
Activity Report 2011

# Project-Team PARIETAL

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

RESEARCH CENTER
**Saclay - Île-de-France**

THEME
**Computational Medicine and Neuro-sciences**

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# Project-Team PARIETAL

**Keywords:** Medical Images, Image Processing, Biological Images, Brain Computer Interface, Machine Learning

*Parietal is part of the Neurospin platform (CEA, DSV, I2BM) at Saclay.*

# 1. Members

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# 2. Overall Objectives

## 2.1. Overall Objectives

The research domain of Parietal is the design of statistical analysis and machine learning tools for the analysis of neuroimaging data. Such data have a limited signal-to-noise ratio, and generally display weakly contrasted structures. More importantly, due to the cost and complexity related to acquisition and analysis process, the estimation of reliable models is plagued by the lack of data, leading to little statistical power.

We try to solve these challenges by combining different modalities, by improving the crucial registration steps and by designing tools to assess efficiently the structure of the data. We design adapted learning algorithms to classify and make inference on these images; we also develop a framework to carry out statistical analysis in high-performance frameworks, such as clouds and grids.

# 3. Scientific Foundations

## 3.1. Human neuroimaging data and its use

Human neuroimaging consists in acquiring non-invasively image data from normal and diseased human populations. Magnetic Resonance Imaging (MRI) can be used to acquire information on brain structure and function at high spatial resolution.

- T1-weighted MRI is used to obtain a segmentation of the brain into different different tissues, such as gray matter, white matter, deep nuclei, cerebro-spinal fluid, at the millimeter or sub-millimeter resolution. This can then be used to derive geometric and anatomical information on the brain, e.g. cortical thickness.
- Diffusion-weighted MRI measures the local diffusion of water molecules in the brain at the resolution of 2mm, in a set of directions (30 to 60 typically). Local anisotropy, observed in white matter, can be used to yields a geometric of fiber tracts along which water diffusion occurs, and thus provides essential information of the connectivity structure of the brain.
- Functional MRI measures the blood-oxygen-level-dependent (BOLD) contrast that reflects neural activity in the brain, at a spatial resolution of 2 to 3mm, and a temporal resolution of 2-3s. This yields a spatially resolved image of brain functional networks that can be modulated either by specific cognitive tasks or appear as networks of correlated activity.
- Electro- and Magneto-encephalography (MEEG) are two additional modalities that complement functional MRI, as they directly measure the electric and magnetic signals elicited by neural activity, at the millisecond scale. These modalities rely on surface measurements and do not localize brain activity very accurately in the spatial domain.

## 3.2. High-field MRI

High field MRI as performed at Neurospin (7T on humans, 11.7T in 2013, 17.6T on rats) brings an improvement over traditional MRI acquisitions at 1.5T or 3T, related to to a higher signal-to-noise ratio in the data. Depending on the data and applicative context, this gain in SNR can be traded against spatial resolution improvements, thus helping in getting more detailed views of brain structure and function. This comes at the risk of higher susceptibility distortions of the MRI scans and signal inhomogeneities, that need to be corrected for. Improvements at the acquisition level may come from the use of new coils (such as the new 32 channels coil on the 7T at Neurospin – Fall 2011).

## 3.3. Technical challenges for the analysis of neuroimaging data

The first limitation of Neuroimaging-based brain analysis is the limited Signal-to-Noise Ratio of the data. A particularly striking case if functional MRI, where only a fraction of the data is actually understood, and from which it is impossible to observe by eye the effect of neural activation on the raw data. Moreover, far from traditional i.i.d. Gaussian models, the noise in MRI typically exhibits correlations and long-distance correlation properties (e.g. motion-related signal) and has potentially large amplitude, which can make it hard to distinguish from true signal on a purely statistical basis. A related difficulty is the *lack of salient structure* in the data: it is hard to infer meaningful patterns (either through segmentation or factorization procedures) based on the data only. A typical case is the inference of brain networks from resting-state functional connectivity data.

Regarding statistical methodology, neuroimaging problems also suffer from the relative paucity of the data, i.e. the relatively small number of images available to learn brain features or models, e.g. with respect to the size of the images or the number of potential structures of interest. This leads to several kinds of difficulties, known either as multiple comparison problems or curse of dimensionality. One possibility to overcome this challenge is to increase the amount of data by using images from multiple acquisition centers, at the risk of introducing scanner-related variability, thus challenging the homogeneity of the data. This becomes an important concern with the advent of cross-modal neuroimaging-genetics studies.

# 4. Application Domains

## 4.1. Application Domains

- Multi-modal brain image registration for the estimation of brain templates.
- Segmentation and dictionary learning techniques for the creation of functional brain atlases.
- Detection of statistical association between the genetic variability and brain characteristics.
- Detection of abnormal data in neuroimaging datasets and robust statistics.
- Evaluation of neuro-computational of vision based on functional neuroimaging experiments.
- Inference of brain states or cognitive variables based on activation patterns.
- Extraction of biomarkers from functional connectivity data for neurodegenrative diseases.

# 5. Software

## 5.1. 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).

See also the web page http://mayavi.sourceforge.net/ and the following paper http://hal.inria.fr/inria-00528985/en.

- Version: 3.4.0

## 5.2. Nipy

**Participants:** Bertrand Thirion [correspondant], Virgile Fritsch, Gaël Varoquaux.

Nipy is an open-source Python library for neuroimaging data analysis, 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). It is devoted to algorithmic solutions for various issues in neuroimaging data analysis. All the nipy project is freely available, under BSD licence. It is available in NeuroDebian.

See also the web page http://nipy.org.

- Version: 0.2

## 5.3. MedINRIA

**Participants:** Pierre Fillard [correspondant], Sergio Medina, Viviana Siless.

MedINRIA is a free collection of softwares developed within the ASCLEPIOS, ATHENA and VISAGES research projects. It aims at providing to clinicians state-of-the-art algorithms dedicated to medical image processing and visualization. Efforts have been made to simplify the user interface, while keeping high-level algorithms. MedINRIA is available for Microsoft windows XP/Vista, Linux Fedora Core, MacOSX, and is fully multithreaded.

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

- Version: 2.0

## 5.4. Scikit learn

**Participants:** Bertrand Thirion [correspondant], Gaël Varoquaux, Alexandre Gramfort, Fabian Pedregosa, Virgile Fritsch.

Scikit-learn is open-source a machine learning toolkit written in Python/C that provides generic tools to learn information for the classification of various kinds of data, such as images or texts. It is tightly associated to the scientific Python software suite (numpy/scipy) for which it aims at providing a complementary toolkit for machine learning (classification, clustering, dimension reduction, regression). There is an important focus on code quality (API consistency, code readability, tests, documentation and examples), and on efficiency, as the scikit-learn compares favorably to state-of-the-art modules developed in R in terms of computation time or memory requirements. Scikit-learn is currently developed by about 30 contributors, but the core developer team has been with the Parietal INRIA team at Saclay-Île-de- France since January 2010. The scikit-learn has recently become the reference machine learning library in Python.

- Version: 0.9
- Programming language: Python, C/Cython

# 6. New Results

## 6.1. A supervised clustering approach for fMRI-based inference of brain states

We propose a method that combines signals from many brain regions observed in functional Magnetic Resonance Imaging (fMRI) to predict the subject's behavior during a scanning session. Such predictions suffer from the huge number of brain regions sampled on the voxel grid of standard fMRI data sets: the curse of dimensionality. Dimensionality reduction is thus needed, but it is often performed using a univariate feature selection procedure, that handles neither the spatial structure of the images, nor the multivariate nature of the signal. By introducing a hierarchical clustering of the brain volume that incorporates connectivity constraints, we reduce the span of the possible spatial configurations to a single tree of nested regions tailored to the signal. We then prune the tree in a supervised setting, hence the name supervised clustering, in order to extract a parcellation (division of the volume) such that parcel-based signal averages best predict the target information. Dimensionality reduction is thus achieved by feature agglomeration, and the constructed features now provide a multi-scale representation of the signal. Comparisons with reference methods on both simulated and real data show that our approach yields higher prediction accuracy than standard voxel-based approaches. Moreover, the method infers an explicit weighting of the regions involved in the regression or classification task. See also [14] and Fig. 1.

## 6.2. Multiclass Sparse Bayesian Regression for fMRI-Based Prediction

Inverse inference has recently become a popular approach for analyzing neuroimaging data, by quantifying the amount of information contained in brain images on perceptual, cognitive, and behavioral parameters. As it outlines brain regions that convey information for an accurate prediction of the parameter of interest, it allows to understand how the corresponding information is encoded in the brain. However, it relies on a prediction function that is plagued by the curse of dimensionality, as there are far more features (voxels) than samples (images), and dimension reduction is thus a mandatory step. We introduce in this work a new model, called Multiclass Sparse Bayesian Regression (MCBR), that, unlike classical alternatives, automatically adapts the amount of regularization to the available data. MCBR consists in grouping features into several classes and then regularizing each class differently in order to apply an adaptive and efficient regularization. We detail these framework and validate our algorithm on simulated and real neuroimaging data sets, showing that it performs better than reference methods while yielding interpretable clusters of features. See also [13] and Fig. 2.

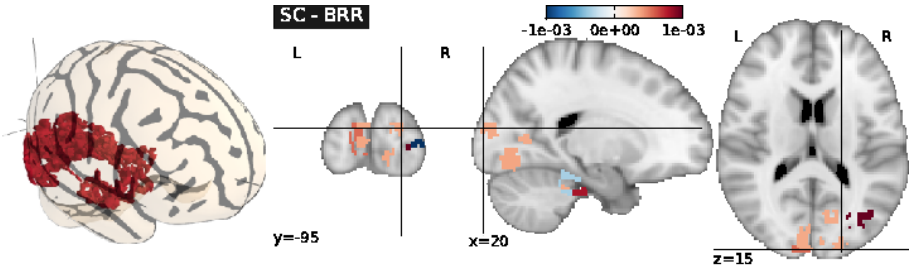


*Figure 1. Results for prediction of object size. Maps of weights found by supervised cut in the prediction of the size of an object. The proposed algorithm creates very interpretable clusters, compared to the reference methods that do not consider the spatial structure of the image.*

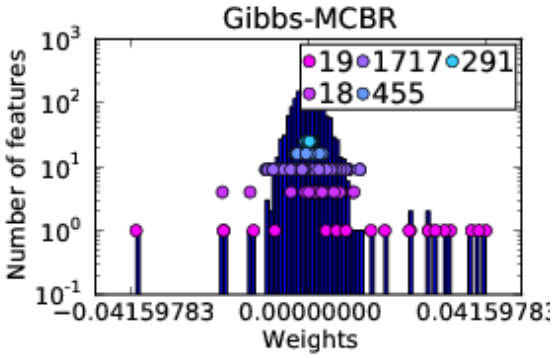


*Figure 2. Mental representation of size - Inter-subject analysis. Histogram of the weights found by Gibbs-MCBR, and corresponding class membership values (each color of dots represents a different class), for the inter-subject analyzes on the mental representation of size. We can see that Gibbs-MCBR creates clusters of informative and non informative voxels, and that the different classes are regularized differently, according to the relevance of the features within them.*

## 6.3. Total variation regularization for fMRI-based prediction of behaviour

While medical imaging typically provides massive amounts of data, the extraction of relevant information for predictive diagnosis remains a difficult challenge. Functional MRI (fMRI) data, that provide an indirect measure of task related or spontaneous neuronal activity, are classically analyzed in a mass-univariate procedure yielding statistical parametric maps. This analysis framework disregards some important principles of brain organization: population coding, distributed and overlapping representations. Multivariate pattern analysis, i.e., the prediction of behavioural variables from brain activation patterns better captures this structure. To cope with the high dimensionality of the data, the learning method has to be regularized. However, the spatial structure of the image is not taken into account in standard regularization methods, so that the extracted features are often hard to interpret. More informative and interpretable results can be obtained with the $\ell_1$ norm of the image gradient, a.k.a. its Total Variation (TV), as regularization. We apply for the first time this method to fMRI data, and show that TV regularization is well suited to the purpose of brain mapping while being a powerful tool for brain decoding. Moreover, this article presents the first use of TV regularization for classification. See also [15] and Fig. 3.

## 6.4. Quantitative evaluation of 10 tractography algorithms on a realistic diffusion MR phantom.

As it provides the only method for mapping white matter fibers in vivo, diffusion MRI tractography is gaining importance in clinical and neuroscience research. However, despite the increasing availability of different diffusion models and tractography algorithms, it remains unclear how to select the optimal fiber reconstruction method, given certain imaging parameters. Consequently, it is of utmost importance to have a quantitative comparison of these models and algorithms and a deeper understanding of the corresponding strengths and weaknesses. In this work, we use a common dataset with known ground truth and a reproducible methodology to quantitatively evaluate the performance of various diffusion models and tractography algorithms. To examine a wide range of methods, the dataset, but not the ground truth, was released to the public for evaluation in a contest, the "Fiber Cup". 10 fiber reconstruction methods were evaluated. The results provide evidence that: 1. For high SNR datasets, diffusion models such as (fiber) orientation distribution functions correctly model the underlying fiber distribution and can be used in conjunction with streamline tractography, and 2. For medium or low SNR datasets, a prior on the spatial smoothness of either the diffusion model or the fibers is recommended for correct modelling of the fiber distribution and proper tractography results. The phantom dataset, the ground truth fibers, the evaluation methodology and the results obtained so far will remain publicly available on http://www.lnao.fr See also [10].

## 6.5. Multi-subject dictionary learning (MSDL) to segment an atlas of brain spontaneous activity

Fluctuations in brain on-going activity can be used to reveal its intrinsic functional organization. To mine this information, we give a new hierarchical probabilistic model for brain activity patterns that does not require an experimental design to be specified. We estimate this model in the dictionary learning framework, learning simultaneously latent spatial maps and the corresponding brain activity time-series. Unlike previous dictionary learning frameworks, we introduce an explicit difference between subject-level spatial maps and their corresponding population-level maps, forming an atlas. We give a novel algorithm using convex optimization techniques to solve efficiently this problem with non-smooth penalties well-suited to image denoising. We show on simulated data that it can recover population-level maps as well as subject specificities. On resting-state fMRI data, we extract the first atlas of spontaneous brain activity and show how it defines a subject-specific functional parcellation of the brain in localized regions. See also [25] and Fif 4.

## 6.6. Functional brain imaging with M/EEG using structured sparsity in time-frequency dictionaries

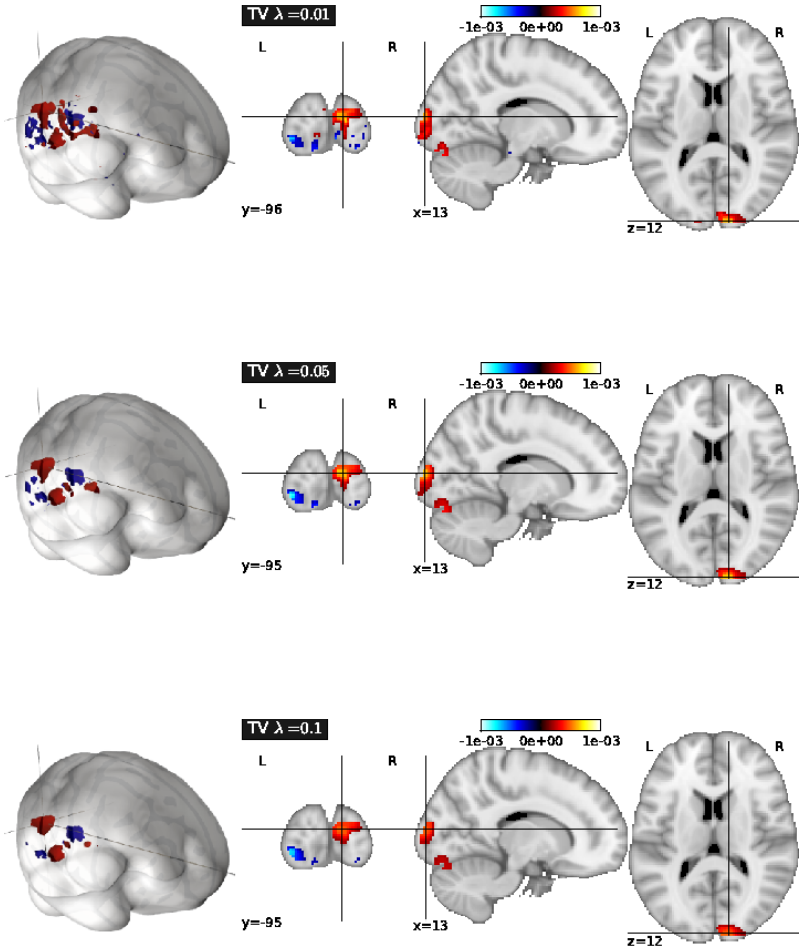


*Figure 3. Regression - Sizes prediction experiment - Inter-subject analysis. Maps of weights found by TV regression for various values of the regularization parameter λ. When λ decreases, the TV regression algorithm creates different clusters of weights with constant values. These clusters are easily interpretable, compared to voxel-based map (see below). The TV regression algorithm is very stable for different values of λ.*

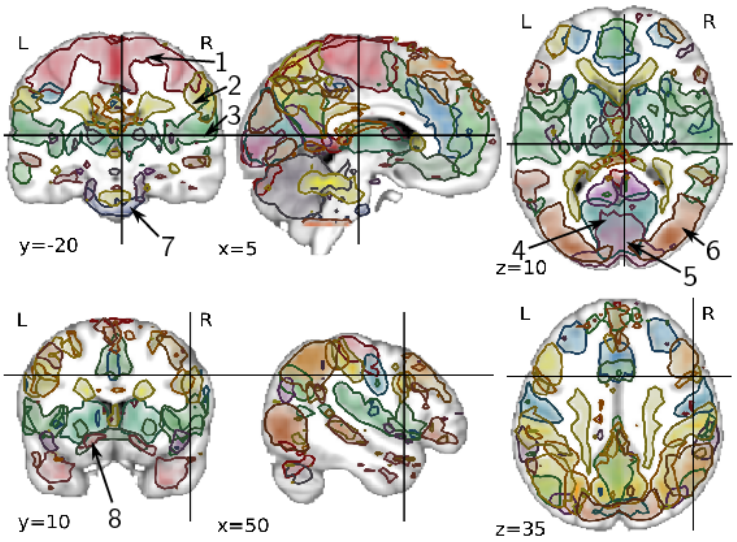


*Figure 4. Outlines at 33% of all dictionary elements estimated by MSDL for 2 different set of cutting planes. The motor system is divided in (**1**) dorsal, (**2**) lateral, and (**3**) ventral regions. Similarly, the visual system is divided in (**4**) a primary region centered on the Calcarine sulcus, overlapping with (**5**) a region centered on the striate cortex, and (**6**) extrastriate regions. (**7**), (**8**): fine details of the vascular system segmented in several maps.*

Magnetoencephalography (MEG) and electroencephalography (EEG) allow functional brain imaging with high temporal resolution. While time-frequency analysis is often used in the field, it is not commonly employed in the context of the ill-posed inverse problem that maps the MEG and EEG measurements to the source space in the brain. In this work, we detail how convex structured sparsity can be exploited to achieve a principled and more accurate functional imaging approach. Importantly, time-frequency dictionaries can capture the non-stationary nature of brain signals and state-of-the-art convex optimization procedures based on proximal operators allow the derivation of a fast estimation algorithm. We compare the accuracy of our new method to recently proposed inverse solvers with help of simulations and analysis of real MEG data. See also [22].

## 6.7. A probabilistic framework to infer brain functional connectivity from anatomical connections

We present a novel probabilistic framework to learn across several subjects a mapping from brain anatomical connectivity to functional connectivity, i.e. the covariance structure of brain activity. This prediction problem must be formulated as a structured-output learning task, as the predicted parameters are strongly correlated. We introduce a model selection framework based on cross-validation with a parametrization-independent loss function suitable to the manifold of covariance matrices. Our model is based on constraining the conditional independence structure of functional activity by the anatomical connectivity. Subsequently, we learn a linear predictor of a stationary multivariate autoregressive model. This natural parameterization of functional connectivity also enforces the positive-definiteness of the predicted covariance and thus matches the structure of the output space. Our results show that functional connectivity can be explained by anatomical connectivity on a rigorous statistical basis, and that a proper model of functional connectivity is essential to assess this link. See also [20] and Fig. 5.

*Figure 5. Identifying structural connections associated with the default mode network. With yellow is represented the lateral parietal cortex, green areas represent the posterior cingulate gyrus (PCC ), blue and light blue represent the medial prefrontal and orbito-frontal areas, respectively. The right model performs much better in terms of cross-validated data likelihood.*

## 6.8. M/EEG source reconstruction based on Gabor thresholding in the source space

Thanks to their high temporal resolution, source reconstruction based on Magnetoencephalography (MEG) and/or Electroencephalography (EEG) is an important tool for noninvasive functional brain imaging. Since the MEG/EEG inverse problem is ill-posed, inverse solvers employ priors on the sources. While priors are generally applied in the time domain, the time-frequency (TF) characteristics of brain signals are rarely employed as a spatio-temporal prior. In this work, we present an inverse solver which employs a structured sparse prior formed by the sum of $\ell_{21}$ and $\ell_1$ norms on the coefficients of the Gabor TF decomposition of the source activations. The resulting convex optimization problem is solved using a first-order scheme based on proximal operators. We provide empirical evidence based on EEG simulations that the proposed method is able to recover neural activations that are spatially sparse, temporally smooth and non-stationary. We compare our approach to alternative solvers based also on convex sparse priors, and demonstrate the benefit of promoting sparse Gabor decompositions via a mathematically principled iterative thresholding procedure. See also [24].

## 6.9. Multifractal Analysis of Resting State Networks in Functional MRI

It has been know for at least one decade that functional MRI time series display long-memory properties, such as power-law scaling in the frequency spectrum. Concomitantly, multivariate model-free analysis of spatial patterns, such as spatial Independent Component Analysis (sICA), has been successfully used to segment from spontaneous activity Resting-State Networks (RSN) that correspond to known brain function. As recent neuroscientific studies suggest a link between spectral properties of brain activity and cognitive processes, a burning question emerges: can temporal scaling properties offer new markers of brain states encoded in these large scale networks? In this work, we combine two recent methodologies: group-level canonical ICA for multi-subject segmentation of brain network, and wavelet leader-based multifractal formalism for the analysis of RSN scaling properties. We identify the brain networks that elicit self-similarity or multifractality and explore which spectral properties correspond specifically to known functionallyrelevant processes in spontaneous activity. See also [19].

## 6.10. Multi-scale Mining of fMRI Data with Hierarchical Structured Sparsity

Inverse inference, or "brain reading", is a recent paradigm for analyzing functional magnetic resonance imaging (fMRI) data, based on pattern recognition tools. By predicting some cognitive variables related to brain activation maps, this approach aims at decoding brain activity. Inverse inference takes into account the multivariate information between voxels and is currently the only way to assess how precisely some cognitive

information is encoded by the activity of neural populations within the whole brain. However, it relies on a prediction function that is plagued by the curse of dimensionality, as we have far more features than samples, i.e., more voxels than fMRI volumes. To address this problem, different methods have been proposed. Among them are univariate feature selection, feature agglomeration and regularization techniques. In this work, we consider a hierarchical structured regularization. Specifically, the penalization we use is constructed from a tree that is obtained by spatially constrained agglomerative clustering. This approach encodes the spatial prior information in the regularization process, which makes the overall prediction procedure more robust to inter-subject variability. We test our algorithm on a real data acquired for studying the mental representation of objects, and we show that the proposed algorithm yields better prediction accuracy than reference methods. See also [29] and Fig. 6.

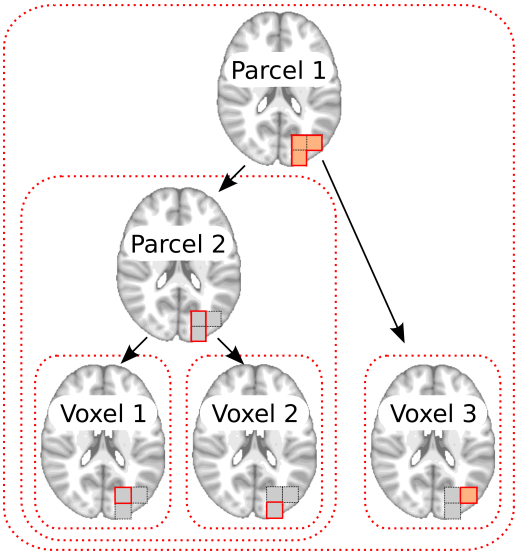


*Figure 6. Principle of structured sparsity: Example of a tree $\mathcal{T}$ when $p = 5$, with three voxels and two parcels. The parcel 2 is defined as the averaged intensity of the voxels $\{1, 2\}$, while the parcel 1 is obtained by averaging the parcel 2 and voxel 3. In red dashed lines are represented the five groups of variables that compose $\mathcal{G}$. If the group containing the parcel 2 is set to zero, the voxels $\{1, 2\}$ are also (and necessarily) zeroed out.*

## 6.11. Detecting Outlying Subjects in High-Dimensional Neuroimaging Datasets with Regularized Minimum Covariance Determinant

Medical imaging datasets used in clinical studies or basic research often comprise highly variable multi-subject data. Statistically-controlled inclusion of a subject in a group study, i.e. deciding whether its images should be considered as samples from a given population or whether they should be rejected as outlier data, is a challenging issue. While the informal approaches often used do not provide any statistical assessment that a given dataset is indeed an outlier, traditional statistical procedures are not well-suited to the noisy, high-dimensional, settings encountered in medical imaging, e.g. with functional brain images. In this work, we modify the classical Minimum Covariance Determinant approach by adding a regularization term, that ensures that the estimation is well-posed in high-dimensional settings and in the presence of many outliers. We show on simulated and real data that outliers can be detected satisfactorily, even in situations where the number of dimensions of the data exceeds the number of observations. See also [21] and Fig. 7.

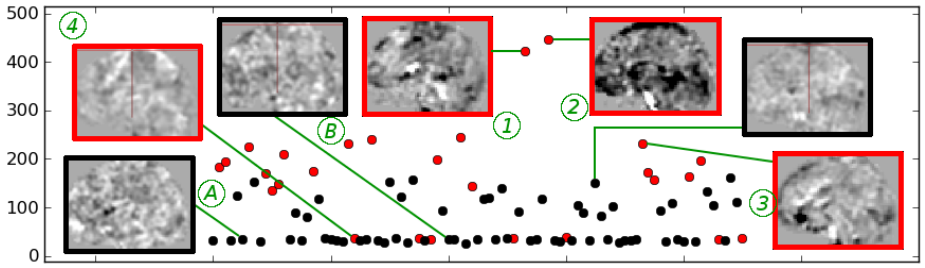


*Figure 7. Regularized-MCD-based Mahalanobis distances of a small sample. The higher the Mahalanobis distance, the higher the probability for an observation to be tagged as outlying. Points in red are outliers subjects according to the whole population.*

## 6.12. Connectivity-informed fMRI Activation Detection

A growing interest has emerged in studying the correlation structure of spontaneous and task-induced brain activity to elucidate the functional architecture of the brain. In particular, functional networks estimated from resting state (RS) data were shown to exhibit high resemblance to those evoked by stimuli. Motivated by these findings, we propose a novel generative model that integrates RS-connectivity and stimulus-evoked responses under a unified analytical framework. Our model permits exact closed-form solutions for both the posterior activation effect estimates and the model evidence. To learn RS networks, graphical LASSO and the oracle approximating shrinkage technique are deployed. On a cohort of 65 subjects, we demonstrate increased sensitivity in fMRI activation detection using our connectivity-informed model over the standard univariate approach. Our results thus provide further evidence for the presence of an intrinsic relationship between brain activity during rest and task, the exploitation of which enables higher detection power in task-driven studies. See also [23] and Fig 8.

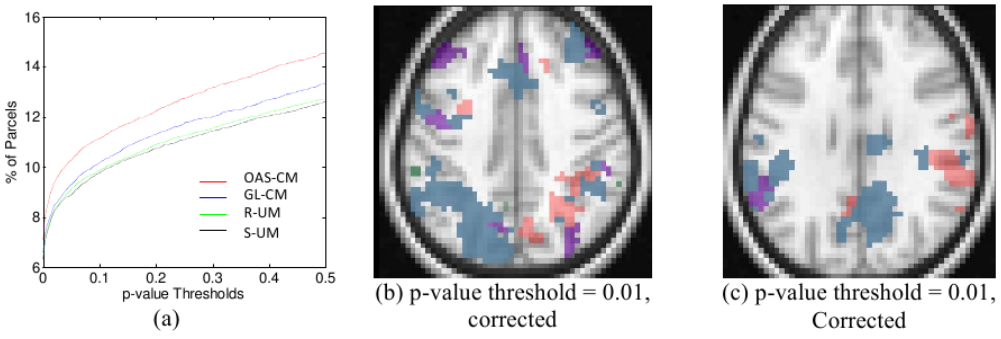


*Figure 8. Real data results. (a) rate of parcels with significant activation differences averaged across contrasts vs. p-value thresholds. (b) Parcels detected by contrasting computation against sentence processing task, and (c) auditory against visual task. Red = detected by only OAS- CM. Purple = detected by both OAS-CM and GL-CM. Blue = detected by all methods.*

## 6.13. Beyond brain reading: identify and predict with clustering and randomized sparsity

The prediction of behavioral covariates from functional MRI (fMRI) is known as brain reading. From a statistical standpoint, this challenge is a supervised learning task. The ability to predict cognitive states from new data gives a model selection criterion: prediction accuracy. While a good prediction score implies that some of the voxels used by the classifier are relevant, one cannot state that these voxels form the brain regions involved in the cognitive task. The best predictive model may have selected by chance non-informative regions, and neglected relevant regions providing duplicate information. In this contribution, we address the support *identification* problem. The proposed approach relies on randomization techniques which have been proved to be consistent for support recovery. To account for the spatial correlations between voxels, our approach makes use of a spatially constrained hierarchical clustering algorithm. Results are provided on simulations and a visual experiment. See Fig. 9.

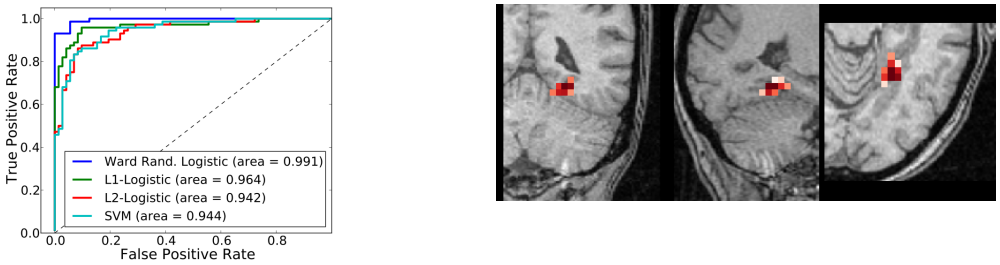


*Figure 9. Results on fMRI object recognition task (face vs. house). The selected voxels are in the Fusiform Face Area.* ***left.*** *Prediction Receiver-Operating Characteristic.* ***right.*** *Scores with Ward Randomized Logistic regression.*

## 6.14. Joint T1 and Brain Fiber Diffeomorphic Registration Using the Demons

Non-linear image registration is one of the most challenging tasks in medical image analysis. In this work, we propose an extension of the well-established diffeomorphic Demons registration algorithm to take into account geometric constraints. Combining the deformation field induced by the image and the geometry, we define a mathematically sound framework to jointly register images and geometric descriptors such as fibers or sulcal lines. We demonstrate this framework by registering simultaneously T1 images and 50 fiber bundles consistently extracted in 12 subjects. Results show the improvement of fibers alignment while maintaining, and sometimes improving image registration. Further comparisons with non-linear T1 and tensor registration demonstrate the superiority of the Geometric Demons over their purely iconic counterparts. See also [28] and Fig. 10.

# 7. Contracts and Grants with Industry

## 7.1. Grants with Industry: Abrain project

Participants : Bertrand Thirion [Correspondant] , Jean-Baptiste Poline.

*Figure 10.* ***Influence of the fiber weighting term on the registration accuracy.*** *Fibers of 11 subjects were overlapped after registration with the Geometric Demons for three values of the fiber weighting parameter. Corresponding fibers in different subjects share colors.*

Joint acquisition of neuroimaging and genetic data on large cohorts of subjects is a new approach used to assess and understand the variability that exists between individuals, and that has remained poorly understood so far. As both neuroimaging- and genetic-domain observations represent a huge amount of variables (of the order of $10^6$ ), performing statistically rigorous analyses on such amounts of data represents a computational challenge that cannot be addressed with conventional computational techniques. In this project, we plan to introduce grid and cloud computing techniques to address the computational challenge using cloud computing tools developed at INRIA (Kerdata team) and the Microsoft Azure cloud computing environment.

The ABrain project(2010-2013), funded by INRIA-Microsoft common lab.

# 8. Partnerships and Cooperations

## 8.1. Regional Initiatives

### *8.1.1. Digiteo: Hidinim Project*

**Participants:** Bertrand Thirion [Correspondant], Virgile Fritsch.

High-dimensional Neuroimaging– Statistical Models of Brain Variability observed in Neuroimaging

This is a joint project with Select project team and with SUPELEC Sciences des Systèmes (E3S), Département Signaux & Systèmes Électroniques (A. Tennenhaus).

Statistical inference in a group of subjects is fundamental to draw valid neuroscientific conclusions that generalize to the whole population, based on a finite number of experimental observations. Crucially, this generalization holds under the hypothesis that the population-level distribution of effects is estimated accurately. However, there is growing evidence that standard models, based on Gaussian distributions, do not fit well empirical data in neuroimaging studies.

In particular, Hidinim is motivated by the analysis of new databases hosted and analyzed at Neurospin that contain neuroimaging data from hundreds of subjects, in addition to genetic and behavioral data. We propose to investigate the statistical structure of large populations observed in neuroimaging. In particular, we will investigate the use of region-level averages of brain activity, that we plan to co-analyse with genetic and behavioral information, in order to understand the sources of the observed variability. This entails a series of modeling problems that we will address in this project: i) Distribution normality assessment and variables covariance estimation, ii) model selection for mixture models and iii) setting of classification models for heterogeneous data, in particular for mixed continuous/discrete distributions.

### 8.1.2. Digiteo: MMoVNI project

**Participants:** Bertrand Thirion [Correspondant], Pierre Fillard, Viviana Siless, Stéphanie Allassonnière, Hao Xu.

This is a joint project with CMAP http://www.cmapx.polytechnique.fr/~allassonniere/, for the 2010-2013 period.

Modelling and understanding brain structure is a great challenge, given the anatomical and functional complexity of the brain organ. In addition to this, there is a large variability of these characteristics among the population. To give a possible answer to these issues, medical imaging researchers proposed to construct a template image. Most of the time, these analysis only focus on one category of signals (called modality), in particular, the anatomical one was the main focus of research these past years. Moreover, these techniques are often dedicated to a particular problem and raise the question of their mathematical foundations. The MMoVNI project aims at building atlases based on multi-modal images (anatomy, diffusion and functional) data bases for given populations. An atlas is not only a template image but also a set of admissible deformations which characterize the observed population of images. The estimation of these atlases will be based on a new generation of deformation and template estimation procedures that builds an explicit statistical generative model of the observed data. Moreover, they enable to infer all the relevant variables (parameters of the atlases) thanks to stochastic algorithms. Lastly, this modeling allows also to prove the convergence of both the estimator and the algorithms which provides a theoretical guarantee to the results. The models will first be proposed independently for each modality and then merged together to take into account, in a correlated way, the anatomy, the local connectivity through the cortical fibers and the functional response to a given cognitive task. This model will then be generalized to enable the non-supervised clustering of a population. This leads therefore to a finer representation of the population and a better comparison for classification purposes for example. The Neurospin center, partner of this project, will allow us to have access to databases of images of high-quality and high-resolution for the three modalities: anatomical, diffusion and functional imaging. This project is expected to contribute to making neuroimaging a more reliable tool for understanding inter-subject differences, which will eventually benefit to the understanding and diagnosis of various brain diseases like Alzheimer's disease, autism or schizophrenia.

## 8.2. National Initiatives

### 8.2.1. ANR IRMGroup

**Participants:** Bertrand Thirion [Correspondant], Alexandre Gramfort, Michael Eickenberg.

This is a joint project with Polytechnique/CMAP http://www.cmap.polytechnique.fr/ : Stéphanie Allassonnière and Stéphane Mallat (2010-2013).

Much of the visual cortex is organized into visual field maps, which means that nearby neurons have receptive fields at nearby locations in the image. The introduction of functional magnetic resonance imaging (fMRI) has made it possible to identify visual field maps in human cortex, the most important one being the medial occipital cortex (V1,V2,V3). It is also possible to relate directly the activity of simple cells to an fMRI activation pattern and Parietal developed some of the most effective methods. However, the simple cell model is not sufficient to account for high-level information on visual scenes, which requires the introduction of specific semantic features. While the brain regions related to semantic information processing are now well understood, little is known on the flow of visual information processing between the primary visual cortex and the specialized regions in the infero-temporal cortex. A central issue is to better understand the behavior of intermediate cortex layers.

Our proposition is to use our mathematical approach to formulate explicitly some generative model of information processing, such as those that characterize complex cells in the visual cortex, and then to identify the brain substrate of the corresponding processing units from fMRI data. While fMRI resolution is still too coarse for a very detailed mapping of detailed cortical functional organization, we conjecture that some of the functional mechanisms that characterize biological vision processes can be captured through fMRI; in parallel we will push the fMRI resolution to increase our chance to obtain a detailed mapping of visual cortical regions.

### *8.2.2. ANR Vimagine*

**Participants:** Bertrand Thirion [Correspondant], Alexandre Gramfort, Michael Eickenberg, Fabian Pedregosa.

Vimagine is an 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, T. Papadopoulos (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.

### *8.2.3. ANR BrainPedia*

**Participants:** Bertrand Thirion [Correspondant], Yannick Schwartz, Virgile Fritsch.

BrainPedia is an ANR JCJC (2011-2015) which addresses the following point:

Neuroimaging produces huge amounts of complex data that are used to better understand the relations between brain structure and function. While the acquisition and analysis of this data is getting standardized in some aspects, the neuroimaging community is still largely missing appropriate tools to store and organise the knowledge related to the data. Taking advantage of common coordinate systems to represent the results of group studies, coordinate-based meta-analysis approaches associated with repositories of neuroimaging publications provide a crude solution to this problem, that does not yield reliable outputs and looses most of the data-related information. In this project, we propose to tackle the problem in a statistically rigorous framework, thus providing usable information to drive neuroscientific knowledge and questions.

## 8.3. International Initiatives

### *8.3.1. INRIA Associate Teams*

#### *8.3.1.1. CAPNEONATES*

Title: Analysis of structural MR and DTI in neonates

INRIA principal investigator: Pierre Fillard

International Partner:

Institution: University of Southern California (United States)

Laboratory: Image Lab at Children Hospital at Los Angeles

Researcher: Natasha Lepore

International Partner:

Institution: University of Pennsylvania (United States)

Laboratory: Penn Image Computing and Science Laboratory

Researcher: Caroline Brun

Duration: 2011 - 2013

See also: http://www.capneonates.org/

While survival is possible at increasingly lower gestational ages at birth, premature babies are at higher risk of developing mental disorders or learning disabilities than babies born at term. A precise identification of the developmental differences between premature and control neonates is consequently of utmost importance. Nowadays, the continuously improving quality and availability of MR systems makes it possible to precisely determine, characterize and compare brain structures such as cortical regions, or white matter fiber bundles. The objective of this project is to understand the developmental differences of premature versus normal neonates, using structural and diffusion MRI. This work will consist in identifying, characterizing and meticulously studying the brain structures that are different between the two groups. To do so, we propose to join forces between the Parietal team at INRIA and the University of Southern California. Parietal has a recognized expertise in medical image registration and in statistical analyses of groups of individuals. USC has a broad knowledge in MR image processing. In particular, the Children's Hospital at Los Angeles (CHLA), which is part of USC, is in the process of collecting a unique database of several hundreds of premature and normal neonates MR scans. This joint collaboration is consequently a unique chance of addressing key questions pertaining to neonatal and premature development. It will make it possible to elaborate new tools to analyze neonate MR images while tremendously increasing our knowledge of neuroanatomy at such an early stage in life.

### *8.3.2. INRIA International Partners*

- LIAMA http://www.nlpr.ia.ac.cn/jiangtz/: B.Thirion visited LIAMA (contact person: Shan Yu) in May and gave a presentation. We plan to develop come collaborations on fMRI data analysis and functional connectivity in the future.
- Donders institute https://sites.google.com/a/distrep.org/distrep/marcel-van-gerven: We share with M. van Gerven some interest on biological vision and on the use of fMRI to probe specific hypotheses related to computational models of vision. We hope to have a student in common in the future.
- Biomedical Image analysis group, Imperial College, London http://www.doc.ic.ac.uk/~dr/: We have started some joint work on the comparison of functional and anatomical connectivity using machine learning tools. We showed preliminary common contributions at IPMI and MLINI 2011.
- MIT, CSAIL http://www.csail.mit.edu/, P.Golland's group : we regularly visit each other and share common interests in the use of machine learning for neuroimaging, in the introduction of functional information into co-registration procedures, and in the study and comparison of anatomical and functional connectivity. We plan a common project and more visits for next year.

### *8.3.3. Visits of International Scientists*

Bernard Ng, from Biomedical Image and Signal Computing Laboratory, British Columbia University http://bisicl.ece.ubc.ca/, has visited Parietal from Sept 1st, 2010 to March 1st, 2011. The collaboration is about the introduction of functional connectivity into the analysis of fMRI activation data.

### *8.3.4. Participation In International Programs*

Parietal has taken part to the program INRIA@SiliconValley, and had a 18-months post-doc funded to work on the comparison of anatomical and fuctional connectivity (18 months, 2011-2013):

In this project, we would like to build probabilistic models that relates quantitatively the observations in anatomical and functional connectivity. For instance given a set of brain regions, the level of functional integration might be predicted by the anatomical connectivity measurement derived from the fibers in a given population of subjects. More generally, we will seek to extract latent factors explaining both connectivity measures across the population. Such models require specifically that a generative model is proposed to explain the observations in either domain, so that a meaningful and testable link is built between the two modalities. The inference problem can then be formulated as learning the coupling parameters that are necessary to model the association between modalities, and tested e.g. by assessing the ability of the learned model to generalize to new subjects. The aim is then to provide the mathematical and algorithmic tools necessary to

build a standardized model of brain connectivity informed by both modalities, associated with confidence intervals to take into account between subject variability. Such an atlas is a long-term project, that requires adequate validation on high-resolution data, but it will probably be tightly linked to this project.

# 9. Dissemination

## 9.1. Animation of the scientific community

- Organization of the euroscipy conference (August 25–28, G. Varoquaux): http://www.euroscipy.org/conference/euroscipy2011.
- Organisation of the Python in neuroscience workshop of the Euroscipy conference on August 29–30 (B.Thirion, G. Varoquaux): http://pythonneuro.sciencesconf.org
- Organization of the Machine learning in Neuroscience workshop in Marseille on November 8–9 (B.Thirion), http://mlni2011.sciencesconf.org/.
- Organization of a Workshop on Neuroimaging and genetics data analysis, November 30, Paris, is conjunction with ITMO Neurosciences, ITMO génétique and ITMO Technology pour la Santé (B.Thirion) https://itneuro.aviesan.fr.
- Co-organization of NIPS 2011 workshop on machine learning and interpretation in neuroimaging, Dec. 17–18 https://sites.google.com/site/mlini2011/
- Worskshops at the OHBM 2011 conference (J.B. Poline, B. Thirion, G. Varoquaux):
  - Group Inference for On-Going Activity: How to Compare Intrinsic Functional Connectivity
  - Imaging Genetics: Multivariate Analyses for Neural and Genetic Circuitry
  - Neuroimaging data sharing
- Course at scipy and scipy India by G. Varoquaux.

## 9.2. Teaching

Master MVA: Imagerie fonctionnelle cérébrale et interface cerveau machine, 12h, M2, ENS Cachan, France

Master biostatistiques: cours de biostatistique computationnelle, 6h, M2, Paris XI, France

CogMaster : Imagerie fonctionnelle, 24h, M2, ENS Ulm, France

# 10. Bibliography

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## Publications of the year

### Articles in International Peer-Reviewed Journal

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