INRIA

INSTITUT NATIONAL DE RECHERCHE EN INFORMATIQUE ET EN AUTOMATIQUE

# *Project-Team parietal*

# *Modelling brain structure, function and variability based on high-field MRI data*

*Saclay - Île-de-France*

Theme : Computational Medicine and Neurosciences

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# 1. Team

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# 2. Overall Objectives

## 2.1. Parietal@Neuropsin

Bertrand Thirion joined INRIA Futurs/Saclay on November 1st, 2005, where he started to work with J.B.Poline (CEA, DSV, SHFJ) and two students, A. Tucholka and C. Damon. All of them moved to the novel Neurospin research Centre on January 1st, 2007. PARIETAL was created as an INRIA project team on July 1st, 2009. As an INRIA team, the originality of PARIETAL is that it is situated within the CEA/DSV high-field neuroimaging platform, Neurospin .

Neurospin is a leading neuroimaging centre that aims at producing high quality data through novel high field MRI scanners (http://www-dsv.cea.fr/neurospin/): 3T for humans (with a 32 channels antenna), 7T for humans (the only one in France), a 7T MRI scanner for rats, EEG EEG-MRI compatible and MEG equipment. By 2013, Neurospin should have the first 11.7T MRI scanner for humans in the world.

These formidable equipment will produce better quality and/or higher resolution images. While most current data analysis solutions might not allow neuroscientists to take fully advantage of high-quality data, PARIETAL commits itself to developing original methods to analyse anatomical and functional brain images in order to better capture their informative content. This can be achieved by introducing new modelling tools (mathematical morphology, shape analysis) statistical techniques (such as descriptive statistics, data mining, inference, model selection), and through the use of intensive computation to analyse the large volumes of data. PARIETAL also shares its tools with various developers of neuroscientific applications and neuroscientists (medINRIA, nipy project, functional toolbox of Brainvisa).

## 2.2. Highlights of the year

- PARIETAL has officially been created on July 1st, 2009. Moreover, the team has welcomed P. Fillard as a new permanent researcher.
- B. Thirion defended his Habilitation à diriger des recherches, entitled *Structural and probabilistic methods for group analysis in functional neuroimaging* on July 30th, at ENS Cachan doctoral school, in front a of a committee that comprised Yves Meyer, Alain Trouvé, Nicholas Ayache, Polina Golland, Steve Smith, Gilles Celeux and Olivier Faugeras.

# 3. Scientific Foundations

## 3.1. Information technology for neuroimaging

The goal of neuroimaging is to analyse brain structure and function through image-based information. This is challenging because of *i)* the intrinsic complexity of the brain structure , *ii)* the limitations of image-based observations (noise, artifacts, resolution), *iii)* the variability of brain structure across individuals, which makes subject-to-subject comparison a very difficult topic.
For these reasons, we propose to build advanced analytical tools with the best statistical, machine learning and image processing tools to extract relevant information from the data.

# 4. Application Domains

## 4.1. High-field neuroimaging

PARIETAL aims at proposing innovative techniques to study brain function through the analysis of anatomical and functional brain images. Although much work has been performed in this field since the mid 90's, and standard solutions have been proposed - in particular a procedure called statistical parametric mapping (SPM), which has been progressively elaborated from 1995 to ca 2005 and implemented in several software packages- some important issues still need to be addressed:

- First, quite surprisingly, standard frameworks do not fit with the way neuroscientists think of their data, that is the output of a highly modular and densely connected network, with a spatial layout that can be characterized through generic anatomical constraints.
- Second, in spite of the intuitive evidence -most of the blood oxygen-level dependent (BOLD) activity seen in functional Magnetic Resonance Imaging (fMRI) originates mainly from the cortex- analysis on the cortical surface is not a standard yet. Spatial models are thus quite coarse and not informed by the anatomy.
- Third, a crucial problem within the standard approach is that it still relies on poor approximations to deal with multiple comparison problems in statistical inference procedures. More work is needed in inter-subject modelling and reproducibility assessment.
- Finally, it is still necessary to understand and characterize the informative content of neuroimaging activation maps, beyond the traditional maps of activity. In particular, the neuroimaging community should benefit from the current advances in machine learning and computational neuroscience.

## 4.2. Parietal research axes

In order to address these questions, PARIETAL currently develops three main research axes:

1. Create some tools to understand brain functional architecture, i.e. the relationship between brain structure (anatomy) and its functional organization. For instance, there is currently much interest in modelling the links between anatomical connectivity, characterised through fibre tracts that connect distant regions, and functional connectivity, i.e. the correlation in the activity between distant brain regions across time. In particular, our aim is to extract the main salient brain structures that can be observed in neuroimaging datasets from several subjects. The final aim of this axis is to build atlases of the brain that will be based on multi-modal information (anatomical, functional and diffusion MRI).
2. The second axis is more classically related to the methodology for group analysis of neuroimaging data based on regression and classification techniques, thus trying to quantify and explain inter-subject differences, in particular when behavioral or genetic information are available to characterize the patients.
3. The third axis consists in finding some *coding schemes* that express how the brain processes encode some particular information, either in perception or action context. A very promising approach, called *inverse inference*, proceeds by predicting mental state from functional neuroimaging data. Moreover, the co-occurrence of signals modulation across regions, called *functional connectivity*, is a fundamental marker of brain functional organization that complements the description obtained through decoding approaches.

An important motivation for these developments is that the advent of high-field Magnetic Resonance Imaging (MRI) will allow an increase of image resolution and quality which should be used to enhance image understanding and analysis. As a member of Neurospin platform, PARIETAL aims at proposing novel analyzing techniques that will take advantage of the high-quality data.

# 5. Software

## 5.1. Nipy

**Participants:** Bertrand Thirion [Correspondant], Gaël Varoquaux, Merlin Keller, Vincent Michel, Alan Tucholka.

NIPY is a development framework in python for the neuroimaging community (publicly available at https://code.launchpad.net/nipy), developed mainly at Berkeley, Stanford, MIT and Neurospin. It is open to any contributors and aims at developing code and tools sharing.
Some parts of the library, are completely developed by PARIETAL and LNAO (CEA, DSV, Neurospin) to build algorithmic solutions for various issues in neuroimaging data analysis. All the nipy project is freely available, under BSD licence.
A coding sprint took place at Berkeley this year (March 21st-29th), with G. Varoquaux, B. Thirion and J.B. Poline.
The first release is expected in December 2009.

## 5.2. Mayavi

**Participant:** Gaël Varoquaux [Correspondant].

Mayavi is the most used scientific 3D visualization python software (http://mayavi.sourceforge.net/). It has been developed by Prabhu Ramachandran (IIT Bombay) and Gaël Varoquaux (PARIETAL, INRIA Saclay). Mayavi can be used as a visualization tool, through interactive command line or as a library. It is distributed under Linux through Ubuntu, Debian, Fedora and Mandriva, as well as in PythonXY and EPD Python scientific distributions. Mayavi is used by several software platforms, such as PDE solvers (fipy, sfepy), molecule visualization tools (http://pyrx.scripps.edu) and brain connectivity analysis tools (connectomeViewer).

## 5.3. Medinria

**Participant:** Pierre Fillard [Correspondant].

During the evaluation seminar of the INRIA's living science theme, the MedINRIA software (initiated by Pierre Fillard) was presented as a potential common platform to transfer towards clinics the methodological advances made at INRIA. After the recruitment of Pierre Fillard at PARIETAL, efforts were deployed to finalize the next generation of MedINRIA (aka Medular) Fig. 1 With the help of Olivier Clatz and Julien Wintz (both at ASCLEPIOS), and with the support of INRIA (with the ADT MedINRIA), we expect to release a beta version early next year. Technological transfer will follow, starting with the advances initially implemented in the former version of MedINRIA (image registration and diffusion MRI processing), completed by new progress in function MRI developed by PARIETAL.

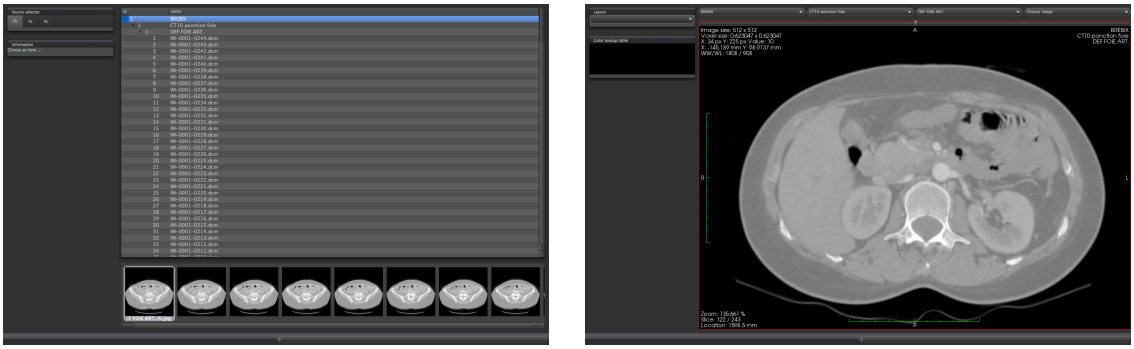

*Figure 1. Left: The database screen of MedINRIA 2.0 allows to browse into the dicom folders present on the doctor's computer and to preview images (bottom row of images). Right: the viewer screen is shown where most of the space is occupied by the image.*

The future of MedINRIA includes the proposal of an INRIA large scale initiative to federate the INRIA teams ASCLEPIOS, PARIETAL, ATHENA, VISAGES around software development, and with the proposal of a European project. The goal of this European project is to federate several European teams around a common toolkit for medical imaging software integration. Furthermore, this toolkit should be compliant with the US initiative called the CTK (Common ToolKit - http://www.commontk.org). Finally, possible connections between MedINRIA and the Brainvisa software are being investigated: MedINRIA can benefit from the database management of Brainvisa to process large sets of data, while Brainvisa can benefit from the clinical aspect of MedINRIA.

## 5.4. fMRI toolbox in Brainvisa

**Participants:** Bertrand Thirion [Correspondant], Lise Favre, Alan Tucholka.

PARIETAL is involved in the development of a functional neuroimaging analysis toolbox in *Brainvisa*: this project includes the implementation of standard toolkit for the analysis of fMRI data, which is an important building block of Neurospin software platform, but it is an interface for the diffusion of the methods developed in our team, in particular those developed in nipy. It benefits from the general infrastructure of *Brainvisa*, which has been set since 2001 by the LNAO laboratory (CEA, DSV, Neurospin) and several other teams from IFR 49 (http://www.ifr49.org/, http://brainvisa.info/).
The toolbox has been presented at *Journées Inter-Régionales de Formation en NeuroImagerie*, Marseille, May 25-29, at a session organized by LNAO, Paris, November 16-20, and at HBM conference [23].

# 6. New Results

## 6.1. Joint modelling of anatomical and functional features from neuroimaging data

**Participants:** Bertrand Thirion, Alan Tucholka, Pierre Fillard.

In this research axis, PARIETAL as performed or participated to several contributions that aim at better characterizing the anatomical structure of the brain, but also at unveiling the relationships that might exist between anatomical and functional information.

### *6.1.1. Modelling the anatomical connectivity of the brain: Global Tractography using an Adaptive Spin Glass Model*

Tractography consists in recovering the main fibre tracts in the brain white matter, starting from the local information conveyed by diffusion MRI.

We have introduced a novel framework for global diffusion MRI tractography inspired from a previously proposed spin glass model [32]. The entire white matter fascicle map is parametrized by pieces of fibers called spins. Spins are encouraged to move and rotate to align with the main fiber directions, and to assemble into longer chains of low curvature. Furthermore, they have the ability to adapt their quantity in regions where the spin concentration is not sufficient to correctly model the data. The optimal spin glass configuration is retrieved by an iterative minimization procedure, where chains are finally assimilated to fibers. As a result, all brain fibers appear as growing simultaneously until they merge with other fibers or reach the domain boundaries. In case of an ambiguity within a region like a crossing, the contribution of all neighboring fibers is used to determine the correct axon pathway.

This framework was tested on a Magnetic Resonance phantom representing a 45° crossing and a real brain dataset. Notably, the framework was able to retrieve the triple crossing between the callosal fibers, the corticospinal tract and the arcuate fasciculus (Fig. 2).

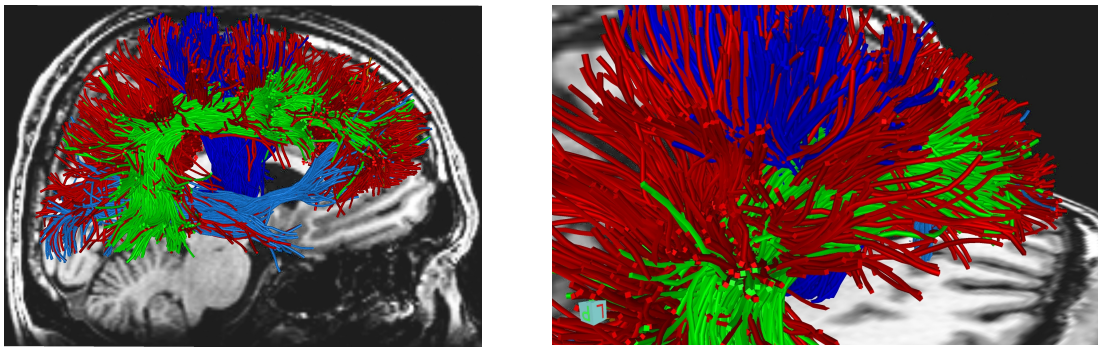

*Figure 2. Intersection between the corpus callosum (red), the corticospinal tract (dark blue), the arcuate fasciculus (green), the cingulum bundle (orange) and the inferior longitudinal fasciculus (light blue) revealed by spin glass tractography. This region is one of the most complex crossing area accessible at this resolution of diffusion images.*

### *6.1.2. Identification of brain sulci*

Sulci recognition is an essential topic for the accurate localization of brain structure and the comparison of anatomical information across subjects.

We have collaborated with researchers from LNAO (CEA, Neurospin) to the setting of automatic recognition algorithms. We have contributed to the study presented in [22] on the recognition of about 60 sulcal structures over a new T1 MRI database of 62 subjects. This was an extension of previous work that improved the localization model of sulci (SPAM). Given that this model is sensitive to the common space chosen during the group study, the focus of the current work consisted in refining this space using registration techniques. Reciprocally, knowing the sulcus-wise localization variability also benefits to normalization accuracy. This results in a consistent Bayesian framework to jointly identify and register sulci, with two complementary normalization techniques and their detailed integration in the model: a global rigid transformation followed by a piecewise rigid-one, sulcus after sulcus. This resulted in an improved sulci labeling quality, reaching a global recognition rate of 86%, together with a basic but robust registration technique.

### *6.1.3. Comparison of surface-based and volume-based analysis*

Being able to detect reliably functional activity in a population of subjects is crucial in human brain mapping, both for the understanding of cognitive functions in normal subjects and for the analysis of patient data. The usual approach proceeds by normalizing brain volumes to a common 3D template. However, a large part of the data acquired in fMRI aims at localizing cortical activity, and methods working on the cortical surface may provide better inter-subject registration than the standard procedures that process the data in 3D. Nevertheless, few assessments of the performance of surface-based (2D) versus volume-based (3D) procedures have been shown so far, mostly because inter-subject cortical surface maps are not easily obtained.

We have presented in [27] a systematic comparison of 2D versus 3D group-level inference procedures, by using cluster-level and voxel-level statistics assessed by permutation, in random effects (RFX) and mixed-effects analyses (MFX). We found that, using a voxel-level thresholding, and to some extent, cluster-level thresholding, the surface-based approach generally detects more, but smaller active regions than the corresponding volume-based approach for both RFX and MFX procedures (see Fig. 3). Finally we showed that surface-based supra-threshold regions are more reproducible by bootstrap.

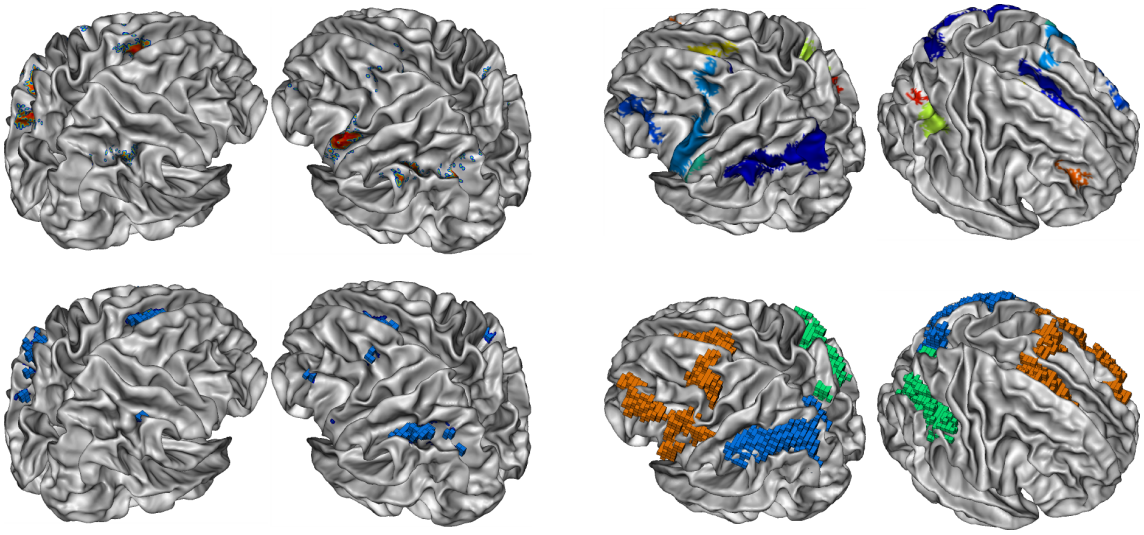

*Figure 3.* ***Left****: Surface-based (top line) versus volume-based (bottom line) voxel-level RFX group analysis results for the computation task.* ***Right****: Cluster-level RFX group analysis for the computation task on the surface (top line) and in the volume (bottom line).*

### *6.1.4. Joint analysis of anatomical and functional features*

We have taken part to a medical study where the joint analysis of functional and anatomical connectivity data was crucial to draw meaningful results [14]. We take this is as an incentive to provide more tools for the joint study of anatomical and functional features in neuroimaging studies.

The objective of the study was to examine the functional neuro-anatomy that could account for pure Gerstmann syndrome, which is the selective association of acalculia, finger agnosia, left-right disorientation, and agraphia. We used structural and functional neuroimaging at high spatial resolution in healthy subjects to seek a shared cortical substrate of the Grundstörung posited by Gerstmann, i.e., a common functional denominator accounting for this clinical tetrad. We construed a functional activation paradigm that mirrors each of the four clinical deficits in Gerstmann syndrome and determined cortical activation patterns. We then applied fiber tracking to diffusion tensor images and used cortical activation foci in the four functional domains as seed regions.

None of the subjects showed parietal overlap of cortical activation patterns from the four cognitive domains. In every subject, however, the parietal activation patterns across all four domains consistently connected to a small region of sub-cortical parietal white matter at a location that is congruent with the lesion in a well-documented case of pure Gerstmann syndrome. Our functional neuroimaging findings are not in agreement with Gerstmann's postulate of damage to a common cognitive function underpinning clinical semiology. Our evidence from intact functional neuro-anatomy suggests that pure forms of Gerstmann's tetrad do not arise from lesion to a shared cortical substrate but from intraparietal disconnection after damage to a focal region of sub-cortical white matter.

## 6.2. Group inference and comparison of neuroimaging data with genetic data

**Participants:** Bertrand Thirion, Jean-Baptiste Poline, Merlin Keller, Cécilia Damon.

### *6.2.1. A Bayesian model for brain activity detection*

To overcome the limitations of standard voxel-based testing methods, such as Statistical Parametric Mapping (SPM), we have introduced a new approach for fMRI group data analysis. This is a region-based procedure that aims at outlining global networks instead of local (voxel-based) analysis. Using a Bayesian model selection framework, the functional network associated with a certain cognitive task is selected according to the posterior probabilities of mean region activations, given a pre-defined anatomical parcellation of the brain. This approach enables us to control a Bayesian risk that balances false positives and false negatives, unlike the SPM-like approach, which only controls false positives. On data from a mental calculation experiment, it detected the functional network known to be involved in number processing, whereas the SPM-like approach either swelled or missed the different activation regions.

### *6.2.2. First joint analysis of neuroimaging and genetic data*

Imaging genetic studies linking functional MRI data and Single Nucleotide Polyphormisms (SNPs) data may face a dire multiple comparisons issue. In the genome dimension, genotyping DNA chips allow to record of several hundred thousands values per subject, while in the imaging dimension an fMRI volume may contain 50k voxels. Finding the brain and genome regions that may be involved in this link entails a huge number of hypotheses, hence a drastic correction of the statistical significance of pairwise relationships, which in turn reduces crucially the sensitivity of statistical procedures that aims at detecting the association. It is therefore desirable to set up as sensitive techniques as possible to explore where in the brain and where in the genome a significant link can be detected, while correcting for family-wise multiple comparisons (controlling for false positive rate).

In neuroimaging, the problem has been addressed during the past last 15 years with a numerous methods and software. The most popular tests developed in neuroimaging are testing in a statistical map for either the voxel intensity, or the size or mass of clusters defined by thresholding the statistical map, with permutation-based statistical validation. In the analysis of SNP data, a number of techniques have been designed as well. Most are based on the idea that the combination of p-values found at adjacent SNPs will be more significant and more biologically relevant than considering the SNPs independently.

We are working, in collaboration with V.Frouin (CEA, Neurospin) on a simple test for imaging genetic data (voxel x SNPs) based on the idea that we wish to detect contiguous brain regions linked to neighbour SNPs on the genome. The method detects clusters defined by a threshold in the product (four-dimensional) data-set, and calibrates the null hypothesis using permutations. While computationally intensive, the technique is conceptually simple, corrects for the multiple comparisons in both the imaging and the genetic dimensions, accounts for the spatial structure of the data (correlation of the imaging data and the linkage disequilibrium of the genetic data. We are currently evaluating this approach on a data-set that includes 94 subjects for which fMRI and SNP data.

## 6.3. Brain decoding techniques

**Participants:** Bertrand Thirion, Vincent Michel, Gaël Varoquaux.

Traditional inference in neuroimaging consists in describing the fluctuations of brain activity related to the modification of a stimulation parameter (a functional contrast). There might exist a relationship that relates functional contrasts and brain states. Inferring functional contrasts from a certain dataset is known as *inverse inference*. The quality of this inference is easily characterized by a correct classification rate if the target variable belongs to some finite set. Such estimation of is usually carried out using classifiers.

### *6.3.1. Classification and decoding*

We have used classification techniques to study various brain systems:

First we compared brain activation in two different tasks: eye saccades and mental computation. Throughout the history of mathematics, concepts of number and space have been tightly intertwined. We tested the hypothesis that cortical circuits for spatial attention contribute to mental arithmetic in humans. We trained a multivariate classifier algorithm to infer the direction of an eye movement, left or right, from the brain activation measured in the posterior parietal cortex. Without further training, the classifier then generalized to an arithmetic task. Its left versus right classification could be used to sort out subtraction versus addition trials, whether performed with symbols or with sets of dots. These findings are consistent with the suggestion that mental arithmetic co-opts parietal circuitry associated with spatial coding. [11]

We also applied these techniques to study the mental representation of quantities, assessing e.g. the number of points that were perceived and mentally processed by some subjects. We could find that some brain regions are particularly important to encode the quantity information when presented either as a set of dots or as a symbolic number [10].

We were less successful in applying these techniques to a pleasantness experiment [12]. We observed that in that case, traditional data analyses were more sensitive than classification-based analysis.

### *6.3.2. Regularized regression approach*

In some cases, the information $y$ that has to be predicted is a continuous variable (such as a reaction time or a number); then it can be predicted through regression techniques. We have presented a novel method for regularized regression and apply it to the prediction of a behavioural variable from brain activation images [25]. In the context of neuroimaging, regression or classification techniques are often plagued by the curse of dimensionality, due to the extremely high number of voxels and the limited number of activation maps. A commonly used solution is regularization of the weights used in the parametric prediction function. To solve the difficult issue of choosing the correct amount of regularization in the model, we have proposed a Bayesian framework, with efficient model specification and evaluation techniques to balance adaptiveness and sparsity.

We have thus introduced an adaptive mixture regularization that generalizes previous approaches. Based on a Variational Bayes estimation framework, our algorithm is robust to over-fitting and more adaptive than other regularization methods. Results on both simulated and real data show the accuracy of the method in the context of brain activation images [25].

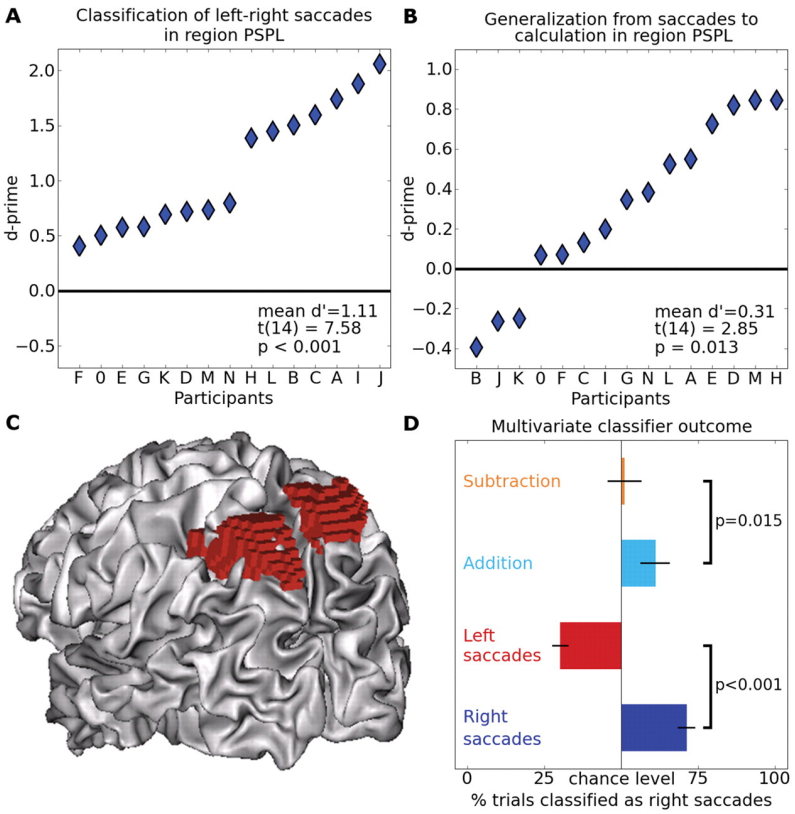


*Figure 4. Results of the joint decoding of left/right saccades versus additions/subtractions. A) Classification performance (classification index d') for each participant in the saccades task (participants are sorted according to d'). (B) Classification performance (d') per participant for generalization of the classifier trained on left/right saccades to subtraction/addition trials. (C) Voxel clusters in left and right posterior parietal region that resulted from the saccade localizer task and served as region of interest for the classifier, rendered on the white matter/gray matter boundary. (D) Percentages of trials classified as right saccades for subtraction (orange), addition (light blue), and left and right saccades (red and dark blue, respectively).*

### 6.3.3. Extracting resting-state networks with Independent Component Analysis

Spatial Independent Component Analysis (ICA) is an increasingly used data-driven method to analyze functional Magnetic Resonance Imaging (fMRI) data. To date, it has been used to extract meaningful patterns without prior information. However, ICA is not robust to mild data variation and remains a parameter-sensitive algorithm. The validity of the extracted patterns is hard to establish, as well as the significance of differences between patterns extracted from different groups of subjects.

PARIETAL has introduced an innovative approach for ICA data analysis, [15], [28]: This approach builds on a generative model of the fMRI group data to introduce a probabilistic ICA pattern-extraction algorithm, called CanICA (Canonical ICA). This approach includes an explicit noise model and identifies noise and signal of interest subspace automatically, with an automatic calibration of the parameters. The group level model is built through canonical correlation analysis, and identifies the group-reproducible data subspace before performing ICA. We have compared our method to state-of-the-art multi-subject fMRI ICA methods and shown that the features extracted are more reproducible [28].

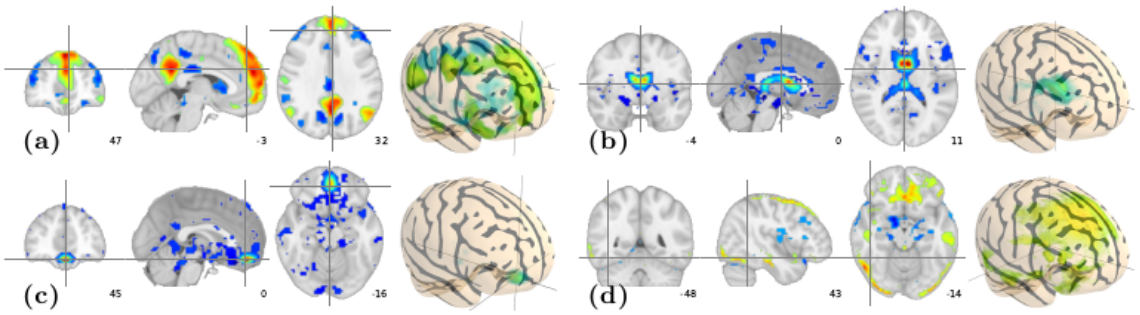


*Figure 5. Example of various ICA maps extracted from a resting-state data (a) a known functional networks (default mode network), (b) a ventricular component that displays mainly cardiac/respiratory signals, (c) and (d) physiological noise and motion components.*

### 6.3.4. connectivity analysis

The correlation between the activity of distant regions may be an important marker of the disruption of certain cognitive networks in patient populations. This measure can provide important information for characterizing the impact of various diseases on brain function, especially when only some sub-networks show a differential effect across populations.

Technically, this analysis requires unbiased measure of functional connectivity (correlation between distant regions) based on the time courses observed in fMRI datasets, and adequate statistical procedures to detect significant differences across individuals.

PARIETAL is actively collaborating with psychiatrists to release adapted modelling and statistical analysis tools, and help them to reach meaningful conclusions from their data. This is illustrated in fig. 6, with an ongoing study that addresses the differences between schizophrenic and normal subjects in a task that implies memory processing.

### 6.3.5. Retinotopic mapping

Pushing the resolution of neuroimaging data is an important issue and it is a major incentive to turn to high-field neuroimaging.

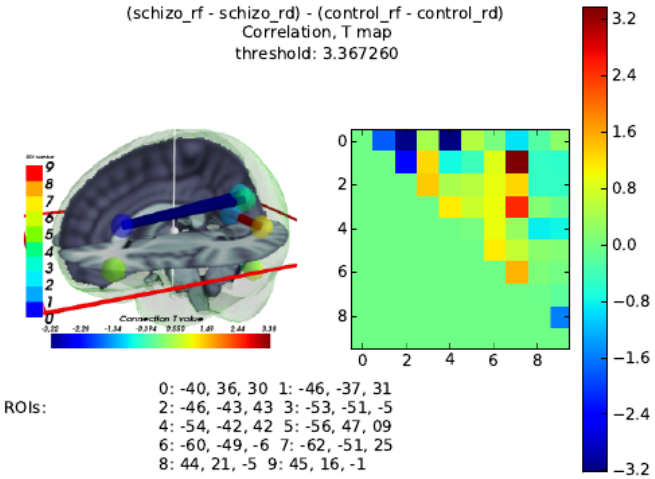


*Figure 6. Exploring functional connectivity differences between different populations of subjects. We have compared the correlation in the BOLD response of distant regions for two different cognitive tasks (noted here rf and rd), and found that the correlation difference is larger in a control group than in schizophrenic subjects when we consider specifically the fronto-parietal region.*

In 2009, PARIETAL researchers have performed the first acquisition of functional images on a 7T scanner in France. The result is qualitatively satisfactory (see fig. 7). This image reveals the functional organisation of visual regions at a $1.5mm$ resolution. This will be useful to decode the content of these images.

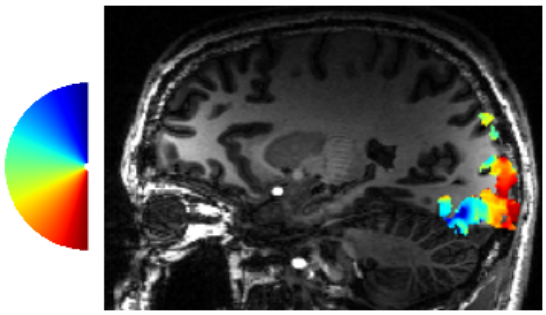

*Figure 7. Result of the first fMRI data acquisition in France: the spatially resolved $(1.5mm^3)$ retinotopic organization of the primary visual cortex.*

# 7. Other Grants and Activities

## 7.1. National Actions

**Participants:** Bertrand Thirion, Vincent Michel, Alexandre Gramfort, Pierre Fillard, Gaël Varoquaux.

### 7.1.1. Vimagine

**Vimagine** is an accepted ANR blanc project (2008-2012), which aims at building a novel view on the retinotopic organization of the visual cortex, based on MEG and MRI. Vimagine should open the way to understanding the dynamics of brain processes for low-level vision, with an emphasis on neuropathologies. This project is leaded by S. Baillet ( MMiXT, CNRS UPR640 LENA, Pitié-Salpêtrière), in collaboration with M.Clerc, O. Faugeras (INRIA Sophia-Antipolis, Odyssée) and J. Lorenceau(LPPA, CNRS, Collège de France). The fMRI part of the project will be done by PARIETAL, and will consist in a study of spatially resolved retinotopic maps at the mm scale, the decoding of retinotopic information and the comparison of retinotopy with sulco-gyral anatomy.

### 7.1.2. Karametria

**KaraMetria** is an ANR lead by Alexis Roche (LNAO) and Pierre Fillard (PARIETAL) whose goal is to develop new methods for feature-based morphometry (FBM) as opposed to voxel-based morphometry (VBM). In VBM, a subject or group of subjects is compared to another group of subjects based on the grey values of their MR images only. The inconvenient is that the interpretation of a change in grey-value is rather unclear (what are we detecting?). Conversely, in KaraMetria we propose to rely on anatomically well-defined features such as the gyri and sulci, the white matter fibers, or other brain internal structures such as the grey nuclei, where the detection of a change of shape is easier to interpret. Practically, our aim is to develop a registration framework able to produce a spatial transformation mapping at the same time all anatomical features of one subject onto the anatomical features of another. This transformation can then be used to build atlases of features, such as sulci or fibers, which are not available yet. Those atlases, in turn, can be used as a reference to compare individuals and determine if they statistically differ from a normal population and if yes, where and how they differ. A study on depressed teenagers lead by a clinical partner (INSERM UMR 797) will serve as proof of concept for the proposed framework. The actors of KaraMetria are the INRIA teams PARIETAL and ASCLEPIOS, the LNAO, the MAP5 (University Paris 5) and the INSERM UMR 797. The project will start in January 2010 for a time period of 3 years (budget: 615Keuros).

### 7.1.3. Resting-State project

The **Resting-State project** is a joint INRIA-INSERM research project (2008-2010), leaded by B. Thirion, and dedicated to the study of the connectivity of the brain during resting state based on fMRI data. It is a collaborative project with INSERM U562, U678, the Alchemy INRIA Saclay team and LNAO (CEA, DSV, Neurospin).
It was launched in February 2008 in an INRIA-INSERM joint *young researchers* seminary. The post-doc of Gaël Varoquaux is funded by this project, and will consist in inferring the structure of the main resting-state networks of the brain and the modulation of this spontaneous activity in various experimental contexts.

### 7.1.4. Work groups

- PARIETAL is animating a working group on Classification, Statistics and fMRI imaging with SELECT and the LNAO team (CEA, DSV, Neurospin). One meeting per month took place in 2009 at Neurospin.
- J.B Poline leads a Neurospin research program on the study of genetics and neuroimaging data (Genim) at Neurospin. This group includes researchers from LNAO (CEA, DSV, Neurospin), PARIETAL, INSERM U562, INSERM U797, Supelec and CNG (Evry), with two meetings per month.

## 7.2. European actions

**Participants:** Jean-Baptiste Poline, Bertrand Thirion, Merlin Keller, Cécilia Damon.

IMAGEN is an Integrated Project funded by the European Commission in the 6th Framework Program LSH-2005-2.1.3-1: Neuroimaging (2007-2012): "Bridging genetics and neural function". J.B. Poline is involved as the responsible for the bio-informatics and bio-statistics work package, and directly fits with PARIETAL's research axes. Half of the PhD theses of M.Keller and C.Damon are funded by IMAGEN, given that their work will contribute to Imagen data analysis part.
Imagen consists in acquiring in 8 centers across Europe, neuroimaging (anatomical, functional and diffusion-weighted), genetic and behavioral data from teenagers, in order to find risk factors of addiction for this population. The database (2000 subjects) is stored and analysed at Neurospin, and handled by a team with three engineers (CEA, DSV, Neurospin) headed by J.B. Poline. In 2009, the databasing system was confronted with the massive arrival of 1000 datasets (neuroimaging and behavioural data), and a first batch of 500 genetic datasets. Quality assessment has been performed systematically on the data to ensure an homogeneous quality and meaningful subsequent analysis.

# 8. Dissemination

## 8.1. Scientific Community animation

### *8.1.1. Invited conferences*

**Participants:** Bertrand Thirion, Jean-Baptiste Poline.

- B.Thirion gave a presentation at the Frontiers of Science France-Taïwan workshop, June 21-23, Saint Malo.
- B. Thirion was invited to give a presentation at the MIT/CSAIL lab, Boston, on May 8th.
- J.-B. Poline was invited to teach to the 2009 SPM course.

### *8.1.2. Scientific animation*

**Participants:** Bertrand Thirion, Jean-Baptiste Poline, Pierre Fillard, Gaël Varoquaux.

- JB. Poline organized a workshop on Biostatistics for neuroimaging and genetic studies on March 13, Paris, as part of the Imagen project. B. Thirion gave a talk at this occasion (25 participants).
- A nipy coding sprint took place at Berkeley (21-29 March 2009) (15 participants); G. Varoquaux, B.Thirion and J.-B. Poline took part to it.
- B. Thirion took part to the INRIA-NIH symposium that took part at Rocquencourt, June 3-4.

### *8.1.3. Conference organization*

**Participants:** Gaël Varoquaux, Bertrand Thirion, Pierre Fillard.

#### *8.1.3.1. Scipy 2009*

Scipy 2009 conference: G. Varoquaux was the president of the scientific committee for the 8th international scipy conference (Caltech, August 2009) on scientific use of python language. Articles selected by a review committee are published on http://conference.scipy.org/proceedings/SciPy2009/

#### *8.1.3.2. fMRI workshop at MICCAI'2009*

B. Thirion was the main organizer, with A. Roche, P.Ciuciu (CEA, Neurospin) and T.Nichols (GSK) of the fMRI workshop at MICCAI 2009, that took place in London, 24 September (30 participants, 9 papers):

Functional MRI (fMRI) provides a unique view on brain activity, which is used both for a better understanding of brain functional anatomy and the assessment of various mental diseases. The analysis of fMRI data entails detection issues, in which it has to be decided whether certain regions shows an activity significantly correlated to some variables of interest. This problem can be formulated in a given individual dataset (in which case the variable of interest is the experimental paradigm) or in a multi-subject dataset (the variable of interest is then a behavioral, clinical, or genetic factor of interest). Moreover, this problem can be handled as a modeling problem when addressing the temporal structure of the BOLD response and various fluctuations observed in fMRI datasets, or when delineating brain regions, especially across individuals, as well as a statistical problem: for instance, a typical concern is to warrant a certain control over false positives (specificity) for a testing procedure, or to achieve an optimal compromise between sensitivity and specificity by using judicious decision statistics.

While some of these questions may be familiar to the medical imaging community, partly for historical reasons, the neuroimaging community has developed specific contributions to solve these issues, and all the questions mentioned above are still the object of active research. This workshop was an opportunity to discuss and evaluate several solutions that have been proposed to solve these questions, and to confront different points of view.

*8.1.3.3. Fibre cup at MICCAI'2009*

The emergence of numerous models and fiber tracking techniques during the last decade raises the need for a comprehensive comparison of available methods on a common ground truth dataset. Objectives of the Fiber Cup were threefold: 1) to provide a MR phantom containing a plethora of crossing, kissing, splitting and bending fiber configurations, 2) to offer a set of quantitative criteria for algorithm performance evaluation with online results, and 3) to attract many participants by organizing it as a contest during the MICCAI conference in London. Participants were asked to run their algorithms on the phantom dataset and return their results along with a 2-page paper summarizing their method for quantitative evaluation.

6 datasets were made available: 3 of resolution 3x3x3mm (image size: 64x64x3) and 3 b-values (650, 1500 and 2000), and 3 of resolution 6x6x6mm (image size: 64x64x1) and 3 b-values (650, 1500, 2650). Participants could use any of these datasets for the contest, but only one submission was taken into consideration.

Contest rules:

Participants were free to use any combination of available tools, or algorithms, that could help them to reach the best result. It may consists in a combination of preprocessing steps and tractography algorithms. Only manual drawing of the fibers was not allowed.

Results:

The contest was a success and we received 10 submissions from international groups, with a result quality ranging from poor to very good results. The most striking result is undoubtedly the evidence of a large disparity of results (Fig. 8). This large inter-method variability is in itself an very interesting finding as it shows how tractography is method-dependent. The best 3 methods were awarded a diploma during the conference. The Fiber Cup allowed to collect a database of results on the same dataset and to create a common reference to evaluate new algorithms. Thus, we expect the phantom and the comparison methodology to be used thoroughly by groups to evaluate new algorithms. A web application to submit tractography results and obtain instantly the scoring is being investigated.

## 8.2. Teaching

**Participants:** Bertrand Thirion, Jean-Baptiste Poline, Gaël Varoquaux.

- B. Thirion taught in the functional Neuroimaging course (EEG, MEG, fMRI) of MVA master2 (ENS Cachan), conjointly with T. Papadopoulos and M. Clerc (INRIA Odyssée).
- J.B. Poline is responsible for the master neuroimaging modules for Cogmaster (http://lumiere.ens.fr/~cogmaster/www/) and Paris XI medical physics mater.

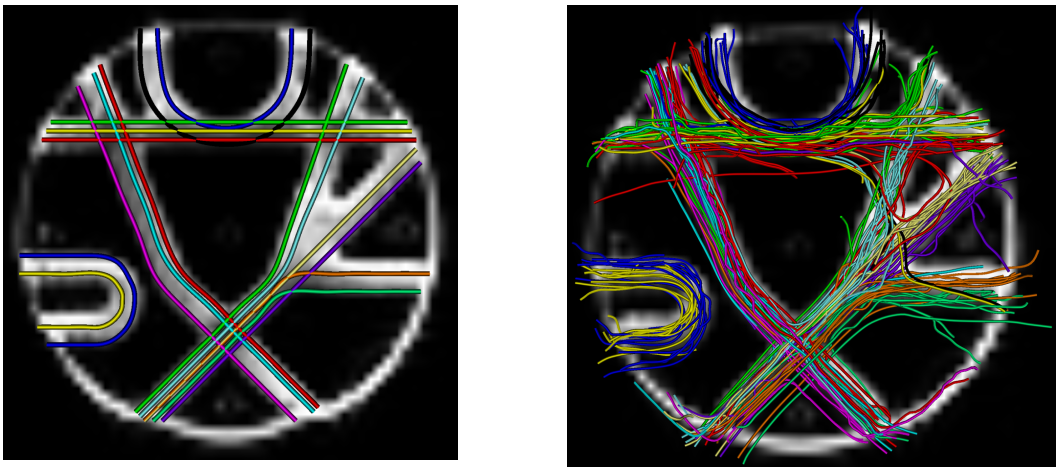

*Figure 8. Left: ground truth. Right: all 10 submissions overlapped. 16 fibers were selected for comparison For each fiber on the left image, 10 fibers with the exact same color are displayed, each fiber corresponding to a submission. This illustrates the inter-method variability.*

- J.B. Poline teaches regularly the basis of functional neuroimaging (ENSEA, BMS).
- B. Thirion gave two lectures at the Jirfni 2009 conference, Marseille, May 21-25.
- G. Varoquaux gave two lectures on scientific computing with Python at the SciPy training course, Passedena August 18-19.

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