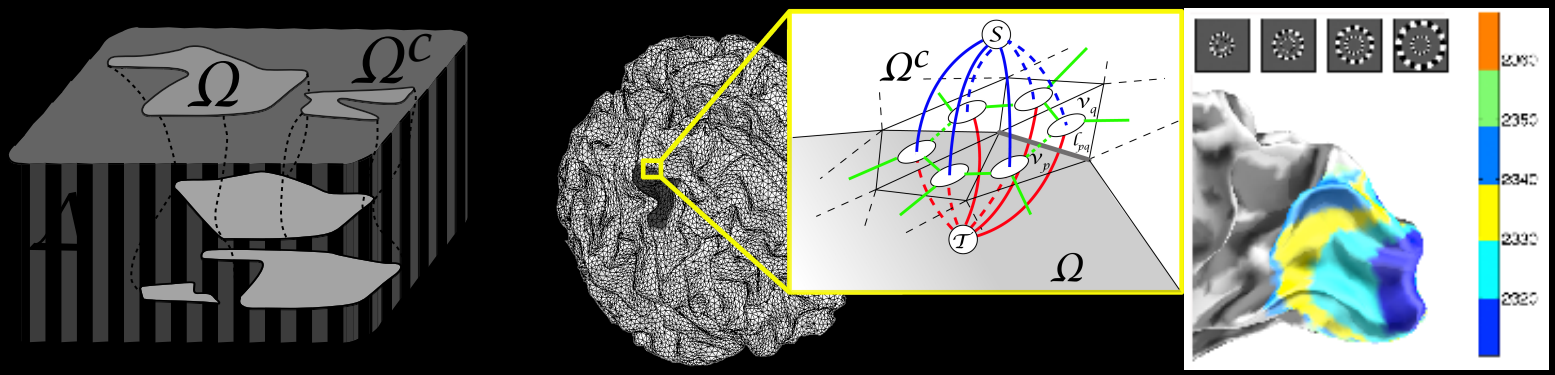


J.M. Badier, P. Chauvel (La Timone), C. Wolters (U. of Munster, Germany), M. Hämäläinen (Harvard).

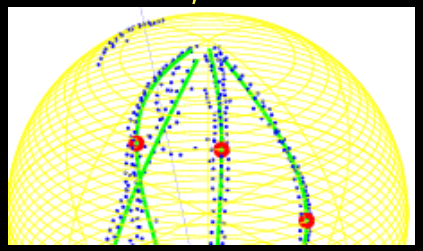
A. Gramfort, T. Papadopoulo, E. Olivi, M. Clerc. OpenMEEG: opensource software for quasistatic bioelectromagnetics, BioMedical Engineering OnLine 9:45, 2010.

MEEG: Inverse problems

Consolidation.



- Combined MEG and EEG workflow (inverse problems, statistics).
- Patch based regularisation.
- Rational approximation FindSources3D.
- Clinical assessment.



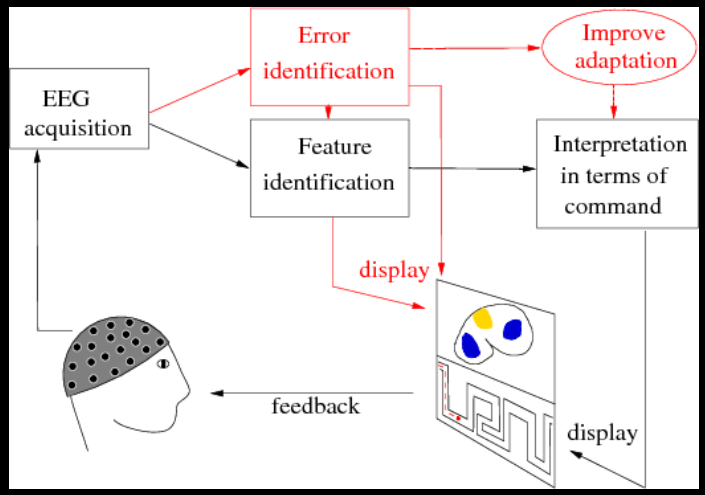
APICS, J.M. Badier, P. Chauvel (La Timone), S. Baillet (U. Wisconsin), M. Hämäläinen (Harvard).

A. Gramfort, T. Papadopoulo, S. Baillet, M. Clerc, Tracking cortical activity from M/EEG using graph-cuts with spatiotemporal constraints. NeuroImage, vol. 54, no. 3, pp. 1930-1941, 2011.

MEEG: Application to Brain Computer Interface (BCI)

Better electrophysiological models into BCI.

- Optimizing BCI in closed loop (Co-adaptation).
- BCI system within an immersive environment.
- Classifiers based on cognitive data (source or sensor space).



Laboratory of Brain-Computer Interfaces, Institute for Knowledge Discovery, Graz University of Technology, 2007.

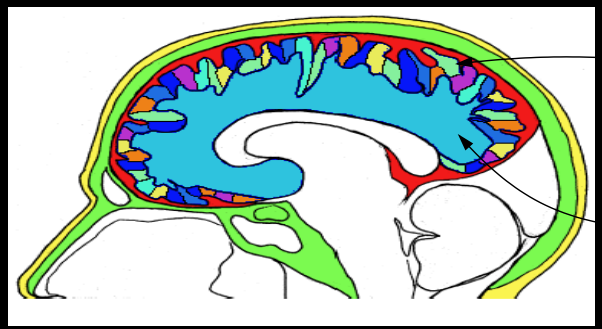
Bunraku, Cortex, Sequel, B. Burle (LNC), O. Bertrand (INSERM U821, Lyon).

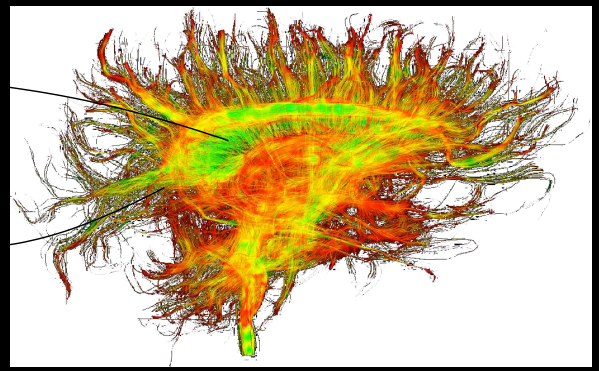
J. Fruitet, A. Carpentier, R. Munos, M. Clerc, Automatic motor task selection via a bandit algorithm for a brain-controlled button,RR-7721, Sept.2011

Combining imaging modalities

Explore the combination of D-MRI/MEEG.

- Augmented connectivity information.
- Regularized inverse problem through D-MRI connectivity priors.
- Electrical conductivity tensor from Diffusion-MRI.





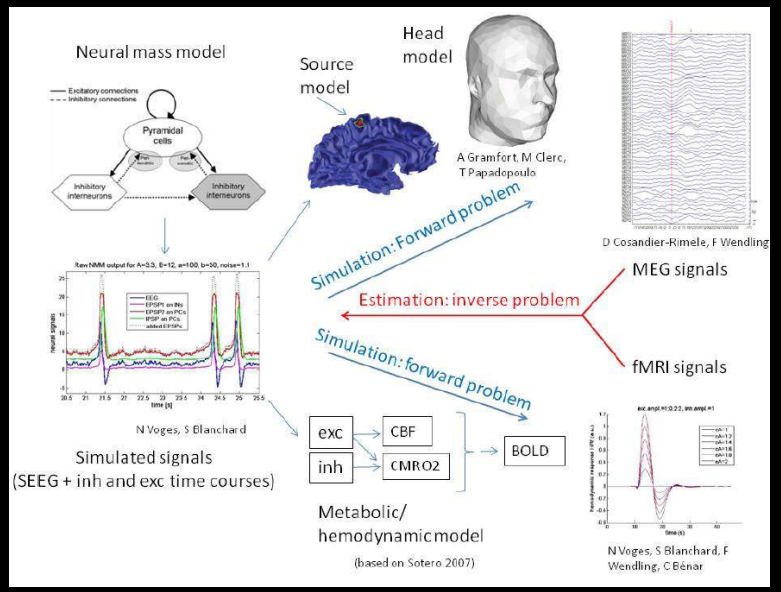
PARIETAL, NEUROMATHCOMP, F. Wendling (U642), H. Benali (U678), C. Bénar (U751), O. David (U594).

A.C Philippe, M. Clerc, T. Papadopoulo, R. Deriche, A nested cortex parcellation combining analysis of meg forward problem and diffusion mri tractography, IEEE International Symposium on Biomedical Imaging, 2-5 May, 2012, Barcelona

Combining imaging modalities

Multi-modal data fusion with biophysical models

- Unified spatio-temporal models of sources.
- Neuronal activity is simulated by a neural mass model. EEG or MEG and fMRI signals can be simulated via realistic model of the head and via a model of the neurovascular coupling.



Parietal, NeuroMathComp, F. Wendling (U642), H. Benali (U678), C. Bénar (U751), O. David (U594).

S. Blanchard, T. Papadopoulo, C. Bénar, N. Voges, M. Clerc, H. Benali, J. Warnking, O. David, F. Wendling Relationship Between Flow and Metabolism in BOLD Signals: Insights from Biophysical Models, Brain Topography, pp. 1-14, Nov. 2010.

Grants

- Associated Team with NIH & UoM (2009–2011) : dMRI.
- Associated Team with CRM (Montreal & Sherbrooke Univ.) (2012-2014) : dMRI & MEEG.
- ANR NucleiPark (2009–2013) : dMRI & Parkinson's Disease.
- ANR Vimagine (2008–2012) : MEG based retinotopy with Diffusion MRI.
- ANR CO-ADAPT (2009–2013) : Co-adaptation in BCI systems.
- ANR MultiModal (2011–2014) : fMRI & MEEG.

- CPER TELIUS (2008–2010) : Building an EEG/BCI system (hardware only).
- ADT MedInria (2011-2012) : Building an Inria Medical Platform

- Various: Ecos-Sud, PAI Bosphore, Stic-Algerie..

Network of Collaborators

National Level

- S. Lehericy - CENIR (CHU Pitié-Salpêtrière), H. Benali - Inserm U678 (CHUPS), C. Poupon & D. Le Bihan - (NeuroSpin), Chauvel & J.M. Badier (Inserm U751 -Marseille),..

European Level

- A. Anwander - MPI for Human Cognitive and Brain Sciences (Leipzig)..

International Level

- P. Basser - NIH (NICHD, Bethesda), K. Ugurbil - Center for Magnetic Resonance Research (Univ. of Minnesota), J.M.Lina & C. Grova & M. Descoteaux (CRM, Québec), R. Verma - Univ. of Pennsylvania (Dpt of Radiology - School of Medicine) - Rossignol (University of Montreal), J. Tianzi - CASIA - LIAMA (Beijing), M. Moakher - ENIT (Tunis)..

Softwares & Libraries

Forward MEEG

- OpenMEEG : C++ package for forward/inverse problems of EEG/MEG using the symmetric BEM Method and a distributed approach (L2, L1 regularization) resp.
- ImplicitMesh : FEM based on MEEG forward pb with anisotropy in the conductivities.

Inverse MEEG

- EMBAL : Matlab Toolbox for MEEG inverse modeling with distributed source models.
- FindSources3D (APICS): Matlab toolbox to solve inverse pb and locate pointwise dipolar sources from EEG.

Diffusion MRI

- DT-MRI and HARDI applications made available as plugins for MedINRIA (Asclepios) and 3DSlicer (NA-MIC...)

Scientific Production since 2005

HDR

- 2 HDR (M. Clerc, T. Papadopoulo)

PhD Thesis

- 7 PhD thesis: C. Lenglet (Research Scientist, Minnesota Univ.), M. Descoteaux (Assistant Prof., Sherbrooke Univ.), J. Piovano (Research Scientist, Polar Rose/Apple), S. Vallaghé (Post-Doc, ENSIMAG/MGH), A. Gramfort (Post-Doc, MGH/Parietal), D. Wassermann (Harvard Medical School), A. Ghosh (Post-Doc, Athena).

Journals & Conferences

- 41 Int.Journals, 113 In. Confs.
- 2 journals and 5 confs. per year & per senior member.

Software/Publications

Dissemination/Transfer of Computational CNS Imaging knowledge.

- Continue to publish in the best international referreed conferences and journals: *NeuroImage (3), IEEE Transactions on Medical Imaging (3), Physics in Medicine and Biology (3), Journal Mathematical Imaging and Vision (3), Magnetic Resonance in Medicine (2), Medical Image Analysis, Inverse Problems, Journal of Neuroscience Methods, Archives of Neurology . . .*
- Continue to develop software, libraries and plugins for our applications.

Brainstorm/BrainVisa/MedINRIA/3DSlicer – INSERM U751 Marseille, INSERM U842 Lyon, LENA, CHU Pitié Salpétrière and CEA-Neurospin, FieldTrip – Oostenveld (Donders Institute for Brain), MNE – Hämäläinen (Harvard), EEGLab – Delorme (Cerco Toulouse), Camino (UCL) . . . .

Relief of the so-called "Contemplative Athena" - Ca. 460 BC. Museum of the Acropolis in Athens