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. Highlights

- Alexandre Gramfort got the *Prix de la meilleure thèse Interdisciplinaire* from the EADS foundation. http://www.fondation.eads.net/fr/laureats-prix-meilleure-these-2010 (his PhD was perform with ODYSSÉE/ATHENA project team).
- Alexandre Gramfort got a Young Investigator award at the Biomag 2010 conference http://www.biomag2010.org/images/stories/biomagawards.pdf
- Merlin Keller defended his PhD thesis, entitled *Sélection de modèles d'activation cérébrale en IRM* on January 11^{th}.
- Alan Tucholka defended his PhD thesis entitled *Prise en compte de l'anatomie cérébrale individuelle dans les études d'IRM fonctionnelle* on July 7^{th}.
- Cécilia Damon defended her PhD thesis entitled *Réduction de dimension et régularisation pour l'apprentissage statistique et la prédiction individuelle en IRMf* on September 29^{th}.
- Vincent Michel defended his PhD thesis, entitled *Understanding the visual cortex by using classification techniques* on December 15^{th}.

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. Modeling and Analysis of Neuroimaging data

- Analysis of structural connectivity data obtained from diffusion-weighted Magnetic Resonance Imaging.
- Modeling and analysis of functional Magnetic Resonance Imaging (fMRI) data.
- Statistical inference for small cohorts in neuroimaging.
- Search of biomarkers and diagnostic based on brain images.
- Comparison of genetic data with brain structure and activation; use of this information for better medical diagnosis.
- Analysis of brain functional connectivity in normal and diseased patients.
- Decoding of brain states from brain activation data.
- Modelling of vision based on fMRI signals in humans.

4.2. Parietal research axes

In order to address the above 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, characterized through fibre tracts that connect distant regions, and functional connectivity, i.e. the correlation in the activity between distant brain regions across time.
   This involves the accurate definition of structures of interest in either modality and the coregistration of such structures across individuals.
   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) without ignoring between-subject differences.
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.
   This involves the use of sophisticated statistical inference and machine learning tools.
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. MedINRIA

Participants: Pierre Fillard [Correspondant], Viviana Siless.

MedINRIA is a free collection of softwares developed within the ASCLEPIOS research project. 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://www-sop.inria.fr/asclepios/software/MedINRIA/.

- Version: 1.9
- Keywords: Medical Image Processing
- Patent: PCT/FR2006/000774
- License: Licence Propriétaire
- Type of human computer interaction: WxWidget
- OS/Middelware: Windows - Linux - MacOSX
- Required library or software: DTI Track (propriétaire)vtkINRIA3D (CeCillB)Baladin (propriétaire)DT-REFInD (propriétaire)
- Programming language: C++

5.2. Nipy

Participants: Bertrand Thirion [Correspondant], Gaël Varoquaux, Merlin Keller, Vincent Michel, Virgile Fritsch.

NIPY is a development framework in python for the neuroimaging community (publicly available at http://nipy.sourceforge.net/), 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 all kinds of neuroimaging data analysis problems. All the nipy project is freely available, under BSD license. The first release is expected in February 2011.

5.3. 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).

5.4. Scikit learn

Participants: Gaël Varoquaux [Correspondant], Fabian Pedregosa, Alexandre Gramfort, Vincent Michel, Virgile Fritsch, Bertrand Thirion.

Scikit learn is meant to be a easy-to-use and general-purpose machine learning in Python: scikits.learn is a Python module integrating classic machine learning algorithms in the tightly-knit world of scientific Python packages (numpy, scipy, matplotlib).

It aims at providing simple and efficient solutions to learning problems that are accessible to everybody and reusable in various contexts: machine-learning as a versatile tool for science and engineering. Current features implemented in scikit learn are:

- Solid: Supervised learning: classification, regression
- Work in progress: Unsupervised learning: Clustering, Gaussian mixture models, manifold learning, ICA
- Planed: Gaussian graphical models, matrix factorization

The license is Open source, commercially usable: BSD license.

Fore more information, demos, examples and code, please see http://scikit-learn.sourceforge.net/. The development of Scikit learn is funded through an INRIA ADT. Three coding sprints have taken place this year in Paris and Saclay: on March 3rd, July 26th and September 8-9th.

5.5. fMRI toolbox in Brainvisa

Participants: Bertrand Thirion [Correspondant], 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, October 27-29.
In 2010, a toolbox was also appended to brainvisa to encapsulate another software, Freesurfer.

6. New Results

6.1. Multi-modal and multi-structure image registration

Participants: Pierre Fillard [Correspondant], Viviana Siless.

In this project, we aim at adding neural fibers information to registration in order to lead a more plausible an accurate alignment of two anatomies.

In medical imaging studies, being able to compare images of hundreds of patients with images of hundreds of normal controls helps to detect abnormalities caused by pathologies. An abnormality can be seen as a deviation from the normal distribution of a structure.

Registration consists in finding a geometrical mapping from one subject's anatomy onto another one in order to align their structures and be able to compare them. Current registration algorithms align structures using solely information obtained from images.

In medical images, the information is mainly carried by the images contours, which is the interface between white and gray matter. Using only the information coming from the contours of the image, could lead to a misalignment of the internal structures, such as neural fibers, as they appear uniformly white in images.

Allowing registration algorithms to collect also information from the neural fibers and use it to constrain the registration will lead to a more plausible registration of anatomies as it will also force a proper fiber alignment.

This project is being developed in C++, using libraries such as ITK and VTK.

The project name is KaraMetria (see also https://sites.google.com/site/karametria/) and it is available at INRIAGForge https://gforge.inria.fr/projects/kmtk.

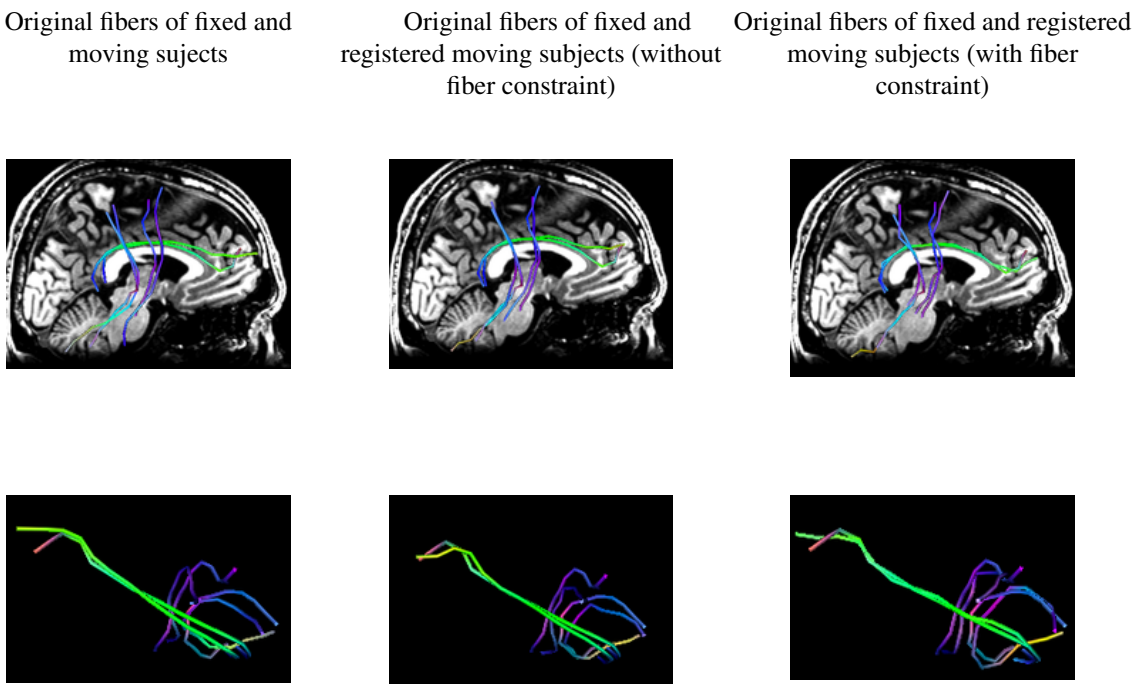

Figure 1. Above we show an example using two subjects. We called moving subject the subject we are registering, which the deformation transformation is applied to. We called fixed subject the one we are trying to align with.

6.2. Surface-based fMRI data analyzes improvement

Participants: Bertrand Thirion [Correspondant], Virgile Fritsch, Alan Tucholka.

Accuracy improvement of the functional activations found over the brain volume in fMRI experiments.

Surface-based analyses of fMRI data become more an more common since they take into account the subjects' anatomy in finding activated regions for a given task. Yet, those analyses are performed on data which actually are the projection of some original 3D data. Due to the folded shape of the human brain surface, some artifacts are hence being observed. For instance, a functional region can be projected on two different gyri, without being spread over the sulcus in-between. This can lead to some misinterpretations as the number of observed activated regions may be way too large. See for example in Fig. 2.

In this project, we aim at providing a better accuracy in the localization of the functional activations found over the brain volume, by using a volume analysis-driven correction. We want to establish a mapping between the activations found in the volume and over the brain surface, and hence try to address - or at least, point out - some errors which have potentially been introduced by the projection step. We could thus have the neuroscientists perform more reliable interpretations of the activation maps that they obtain.

Improving the functional activations localization accuracy should at the same time improve the accuracy of the group analysis results.

6.3. Parcel-based random effects analyses

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

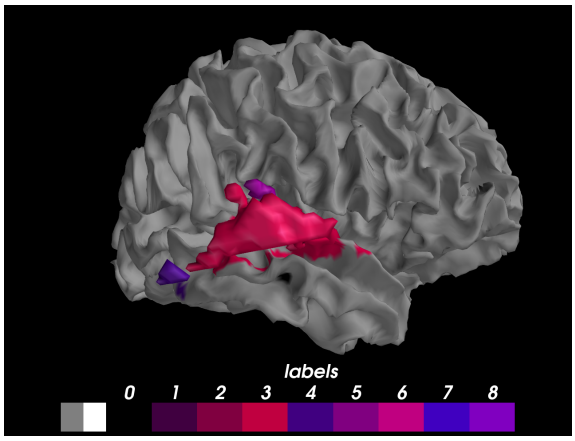

Figure 2. Active regions found in the brain volume and on the cortical surface in one control subject performing a sentence listening task. While a single, well defined activity focus is observed in the volume, several surrounding active patches are found on the cortical surface. This effect can be due to a lack of precision in the projection of fMRI data to the cortical surface. in this project, we aim at detecting this effect, and possibly correcting it.

Activation detection in functional Magnetic Resonance Imaging (fMRI) datasets is usually performed by thresholding activation maps in the brain volume or, better, on the cortical surface. However, basing the analysis on a site-by-site statistical decision may be detrimental both to the interpretation of the results and to the sensitivity of the analysis, because a perfect point-to-point correspondence of brain surfaces from multiple subjects cannot be guaranteed in practice. In this work, we propose a new approach that first defines anatomical regions such as cortical gyri outlined on the cortical surface, and then segments these regions into functionally homogeneous structures using a parcellation procedure that includes an explicit between-subject variability model, i.e. random effects. We show that random effects inference can be performed in this framework. Our procedure allows an exact control of the specificity using permutation techniques, and we show that the sensitivity of this approach is higher than the sensitivity of voxel- or cluster-level random effects tests performed on the cortical surface. An example is given in Fig. 3.

For more information, please see [24].

6.4. Accurate Definition of Brain Regions Position Through the Functional Landmark Approach

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

In many application of functional Magnetic Resonance Imaging (fMRI), including clinical or pharmacological studies, the definition of the location of the functional activity between subjects is crucial. While current acquisition and normalization procedures improve the accuracy of the functional signal localization, it is also important to ensure that functional foci detection yields accurate results, and reflects between-subject variability. Here we introduce a fast functional landmark detection procedure, that explicitly models the spatial variability of activation foci in the observed population. We compare this detection approach to standard statistical maps peak extraction procedures: we show that it yields more accurate results on simulations, and more reproducible results on a large cohort of subjects (see Fig 4). These results demonstrate that explicit functional landmark modeling approaches are more effective than standard statistical mapping for brain functional focus detection.

For more information, please see [25].

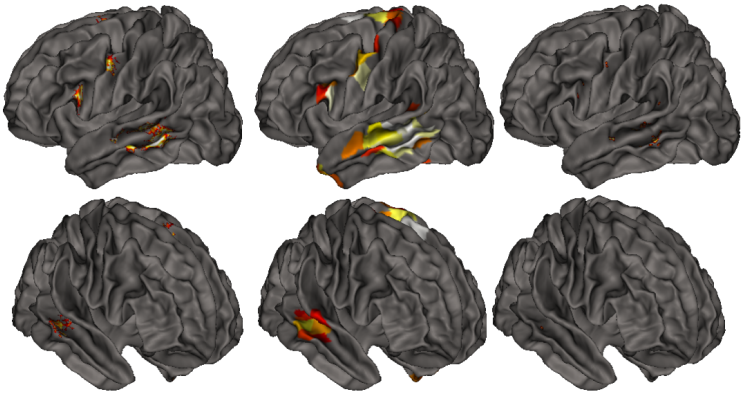

Figure 3. Outcome of the cluster-based (left), parcel-based (middle) and node-based (right) random effects analyses in the left(top) and right (bottom) hemisphere. All the maps are corrected at the p<0.05 cluster-, parcel- and voxel-level, respectively.

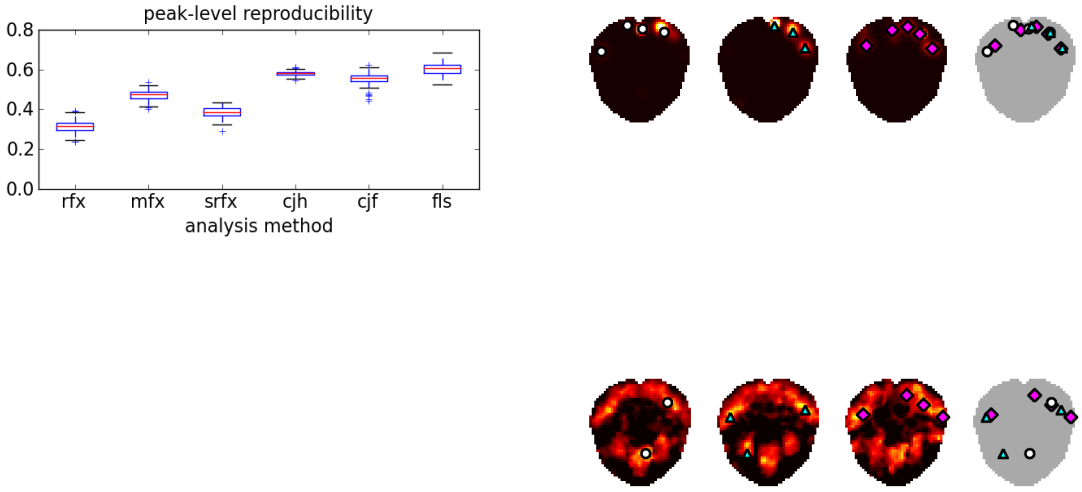

Figure 4. (left) Reproducibility index of peak position obtained in the jackknife subsampling procedure for several group analysis techniques. (Right) 2-dimensional example on an axial slice of the scatter of peaks as observed in 3 groups, using the Functional landmark approach (top), and the random effects statistic (bottom). Functional Landmark typically yield more stable results.

6.5. ICA-based sparse pattern recovery from fMRI

Participants: Gaël Varoquaux [Correspondant], Bertrand Thirion.

We formulate ICA as a sparse-recovery problem to give statistical control on the extracted brain maps based on a probabilistic model of the noise based on sole assumption that the interesting latent factors are sparsely-activated.

Patterns extracted by ICA from fMRI datasets display interpretable salient features, but also some background noise present to a varying degree in the different patterns.

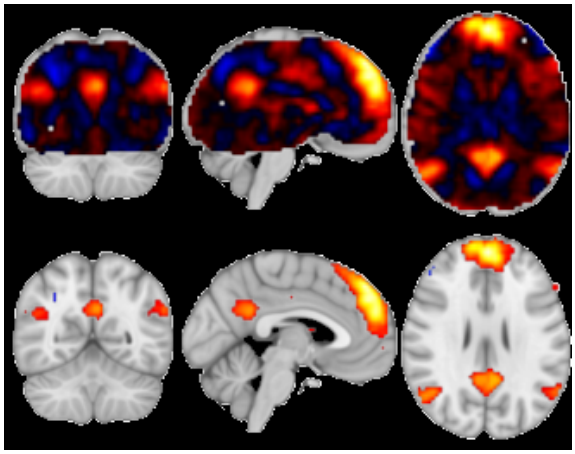

Figure 5. Segmenting the activated regions from a noisy ICA map

We introduce a paradigm-free probabilistic model of the fMRI signal based on the assumption that the interesting latent factors are spatially sparse. From this model, we show that a simple algorithm using ICA can recover sparse activated regions in the fMRI signal with an exact statistical control on specificity and sensitivity.

We shown on real fMRI data that, unlike other existing methods, this algorithm finds the same consistent regions when ran on degraded data. Also, we show that uninterpretable patterns are rejected under the null hypothesis, due to the assumption of sparsity.

For more information, please see [14] and [28].

6.6. Detection of brain functional-connectivity difference in post-stroke patients using group-level covariance modeling

Participants: Gaël Varoquaux [Correspondant], Pierre Fillard, Bertrand Thirion.

Functional brain connectivity, as revealed through distant correlations in the signals measured by functional Magnetic Resonance Imaging (fMRI), is a promising source of biomarkers of brain pathologies. However, establishing and using diagnostic markers requires probabilistic inter-subject comparisons. Principled comparison of functional-connectivity structures is still a challenging issue. We give a new matrix-variate probabilistic model suitable for inter-subject comparison of functional connectivity matrices on the cone of Symmetric Positive Definite (SPD) matrices endowed with a suitable metric. We show that this model leads to a new algorithm for principled comparison of connectivity coefficients between pairs of regions. We apply this model to comparing separately post-stroke patients to a group of healthy controls. We find neurologically-relevant

connection differences and show that our model is more sensitive that the standard procedure. To the best of our knowledge, these results are the first report of functional connectivity differences between a single-patient and a group and thus establish an important step toward using functional connectivity as a diagnostic tool.

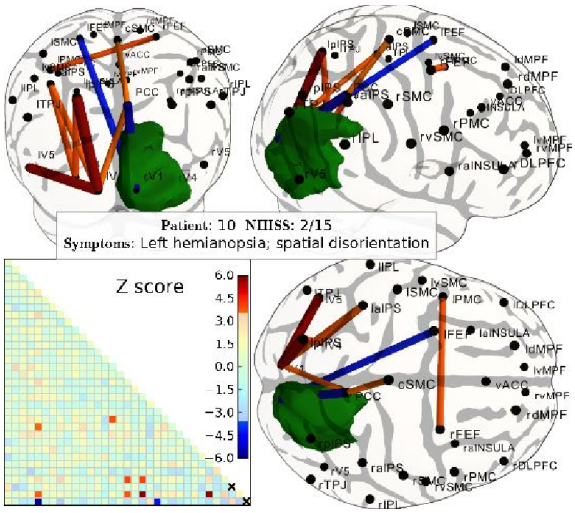

Figure 6. Significant differences on two patients ($p < 0.05$ uncorrected), represented as connections between regions: increased connectivity appears in red, and decreased in blue. The lesion, manually segmented from anatomical images, is represented in green. ROIs fully covered by a lesion are marked with a black cross on the correlation matrix.

For more information, please see [26].

6.7. Connectivity models using population prior

Participants: Gaël Varoquaux [Correspondant], Alexandre Gramfort, Bertrand Thirion.

Spontaneous brain activity, as observed in functional neuroimaging, has been shown to display reproducible structure that expresses brain architecture and carries markers of brain pathologies. An important view of modern neuroscience is that such large-scale structure of coherent activity reflects modularity properties of brain connectivity graphs. However, to date, there has been no demonstration that the limited and noisy data available in spontaneous activity observations could be used to learn full-brain probabilistic models that generalize to new data. Learning such models entails two main challenges: *i)* modeling full brain connectivity is a difficult estimation problem that faces the curse of dimensionality and *ii)* variability between subjects, coupled with the variability of functional signals between experimental runs, makes the use of multiple datasets challenging. We describe subject-level brain functional connectivity structure as a multivariate Gaussian process and introduce a new strategy to estimate it from group data, by imposing a common structure on the graphical model in the population. We show that individual models learned from functional Magnetic Resonance Imaging (fMRI) data using this population prior generalize better to unseen data than models based on alternative regularization schemes. To our knowledge, this is the first report of a cross-validated model of spontaneous brain activity. Finally, we use the estimated graphical model to explore the large-scale characteristics of functional architecture and show for the first time that known cognitive networks appear as the integrated communities of functional connectivity graph.

For more information, please see [27].

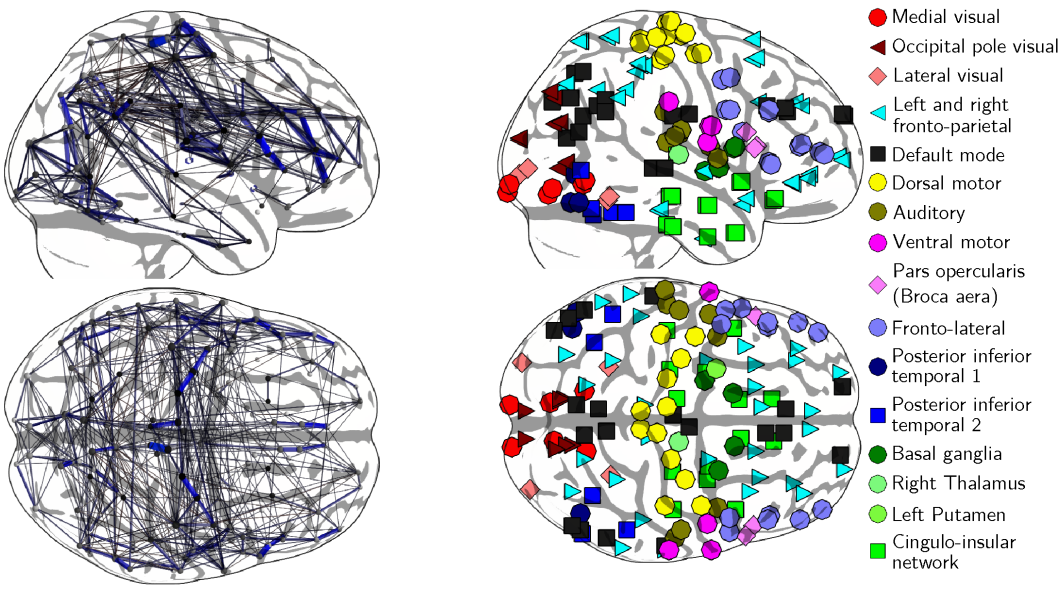

Figure 7. Functional-connectivity graph computed by ℓ_{21}-penalized estimation and corresponding communities. The graph displayed on the left is not thresholded, but on the top view, connections linking one region to its corresponding one on the opposite hemisphere are not displayed.

6.8. A supervised clustering approach for extracting predictive information from brain activation images

Participants: Vincent Michel [Correspondant], Jean-Baptiste Poline, Alexandre Gramfort, Bertrand Thirion.

It is a standard approach to consider that images encode some information such as face expression or biomarkers in medical images; decoding this information is particularly challenging in the case of medical imaging, because the whole image domain has to be considered a priori to avoid biasing image-based prediction and image interpretation. Feature selection is thus needed, but is often performed using mass-univariate procedures, that handle neither the spatial structure of the images, nor the multivariate nature of the signal. Here we propose a solution that computes a reduced set of high-level features which compress the image information while retaining its informative parts: first, we introduce a hierarchical clustering of the research domain that incorporates spatial connectivity constraints and reduces the complexity of the possible spatial configurations to a single tree of nested regions. Then we prune the tree in order to produce a parcellation (division of the image domain) such that parcel-based signal averages optimally predict the target information. We show the power of this approach with respect to reference techniques on simulated data and apply it to enhance the prediction of the subject's behaviour during functional Magnetic Resonance Imaging (fMRI) scanning sessions. Besides its superior performance, the method provides an interpretable weighting of the regions involved in the regression or classification task.

For more information, please refer to [20]. This is a joint work with the SELECT team.

6.9. Multi-Class Sparse Bayesian Regression for Neuroimaging data analysis

Participants: Vincent Michel [Correspondant], Bertrand Thirion.

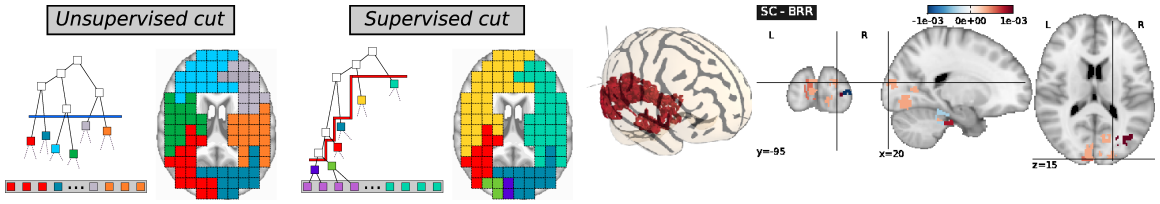

Figure 8. (Left) In the unsupervised cut approach, Ward's hierarchical clustering tree is divided into 6 parcels through a horizontal cut (blue); in the supervised cut approach, by choosing the best cut (red) of the tree given a score function ζ , we focus on some specific regions of the tree that are more informative. (Right) fMRI based study of mental representation of object size: we present a map of the predictive regions found by supervised cut. Unlike current alternatives, the proposed algorithm creates very interpretable clusters.

The use of machine learning tools is gaining popularity in neuroimaging, as it provides a sensitive assessment of the information conveyed by brain images. In particular, finding regions of the brain whose functional signal reliably predicts some behavioral information makes it possible to better understand how this information is encoded or processed in the brain. However, such a prediction is performed through regression or classification algorithms that suffer from the curse of dimensionality, because a huge number of features (i.e. voxels) are available to fit some target, with very few samples (i.e. scans) to learn the informative regions. A commonly used solution is to regularize the weights of the parametric prediction function. However, model specification needs a careful design to balance adaptiveness and sparsity. In this paper, we introduce a novel method, Multi-Class Sparse Bayesian Regression (MCBR), that generalizes classical approaches such as Ridge regression and Automatic Relevance Determination. Our approach is based on a grouping of the features into several classes, where each class is regularized with specific parameters. We apply our algorithm to the prediction of a behavioral variable from brain activation images. The method presented here achieves similar prediction accuracies than reference methods, and yields more interpretable feature loadings.

For more information, please refer to [21]. This is a joint work with the SELECT team.

6.10. Total Variation regularization enhances regression-based brain activity prediction

Participants: Vincent Michel [Correspondant], Alexandre Gramfort, Gaël Varoquaux, Bertrand Thirion.

While medical imaging typically provides massive amounts of data, the automatic extraction of relevant information in a given applicative context remains a difficult challenge in general. With functional MRI (fMRI), the data provide an indirect measurement of brain activity, that can be related to behavioral information. It is now standard to formulate this relation as a machine learning problem where the signal from the entire brain is used to predict a target, typically a behavioral variable. In order to cope with the high dimensionality of the data, the learning method requires a regularization procedure. Among other alternatives, L1 regularization achieves simultaneously a selection of the most predictive features. One limitation of the latter method, also referred to as Lasso in the case of regression, is that the spatial structure of the image is not taken into account, so that the extracted features are often hard to interpret. To obtain more informative and interpretable results, we propose to use the L1 norm of the image gradient, a.k.a., the Total Variation (TV), as regularization. TV extracts few predictive regions with piecewise constant weights over the whole brain, and is thus more consistent with traditional brain mapping. We show on real fMRI data that this method yields more accurate predictions in inter-subject analysis compared to voxel-based reference methods, such as Elastic net or Support Vector Regression.

For more information, please refer to [22].

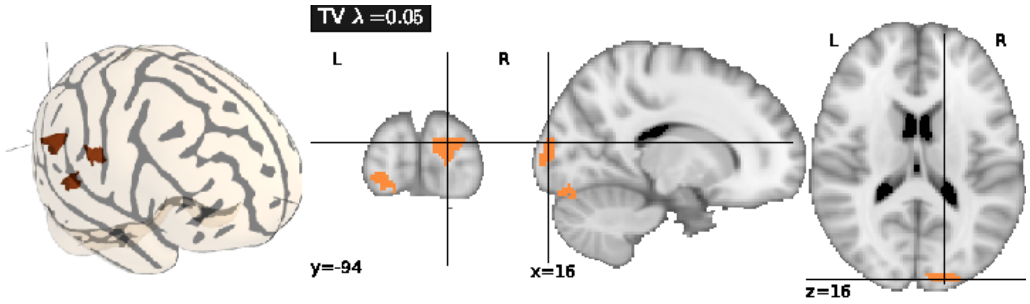

Figure 9. Mental representations of shape and size - Inter-subject analysis: voxels selected within one of the three main clusters by TV regression, in an object sizes prediction experiment. The prediction is very accurate and yields interpretable brain maps.

6.11. Tracking cortical activity from M/EEG using graph-cuts with spatiotemporal constraints

Participant: Alexandre Gramfort.

This work proposes to use magnetoencephalography (MEG) and electroencephalography (EEG) source imaging to provide cinematic representations of the temporal dynamics of cortical activations. Cortical activations maps, seen as images of the active brain, are scalar maps defined at the vertices of a triangulated cortical surface. They can be computed from M/EEG data using a linear inverse solver every millisecond. Taking as input these activation maps and exploiting both the graph structure of the cortical mesh and the high sampling rate of M/EEG recordings, neural activations are tracked over time using an efficient graph-cuts based algorithm. The method estimates the spatiotemporal support of the active brain regions. It consists in computing a minimum cut on a particularly designed weighted graph imposing spatiotemporal regularity constraints on the activations patterns. Each node of the graph is assigned a label (active or non-active). The method works globally on the full time-period of interest, can cope with spatially extended active regions and allows the active domain to exhibit topology changes over time. The algorithm is illustrated and validated on synthetic data. Results of the method are provided on two MEG cognitive experiments in the visual and somatosensory cortices, demonstrating the ability of the algorithm to handle various types of data.

For more information, please refer to [12].

6.12. Graph-Based Variability Estimation in Single-Trial Event-Related Neural Responses

Participant: Alexandre Gramfort.

Extracting information from multi-trial MEG or EEG recordings is challenging because of the very low signal-to- noise ratio (SNR), and because of the inherent variability of brain responses. The problem of low SNR is commonly tackled by averaging multiple repetitions of the recordings, also called trials, but the variability of response across trials leads to biased results and limits interpretability. This paper proposes to decode the variability of neural responses by making use of graph representations. Our approach has several advantages compared to other existing methods that process single-trial data: first, it avoids the a priori definition of a model for the waveform of the neural response, second, it does not make use of the average data for parameter estimation, third, it does not suffer from initialization problems by providing solutions that are global optimum of cost functions, and last, it is fast. We proceed in two steps. First, a manifold learning algorithm based on a graph Laplacian offers an efficient way of ordering trials with respect to the response variability, under the

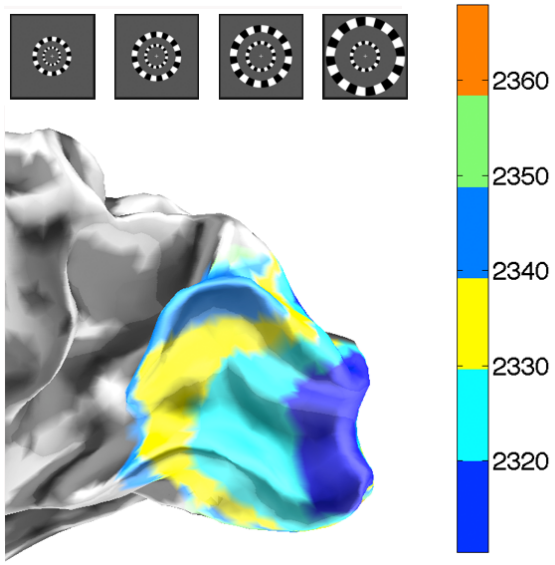

Figure 10. Tracking results obtained with visual stimulation of expanding checkerboard rings. The color codes for the initial apparition of activation during the time window considered, 2310 to 2367 ms after the stimulation. Tracking is performed from MEG data.

condition that this variability itself depends on a single parameter. Second, the estimation of the variability is formulated as a combinatorial optimization that can be solved very efficiently using graph cuts. Details and validation of this second step are provided for latency estimation. Performance and robustness experiments are conducted on synthetic data, and results are presented on EEG data from a P300 oddball experiment.

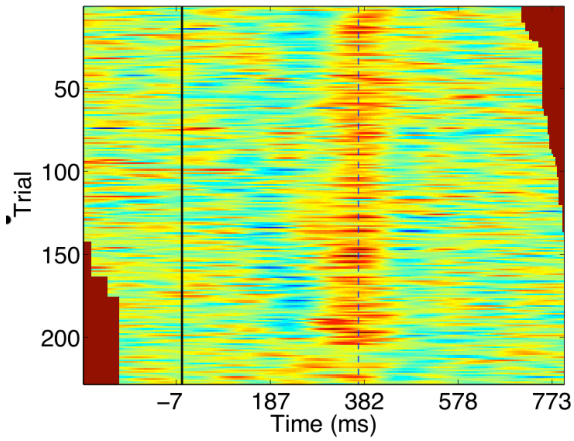

Figure 11. Lags correction on raster plot of time series. EEG data from an oddball paradigm.

For more information, please refer to [11].

6.13. Multi-condition M/EEG inverse modeling with sparsity assumptions: how to estimate what is common and what is specific in multiple experimental conditions

Participant: Alexandre Gramfort.

M/EEG inverse modeling with distributed dipolar source models and penalizations with sparsity inducing norms (e.g. L1 with MCE, L0 with FOCUSS, L2-L1) offer a way to select a set of active dipoles. Indeed, sparsity inducing norms lead to solutions where most of the sources are set to zero and the remaining non zero sources form the set of estimated active dipoles. When running cognitive studies multiple experimental conditions are usually involved and cognitive hypothesis classically consist in quantifying the difference between these conditions. The problem is that when a sparse inverse solver is used independently for each experimental condition, it happens that the selection of dipolar sources is not consistent across conditions, thus limiting further analysis. Even if all conditions share a common dipolar source, due to noise, it can happen that such solvers do not select exactly the same dipole but two neighboring ones. To circumvent this limitation, we propose in this contribution to run the inverse computation with all the experimental conditions simultaneously. We use a penalization that achieves a joint selection of active dipoles while estimating two parts in the reconstructed current distributions: a part that is common to all the different conditions and a part that is specific to each condition. The penalization used in the inverse problem is based on groups of L2-L1 norms. The optimization is achieved with iterative least squares (iterative L2 Minimum Norm) making the solver tractable on large datasets. The method is illustrated on toy data and validated on synthetic MEG data reproducing activations appearing for somesthesic finger stimulations. We call our solver SMC (Sparse Multi-Condition).

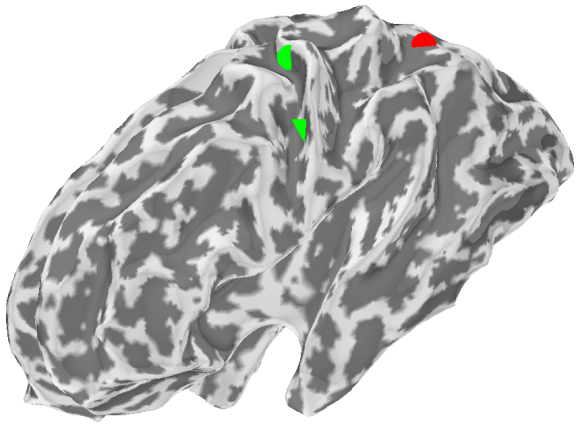

Figure 12. Source configuration with 2 specific generators in the primary somatosensory cortex (green sphere end green pyramid) and 1 common generator in the parietal cortex (red sphere)

For more information, please refer to [17].

6.14. OpenMEEG: opensource software for quasistatic bioelectromagnetics

Participant: Alexandre Gramfort.

BACKGROUND: Interpreting and controlling bioelectromagnetic phenomena require realistic physiological models and accurate numerical solvers. A semi-realistic model often used in practise is the piecewise constant conductivity model, for which only the interfaces have to be meshed. This simplified model makes it possible to use Boundary Element Methods. Unfortunately, most Boundary Element solutions are confronted with accuracy issues when the conductivity ratio between neighboring tissues is high, as for instance the scalp/skull conductivity ratio in electro-encephalography. To overcome this difficulty, we proposed a new method called the symmetric BEM, which is implemented in the OpenMEEG software. The aim of this paper is to present OpenMEEG, both from the theoretical and the practical point of view, and to compare its performances with other competing software packages.

METHODS: We have run a benchmark study in the field of electro- and magneto-encephalography, in order to compare the accuracy of OpenMEEG with other freely distributed forward solvers. We considered spherical models, for which analytical solutions exist, and we designed randomized meshes to assess the variability of the accuracy. Two measures were used to characterize the accuracy: the Relative Difference Measure and the Magnitude ratio. The comparisons were run, either with a constant number of mesh nodes, or a constant number of unknowns across methods. Computing times were also compared.

RESULTS: We observed more pronounced differences in accuracy in electroencephalography than in magnetoencephalography. The methods could be classified in three categories: the linear collocation methods, that run very fast but with low accuracy, the linear collocation methods with isolated skull approach for which the accuracy is improved, and OpenMEEG that clearly outperforms the others. As far as speed is concerned, OpenMEEG is on par with the other methods for a constant number of unknowns, and is hence faster for a prescribed accuracy level.

CONCLUSIONS: This study clearly shows that OpenMEEG represents the state of the art for forward computations. Moreover, our software development strategies have made it handy to use and to integrate with other packages. The bioelectromagnetic research community should therefore be able to benefit from OpenMEEG with a limited development effort.

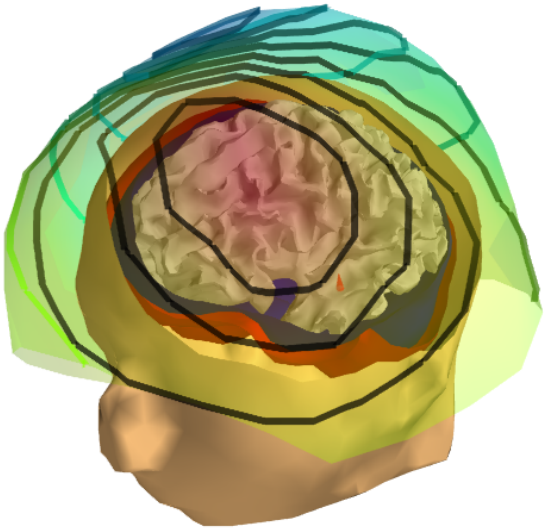

Figure 13. Magnetic field induced by a dipolar source on the left temporal cortex (in red). Computation is done with OpenMEEG and a 3-layer head model.

For more information, please refer to [13].

7. Contracts and Grants with Industry

7.1. AzureBrain project

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

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 Azure brain project(2010-2013), funded by INRIA-Microsoft common lab.

7.2. National Initiatives

7.2.1. Vimagine

Participants: Bertrand Thirion [Correspondant], Vincent Michel, Alexandre Gramfort, Gaël Varoquaux, Alan Tucholka.

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, 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.

7.2.2. Karametria

Participants: Pierre Fillard [Correspondant], Viviana Siless, Bertrand Thirion.

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 started in January 2010 for a time period of 3 years.

7.2.3. Digiteo: Hidinim Project

Participants: Bertrand Thirion, Virgile Fritsch, Jean-Baptiste Poline.

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.

7.2.4. ANR IRMGroup

Participants: Bertrand Thirion, Alexandre Gramfort.

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, as detailed next, 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.

7.2.5. Graph-based decoding CNRS project

Participants: Bertrand Thirion, Gaël Varoquaux.

This is a joint project with Sylvain Takerkart (CNRS/UMR 6193), Daniele Schon (CNRS/UMR 6193), and Liva Ralaivola (CNRS UMR 6166). The time span of the project is 2010-2011.

In this project, we develop new tools for fMRI decoding that specifically address the aforementioned pitfall by explicitly using the spatial information. These tools should broaden the range of applications of this technique and help better improve our understanding of brain functions. Two specific goals are set :

The first goal is methodological. We will demonstrate that we can integrate the information about the spatial locations of the voxels and their neighboring links in the fMRI decoding framework. For that purpose, we will use graphical models to represent spatial patterns of activation and develop graph-based kernels within a SVM framework in order to perform the classification.

The second goal is application-oriented. We will demonstrate that the outputs of the decoder can provide estimates of the robustness of a cortical representation. We will therefore scan two populations with fMRI, and show, using our graph-based decoding technique, that the anatomo-functional representation associated with the task is "stronger" in one population than in the other, thus allowing for finer discrimination.

7.2.6. MNoVNI

Participants: Bertrand Thirion, Pierre Fillard.

This is a joint project with S.Allassonnière (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 an 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 image (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.

7.3. European Initiatives

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 analyzed at Neurospin, and handled by a team with three engineers (CEA, DSV, Neurospin) headed by J.B. Poline. At the end of 2010, the databasing system contains about 1800 datasets (neuroimaging and behavioral data), and about 1000 genetic datasets. Quality assessment has been performed systematically on the data to ensure an homogeneous quality and meaningful subsequent analysis.

7.4. International Initiatives

We have developed collaboration with the following groups:

- University of South California (N. Lepore and C. Brun) http://www-rcf.usc.edu/~nlepore/:
  We are creating a collaborative project, in which we propose to develop a complete set of tools for the analysis of structural MR and DTI in neonates, and to compare our premature neonates to our controls. Both INRIA and USC have recently developed original approaches to medical image registration with which we are able to align different types of data such as T1-weighted images, diffusion images, white matter fibers, cortical surfaces or sulcal lines. Here we propose to compare premature neonates to normal newborns based on their MR data and the structures extracted from them: this involves the extraction and identification of those structures-of-interest, the construction of atlases (i.e., average representation of a group) of neonates structural MR (T1 and DTI) and the structures of interest, and a methodology for the statistical comparison of the two groups and the identification of effects of premature birth. Finally, those methodological advances will be further transferred into MedINRIA as a pediatric extension for clinical use.
- LIAMA http://www.nlpr.ia.ac.cn/jiangtz/:
  B.Thirion and Shan Yu (INRIA/LIAMA) visited each other in September/October. We plan to develop come collaborations on fMRI data analysis and functional connectivity in the future.
- Donders institute http://www.cs.ru.nl/~marcelge/students.html: 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://biomedic.doc.ic.ac.uk/: We have started to develop some joint work on the comparison of functional and anatomical connectivity using machine learning tools. We showed preliminary common contributions at the Connectivity workshop at MICCAI 2010 http://www.ccm.org.cn/index.php/mibc.
- fMRIB, Oxford http://www.fmrib.ox.ac.uk/: Through regular visit to each side of the Channel, we do collaborate on functional connectivity analysis, multivariate models and graphical model tools.
- MIT, CSAIL http://www.csail.mit.edu/: 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.

7.5. Exterior research visitors

Bernard Ng, from Biomedical Image and Signal Computing Laboratory, British Columbia University http://bisicl.ece.ubc.ca/, is visiting 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. Dissemination

8.1. Animation of the scientific community

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

- Euroscipy 2010 http://www.euroscipy.org/conference/eid/867, July 8-10: Gaël Varoquaux was one of the organisers of the conference.
- Jean-Baptiste Poline organized the annual meeting of IFR 49, on genetic/imaging aspects (December 17th).

- B. Thirion organized with Gaël Varoquaux, Sophia Achard, Habib Benali and Andréas Kleinschmidt a workshop on functional connectivity at Neurospin with people coming from different french neuroimaging places, and from Lausanne (November 17th).
- The parietal team was involved in the BCI workshop in Paris (may 25th) organized by TAO http://www.lri.fr/~gouypaic/BCImeetingReport.pdf.
- B.Thirion animated the jirfni 2010 advanced course on fMRI data analysis that took place at Marseille, 27-29 October.

8.2. Teaching

Participants: Bertrand Thirion, Jean-Baptiste Poline, Gaël Varoquaux, Pierre Fillard, Fabian Pedregosa, Alexandre Gramfort.

- B. Thirion taught in the functional Neuroimaging course (EEG, MEG, fMRI) of MVA master2 (ENS Cachan), conjointly with T. Papadopoulos, M. Clerc (INRIA Odyssée) and A. Gramfort http://www.math.ens-cachan.fr/version-francaise/formations/master-mva/.
- J.-B. Poline is responsible for the master neuroimaging modules for Cogmaster (http://lumiere.ens.fr/~cogmaster/www/) and Paris XI medical physics mater.
- J.B. Poline teaches regularly the basis of functional neuroimaging (ENSEA, BMS).
- P Fillard gave an MRI course at ESCPE Lyon (Ecole Sup. de Chimie, Physique, Electronique de Lyon).
- G.Varoquaux and F. Pedregosa gave several tutorial on scientific python at euroscipy 2010 http://www.euroscipy.org.
- A. Gramfort gave some master courses at MIMED master http://perso.telecom-paristech.fr/~angelini/MIMED/MIMED2010-2011.html.

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