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ACTIVITY
REPORT

Project-Team
MIND

Models and Inference for Neuroimaging Data

IN COLLABORATION WITH: CEA Neurospin

DOMAIN

Digital Health, Biology and Earth

THEME

Computational Neuroscience and
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Project-Team MIND

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Computer sciences and digital sciences

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- A3.4.1. – Supervised learning
- A3.4.2. – Unsupervised learning
- A3.4.4. – Optimization and learning
- A3.4.5. – Bayesian methods
- A3.4.6. – Neural networks
- A3.4.8. – Deep learning
- A6.2.4. – Statistical methods
- A6.2.6. – Optimization
- A9.2. – Machine learning
- A9.3. – Signal analysis
- A9.7. – AI algorithmics

Other research topics and application domains

- B1.2. – Neuroscience and cognitive science
 - B1.2.1. – Understanding and simulation of the brain and the nervous system
 - B1.2.2. – Cognitive science
 - B1.2.3. – Computational neurosciences
- B2.6.1. – Brain imaging

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2 Overall objectives

The MIND team, which finds its origin in the PARIETAL team, is uniquely equipped to impact the fields of statistical machine learning and artificial intelligence (AI) in service to the understanding of brain structure and function, in both healthy and pathological conditions.

AI with recent progress in statistical machine learning (ML) is currently aiming to revolutionize how experimental science is conducted by using data as the driver of new theoretical insights and scientific hypotheses. Supervised learning and predictive models are then used to assess predictability. We thus face challenging questions like *Can cognitive operations be predicted from neural signals?* or *Can the use of anesthesia be a causal predictor of later cognitive decline or impairment?*

To study brain structure and function, cognitive and clinical neuroscientists have access to various neuroimaging techniques. The MIND team specifically relies on non-invasive modalities, notably on one hand, magnetic resonance imaging (MRI) at ultra-high magnetic field to reach high spatial resolution and, on the other hand, electroencephalography (EEG) and magnetoencephalography (MEG), which allow the recording of electric and magnetic activity of neural populations, to follow brain activity in real time. Extracting new neuroscientific knowledge from such neuroimaging data however raises a number of methodological challenges, in particular in inverse problems, statistics and computer science. The MINDproject aims to develop the theory and software technology to study the brain from both cognitive to clinical endpoints using cutting-edge MRI (functional MRI, diffusion weighted MRI) and MEG/EEG data. To uncover the most valuable information from such data, we need to solve a large panoply of inverse problems using a hybrid approach in which machine or deep learning is used in combination with physics-informed constraints.

Once functional imaging data is collected the challenge of statistical analysis becomes apparent. Beyond the standard questions (Where, when and how can statistically significant neural activity be identified?), MIND is particularly interested in addressing driving effect or the *cause* of such activity in a given cortical region. Answering these basic questions with computer programs requires the development of methodologies built on the latest research on causality, knowledge bases and high-dimensional statistics.

The field of neuroscience is now embracing more open science standards and community efforts to address the referenced to as “replication crisis” as well as the growing complexity of the data analysis pipelines in neuroimaging. The MINDteam is ideally positioned to address these issues from both angles by providing reliable statistical inference schemes as well as open source software that are compliant with international standards.

The impact of MIND will be driven by the data analysis challenges in neuroscience but also by the fundamental discoveries in neuroscience that presently inspire the development of novel AI algorithms. The PARIETAL team has proved in the past that this scientific positioning leads to impactful research. Hence, the newly created MIND team formed by computer scientists and statisticians with a deep understanding of the field of neuroscience, from data acquisition to clinical needs, offers a unique opportunity to expand and explore more fully uncharted territories.

3 Research program

The scientific project of MIND is organized around four core developments (machine learning for inverse problems, heterogeneous data & knowledge bases, statistics and causal inference in high dimension, and machine Learning on spatio-temporal signals).

3.1 Machine learning for inverse problems

Participants: P. Ciuciu, A. Gramfort, T. Moreau, D. Wassermann

Inverse problems are ubiquitous in observational science. This necessitates the reconstruction of a signal/image of interest, or more generally a vector of parameters, from remote observations that are possibly noisy and scarce. The link between the parameters of interest and the observations is physics, and is commonly well understood. Yet, the recovery of parameters is challenging as the problem is often ill-posed due to the ill-conditioning of the forward model. Machine learning is now more frequently used to address such problems, using likelihood-free inference (LFI) to inverse nonlinear systems, or prior learning using bi-level optimization and reinforcement learning to guide the way to collect observations.

3.1.1 From linear inverse problems to simulation based inference

Expected breakthrough: Boosts in MR image quality and reconstruction speed and in spatio-temporal resolution of M/EEG source imaging

Findings: Development of data-driven regularizing functions for inverse problems, as well as deep invertible and cost-effective network architectures amenable to solve nonlinear inverse problems on neuroscience data.

Solving an inverse problem consists in estimating the unobserved parameters at the origin of some measurements. Typical examples are image denoising or image deconvolution, where, given noisy or low resolution data, the objective is to obtain an underlying high-quality image. Inverse problems are pervasive in experimental sciences such as physics, biology or neuroscience. The common problem across these fields is that the measurements are noisy and generally incomplete.

Mathematically speaking, these inverse problem can be formulated as estimating \mathbf{x} from $\mathbf{y} = \Gamma(\mathbf{x}) + \mathbf{b}$. Here, \mathbf{b} is an additive noise and Γ is a (generally non-injective) mapping to a lower-dimensional space. For example, in magneto- and electroencephalography (M/EEG), Γ is a real linear mapping $\Gamma_{\text{M/EEG}} : \mathbb{R}^N \mapsto \mathbb{R}^M$ and \mathbf{b} is considered white and Gaussian, while in magnetic resonance imaging (MRI), Γ is a complex linear mapping $\Gamma_{\text{MRI}} : \mathbb{C}^N \mapsto \mathbb{C}^M$ and \mathbf{b} is circular complex white Gaussian. Despite the linearity of $\Gamma_{\text{M/EEG}}$ and Γ_{MRI} , estimating \mathbf{x} is a challenging task when the

measurements are incomplete, i.e., $M \ll N$ and the problem is ill-posed. This is often the case due to physical limitations on the measurement device (M/EEG) or the acquisition time (MRI). Moreover, the linear Fourier operator Γ_{MRI} only reflects an ideal acquisition process and part of the acquisition artifacts (e.g. B0 inhomogeneity) can be compensated by considering nonlinear models at the cost of estimating additional parameters along with the MR image.

To tackle these inverse problems, using adequate regularization will promote the right structure for the data to be recovered. Over the last decade the members of MIND have proposed state-of-the-art models and efficient algorithms based on sparsity assumptions [81, 131, 103, 87, 132, 116, 115, 101, 106, 102]. MNE is the reference software developed by the team that implements these methods for MEG/EEG data while `pysap-mri` proposes solvers for MR image reconstruction.

The field is now progressing with novel approaches based on deep learning by either learning the regularization from data in the context of MRI reconstruction [153, 154], or by considering nonlinear models grounded in the physics underlying the data. The team has started to explore this direction using so-called Likelihood-Free Inference (LFI) techniques built on deep invertible networks [156, 114]. A particular application has been on diffusion MRI (dMRI), where we have linked the dMRI signal with physiological tissue models of grey matter tissue [114]. Still in MRI but in susceptibility weighted imaging, another approach [95] has consisted in directly estimating the B0 field map from non-Cartesian k-space data to correct for off-resonance effects in non-Fourier operators Γ_{MRI} . The MIND project will continue along this direction studying nonlinear simulators of imaging data as building blocks. A key aspect of the work proposed is to exploit knowledge on the physics of the data generation mechanisms.

3.1.2 Bi-level optimization

Expected breakthrough: Efficient algorithms to select hyper-parameters and priors for source localisation in MEG and image reconstruction in MRI/fMRI.

Findings: Bi-level optimization solvers exploiting gradients to scale with the large number of samples and hyper-parameters.

In recent years, bi-level optimization – minimizing over a parameter which is itself the solution of another optimization problem – has raised great interest in the machine learning community. Indeed, many methods in ML reduce to this bi-level framework, typically the problem of hyper-parameter optimization.

In most practical cases, hyper-parameter selection is done using cross-validation (CV), which basically consists in splitting the whole dataset in training and validation sets. The parameters of the method are computed by minimizing a loss function on the training set, and the hyper-parameters are then set by minimizing the loss function on the validation set. This approach is a bi-level optimization problem.

Other instances of such problems can be found in dictionary learning, robust training of neural networks or the use of implicit layers in deep learning. In all these applications, the model or the latent variables are learned by minimizing some loss while the parameters or the dictionary are updated by minimizing a second optimization problem depending on the outcome of the first problem. While theoretical results were produced in the early 70's [94], there are still many challenges related to bi-level optimization that need to be addressed to produce methods that are both theoretically well grounded and computationally efficient. Recently, the members of MIND have published several works related to the subject [64, 65, 76, 88]. We intend to pursue this effort in the following directions.

Stochastic bi-level solvers. Bi-level solvers require the use of the whole training set before doing an update on an outer-level problem: In this sense, they are *full-batch* methods [76]. We propose to study *stochastic* methods for this task, where some improvement on the optimization can be achieved using only a few samples from the training data. Stochastic algorithms are notoriously faster than full-batch methods for large datasets, but are also generally harder to analyse from a theoretical standpoint. In addition to being fast, the proposed algorithm should come with some

statistical guarantees. These solvers can have many applications, from stochastic prior learning for inverse problem to hyper-parameters tuning in general machine learning.

Neural Dictionary Learning. Bi-level optimization framework offers a canvas to advance the state of the art in dictionary and prior learning. Indeed, dictionary learning has long been seen as a bi-level optimization problem [130]. Practical algorithms are mainly based on alternate minimization and rarely account for the sub-optimality of each sub-problem. With advances in bi-level optimization and algorithm unrolling [64], we aim at providing efficient and theoretically justified dictionary learning algorithms, that will be able to leverage the technologies of differentiable programming [62, 149].

Deep Equilibrium Models. The use of Deep learning, and in particular unrolled algorithms [110], has introduced a quantum leap in the resolution of inverse problems compared to variational approaches, specifically in terms of computing efficiency and image/signal recovery performance. However, these networks are very demanding in memory for the training, which currently limits their potential. Different methods exist to alleviate this problem both on the modeling (gradient checkpointing, reversible networks) and the implementation side (model parallelism, mixed precision), but come at the expense of larger computational cost. However, a promising research avenue, illustrated by [108], is the use of Deep Equilibrium Models. These models are defined implicitly and amount to unrolling an infinite number of iterations, thereby using much less memory. These implicit layers constitute another instance of bi-level optimization problem and we plan to work on these directions in the near future as a means to address DL image reconstruction in realistic 3D and 4D multi-coil MRI setting, both for structural and functional imaging.

3.1.3 Reinforcement learning for active k-space sampling

Expected breakthrough: New hardware compliant under-sampling patterns in MRI k-space that accelerate anatomical and functional scans while optimizing MR image quality.

Findings: Develop novel principles of active sampling in the reinforcement learning framework which optimizes a sampling policy tightly linked to the reconstructed image quality.

Current under-sampling schemes in MRI allow for shorter scan acquisition times, however at the cost of artifacts in various regions of the reconstructed MR image. These artifacts arise due to uncertainties in some heavily under-sampled regions of the acquired Fourier space (i.e. also called k-space). Modern reconstruction algorithms, with the use of strong priors, either hand-crafted or learned, tend to reduce these uncertainties and behave as if the acquisition is fixed.

To go beyond the state of the art, we argue that there is a need to jointly learn an algorithm that designs the optimal under-sampling pattern in k-space as well as the reconstruction network.

As it can be summarized to learning a sequential decision algorithm, we will rely on reinforcement learning (RL) to build up optimal k-space sampling patterns while enforcing physical constraints on the MRI sequence, as originally proposed in [84, 79, 123].

The k-space acquisition can be modeled by a sampling policy and the rewards for the joint network are based on reconstructed image quality. Under this paradigm, after every fixed scan time, an instantaneous reconstruction can be obtained and the Fourier space uncertainty maps analysed in depth. Based on this, the scan can continue by actively sampling the k-space and enforcing denser samples in regions where uncertainty is larger. In this way, the learned k-space trajectories may become more patient and organ specific. Further, the trajectory can run and lead to instantaneous best results of reconstruction under a given variable scan time budget. These aspects define one of the core directions we will investigate to produce the next generation of state-of-the-art MR data sampling and image reconstruction algorithms. Recent contributions [170, 150] only approach the problem in the Cartesian framework and hence perform 1D variable density sampling along the phase encoding dimension. Given our expertise on non-Cartesian sampling in developing SPARKLING for both for 2D and 3D MR imaging [123, 124, 82], we plan to extend this framework to non-Cartesian acquisition setups while still remaining compatible with hardware

constraints on the gradient system. The access to various MRI scanners at CEA/NeuroSpin is necessary and an added advantage to the success of the MIND team.

3.2 Heterogeneous Data & Knowledge Bases

Participants: B. Thirion, D. Wassermann

Inferring the relationship between the physiological bases of the human brain and its cognitive functions requires articulating different datasets in terms of their semantics and representation. Examples of these are spatio-temporal brain images, tabular datasets, structured knowledge represented as ontologies, and probabilistic datasets. Developing a formalism that can integrate all these modalities requires constructing a framework able to represent and efficiently perform computations on high-dimensional datasets as well as to combine hybrid data representations in deterministic and probabilistic settings. We will take on two main angles to achieve this task: on one hand, the automated inference of cross-dataset features, or coordinated representations and on the other hand, the use of probabilistic logic for knowledge representation and inference. The probabilistic knowledge representation part is now well advanced with the [Neurolang](#) project. It is yet a long-term endeavor. The learning of coordinated representations is less advanced.

3.2.1 Learning coordinated representations

Expected breakthrough: Process semantic information together with image data to bridge large-scale resources and knowledge bases

Findings: Set up a learning model that leverages heterogeneous data: Images, annotations, texts, and coordinate tables.

Inference is the pathway that leads from data to knowledge. One crucial aspect is that in the context of neuroscience, data comes in different forms: Full texts, images and tables. Annotations may be full texts or simply tags associated with observed images. One challenge is thus to develop automated techniques that learn *coordinated representations* across such heterogeneous data sources.

This learning endeavor rests on several key machine learning techniques: Compression, embeddings, and multi-layer networks. Compression (sketching) consists in building a reduced representation of some input that leads from large sparse and complex representation to low-dimension ones, while minimizing some distortion criterion. Embedding techniques also create representations, but possibly bias them to enhance some aspects of the data. It thus incorporates prior information on data distribution or the relevance of features. Finally, multi-layer networks create intermediate representation of data that are suitable to achieve a prediction goal. Such representations are rich enough in particular in multi-task settings, where the outputs of the network are multi-dimensional. Following [70], we call such latent data models *coordinated representations*.

Deep learning is well suited to the goal of learning intermediate representations. As an example, we plan to develop a framework that coalesces in one deep learning formulation, the task of estimating brain structures, cognitive concepts, and their relationships.

Brain structures and cognitive concepts will appear as intermediate representations responsible for linking brain activity to observed behavior. However deep learning cannot be considered as a standard means to understand coordinated representations, due to the limited data available, their poor signal-to-noise ratio (SNR) and their heterogeneity. Deep learning needs instead to be adapted by injecting our expertise on statistical structure of the data (see e.g. [112, 134]). Since the challenge is to train such models on limited and noisy data, we will extend our recent work [69] that has developed regularization schemes for deep-learning models: it relies on structured stochastic regularizations (a.k.a. structured dropout). Such approaches are efficient, powerful and can be used in wide settings. We will enhance them with more generic, cross-layer, grouping schemes. Additionally, we will develop two strategies: *i*) aggregation of predictors for variance reduction and stability of the model [112] and *ii*) data augmentation – i.e. learning to augment, based on unlabeled data – to improve the fit with limited data. For this we will consider plausible generative mechanisms.

3.2.2 Probabilistic Knowledge Representation

Expected breakthrough: A domain-specific language (DSL) capable of articulating heterogeneous probabilistic data sources in neuroimaging is a way to relate physiology to cognition.
Findings: Self-optimizing probabilistic solvers for discrete and continuous hierarchical models able to scale for neuroimaging problems.

Neuroscientific data used to infer the relationships between physiology of the human brain and its cognitive function goes well beyond text, image, and tables. Knowledge graphs representing human knowledge, and the ability to encode reasoning strategies in neuroscience are also key to effectively bridge current data-centric approaches and decades-old domain knowledge. A main challenge in performing inferences combining demographic data-centric approaches, imaging measurements, and domain knowledge, is to be able to infer new knowledge soundly and efficiently taking into account the noisy nature of demographic and imaging measurements, and the common open-world assumption of ontologies and knowledge graphs. Such probabilistic hybrid logic approaches are known to be, in general, intractable in the deterministic [67] as well as in the probabilistic case [167]. Nonetheless, there is an opportunity to be seized in identifying tractable segments of probabilistic hybrid logic representations able to solve open neuroscientific questions.

A noticeable opportunity to incorporate all statistical evidence gathered from noisy data into a usable knowledge base is to formalize the inferred relationships into probabilistic symbolic representations [113]. These representations are much better suited to simultaneously handle data across topologies and logic systems, implementing inferential algorithms avoiding the brittleness of deterministic logic as well as causal probabilistic reasoning.

A typical application of such heterogeneous data processing is meta-analytic applications which combine neuroimaging data with results found in the scientific literature. Current tools to perform this task are **NeuroSynth** or **Neuroquery** (developed by the team). However, knowledge inferred by such tools is tremendously limited by the expressive power of the language used to query the data. Current meta-analytic tools are able to express queries relating test makers, article annotations, and their relationship with reported brain activations, support propositional logic only. Propositional logic requires the user to explicitly express every desired term with their characteristics and their relationships. Our goal is to extend the inference capabilities of such applications by leveraging current advances in probabilistic logic languages and embedding them in the **Neurolang** language. **Neurolang** enables the encoding of complex knowledge in terms of more expressive queries. **Neurolang** queries first-order logic segment, $FO^{\neg\exists}$, with a tractable probabilistic extension allowing for high-dimensional and large dataset computations. Such segment of first order logic enables formalising questions such as “what brain areas are most likely reported active in a study specifically when terms related to consciousness are mentioned in such study”, hence being able to infer, amongst other tasks, specificity and causality [168] of diverse neuroscience phenomena. To disseminate our results allowing complex expressive searches of massively aggregated diverse data, we will leverage **Neurolang**. The latter produces a domain-specific language (DSL) for human neuroscience research, while being able to combine imaging data, anatomical descriptions and ontologies. Three main characteristics of the DSL are key to fulfilling this goal: First, it represents neuroimaging-derived information and spatial relationships in a *syntax close to natural language used by neuroscientists* [169]. Second, through a back-end belonging to the Datalog[±] family, it allows *querying ontologies* with the same expressive power as current standards SPARQL and OWL [73]. Finally, we will extend **Neurolang** to a *probabilistic language able to express graphical models* allowing the implementation of a wide variety of causal inference and machine learning algorithms [72] in high-dimensional settings which are specific to neuroimaging research. In sum, by leveraging *recent advances in deductive database systems* [73] and this **novel DSL** [169] we will provide a more flexible tool to express and infer knowledge on brain structure-function relationships.

3.3 Statistics and causal inference in high dimension

Participants: A. Gramfort, T. Moreau, B. Thirion, D. Wassermann

Statistics is the natural pathway from data to knowledge. Using statistics on brain imaging

data involves dealing with high-dimensional data that can induce intensive computation and low statistical power. Besides, statistical models on large-scale data also need to take potential confounding effects and heterogeneity into account. To address these questions the MIND team will employ causal modeling and post-selection inference. Conditional and post-hoc inference are rather short-term perspectives, while the potential of causal inference stands as a longer-term endeavor.

3.3.1 Conditional inference in high dimension

Expected breakthrough: Obtain statistical guarantees on the parameters of very-high dimensional generalized linear or non-parametric models.

Findings: Develop computationally efficient procedures that allow inference for such models, by leveraging structural priors on the solutions.

Conditional inference consists of assessing the importance of a certain feature in a predictive model, while taking into account the information carried by alternative features. One motivation for using this inference scheme is that brain regions that sustain behavior and cognition are strongly interacting. Taking these interactions into account is critical to avoid confusing correlation with causation in brain/behavior analysis.

Technical difficulties come when the set of explanatory features \mathbf{X} becomes extremely large as frequently met in neuroimaging: Conditioning on many variables (or equivalently, high dimensional variables) is computationally costly and statistically inefficient. The main solutions to date are based either on linear model debiasing [118], as well as simulation-based approaches (knockoff inference [80] or conditional randomization tests [127]). Importantly the latter involves simulating data with statistical characteristics described explicitly (in a parametric family) or implicitly (by samples). There remain two gaps to bridge for these methods: *i*) The computational gap, as the algorithmic complexity of these approaches is typically cubic in the number of samples, unless more efficient generative mechanisms are available; *ii*) the power gap, related to the limited number of available samples. The best solution thus far consists of associating these inference procedures with dimension reduction procedures [142]. The next step is adaptation to more general settings: Conditional inference has been formulated in the linear framework, where it boils down to controlling that the corresponding coefficient is non-zero, hence it has to be generalized to nonlinear models: Non-parametric models like random forests, then possibly deep networks.

3.3.2 Post-selection inference on image data

Expected breakthrough: Statistical control of false discovery proportion (FDP) for data under arbitrary correlation structure.

Findings: A computationally efficient non-parametric statistical test procedure, and a benchmark against alternative techniques.

Large-scale statistical testing is pervasive in many scientific fields, where high-dimensional datasets are collected and compared with an outcome of interest. In such high-dimensional contexts, false discovery rate (FDR) control [75] is attractive because it yields reasonable power, while providing an explicit and interpretable control on false positives. Yet the FDR rate is the expectation of the FDP. Controlling the FDR does not mean that the FDP is controlled, a distinction that is most often ignored by practitioners. For the sake of scientific reproducibility, there is a need for methods controlling the FDP.

Such an approach has been developed in the context of neuroimaging, namely the *all-resolution inference* framework [157] based on classical multiple correction error control bounds. Yet, the empirical behavior of this method remains to be assessed. Moreover, it has been clearly established that the procedure is over-conservative in some settings [77]. Indeed, it relies on the Simes statistical bound, that is not adaptive to the specific type of dependence for a particular data set. To bypass these limitations, [77] have proposed a randomization-based procedure known as λ -calibration, which yields tighter mathematical bounds that are adapted to the dependency observed in the dataset at hand. It rests on a non-parametric (permutation-based) estimation of the null distribution, leading to tight and valid inference under general assumptions.

In this research axis, we propose to fix some of the open issues with the approach described in [77], namely the choice of a template family to calibrate the error distribution in the permutation procedure. We hope to propose a practical choice for this family to avoid putting the burden of choice on practitioners.

We will characterize by simulations and theoretical arguments the behavior of these error control procedures and develop efficient computational methods for the use of these tools in brain imaging analysis.

3.3.3 Causal inference for population analysis

Expected breakthrough: Provide a reference methodology for causal and mediation analysis in high-dimensional settings.

Findings: Benchmark state-of-the-art techniques and further adapt them to the high-dimensional setting.

Modern health datasets present population characteristics with many variables and in multiple modalities. They can ground prediction and understanding of individual outcomes, using machine learning techniques. Still, heterogeneous variables have complex relationships, making it hard to tease apart each factor in an outcome of interest. Potential outcome theory [161] provides a valuable framework to evaluate the impact of treatment (interventions). Treatment effects can be heterogeneous. In particular, interactions between background and treatment variables have to be considered.

The statistical behavior (consistency and efficiency) under non-parametric models is actively investigated [68, 143]. However, their behavior in high-dimensional settings, when both the number of features and the number of samples are large, is still poorly understood. Our objective is thus to extend the theory and algorithms of causal inference to noisy high-dimensional settings, where the noise level implies that effects sizes are proportionally small, and classic methods often become inefficient and potentially inaccurate due to overfitting. More specifically, we plan to explore the following directions.

Mediation analysis and conditional independence Mediation analysis considers the question of whether a variable z mediates all the effect of another variable x onto a target variable y , *a.k.a.* outcome. It turns out that full-mediation analysis amounts to testing whether $x \perp y|z$ (x is independent from y given z), which is handled by a conditional independence test. When the dimensions of these variables (z in particular, but also x and to some extent y) grow, the underlying statistical inference procedures typically lose power, or even possibly error control. We propose to leverage our experience on such high-dimensional inference problems [89, 141] to set up computationally efficient and accurate solutions to this problem.

Latent variable models and confounders The most important aspect of inferring causal effects from observational data is the handling of confounders, *i.e.*, factors that affect both an intervention and its outcome. For instance, age has a clear impact on brain characteristics as well as on behavior, potentially biasing brain/behavior statistical associations. A carefully designed observational study attempts to measure all important confounders. When one does not have direct access to all confounders, there may exist noisy and uncertain measurements of proxies for confounders. A possible solution to this problem relies on generative modeling, such as Variational Autencoders (VAE) and Generative Adversarial Networks (GANs), to sample the unknown latent space summarizing the confounders on datasets with incomplete information; the seminal work of [129] is promising, but still requires improvements to become usable in realistic settings.

The quest of model selection and validation In the classical potential outcome theory [161], causal effects are determined by both factual and counterfactual outcomes, ground-truth effects can never be measured in an observational study. In the absence of such measures, how can we evaluate the performance of causal inference methods? Addressing this question is an important step for practical problems, in which one has to determine if an effect can safely be considered

non-zero, or heterogeneous through a population. We propose to revisit the promising work of [66] analysing in detail the shortcomings of the procedure (regarding both bias and variance), especially when the model becomes high-dimensional.

3.4 Machine Learning on spatio-temporal signals

Participants: P. Ciuciu, A. Gramfort, T. Moreau, D. Wassermann, B. Thirion

The brain is a dynamic system. A core task in neuroscience is to extract the temporal structures in the recorded signals as a means to linking them to cognitive processes or to specific neurological conditions. This calls for machine learning methods that are designed to handle multivariate signals, possibly mapped to some spatial coordinate system (e.g. like in fMRI).

3.4.1 Injecting structural priors with Physics-informed data augmentation

Expected breakthrough: Obtain models with more predictive power when trained on small datasets.

Findings: Efficient data-augmentation strategy tailored to brain signals.

Data augmentation consists of virtually increasing dataset size during learning by applying random, yet plausible, transformations to the input data. In computer vision, this means altering data by applying symmetries, rotations, geometric deformations etc. While such strategies are reasonable for natural or medical images [148], it is still unclear how neural or BOLD signals can be augmented in order to improve prediction performance and robustness.

Some purely data driven strategies have been proposed to augment EEG data using spectral transforms [128] or advanced strategies such as channel, time or frequency masking or phase randomizations [122, 125]. Although dozens of transformations have been considered in the literature to augment EEG signals, it is now apparent that different augmentation strategies should be applied to the data as a function of the prediction task to be handled. For example when considering sleep stage classification or BCI applications, the spatial sampling of electrodes and the duration of signals varies considerably, with the consequence being that different augmentation parameters and even transformations need to be employed.

In this line of work we will develop algorithms that can quickly identify the relevant augmentation techniques, building for example on [92, 127]. The aim is to provide a system that can automatically learn invariance within a class and across subjects in order to maximize the prediction performance on unseen data. The methodology developed will be relevant beyond neuroscience as long as a family of physics-informed transformations is available for prediction tasks at hand.

3.4.2 Learning structural priors with self-supervised learning

Expected breakthrough: Unveiling the latent structure of brain signals from large datasets without human supervision as well as improving the prediction performance when learning from limited data.

Findings: Self-supervised algorithms for multivariate brain signals.

Self-supervised learning (SSL) is a recently developed area of research that provides a compelling approach for exploiting large unlabeled datasets. With SSL, the structure of the data is used to turn an unsupervised learning problem into a supervised one, called a “pretext task”, such as solving Jigsaw puzzles from images [145] or learning how to color gray-scaled images. The representation learned on the pretext task can then be reused for unsupervised data exploration or on a supervised downstream task, with the potential to greatly reduce the number of labeled examples required to train a good predictive model.

In fields like computer vision [145, 136] and time series processing [146], SSL has shown great promise in terms of prediction performance but also in ease of use. Indeed, SSL simplifies model selection and evaluation as it relies on prediction scores and cross-validation, contrarily to unsupervised learning methods like ICA [63].

Recently the team has applied SSL to two large cohorts of clinical EEG data [71] revealing insights on the data without any human supervision. However many challenges remain. For example in MIND, we aim to explore novel SSL strategies applicable to electrophysiology as well as to haemodynamic signals measured with fMRI. As such, our goal is to expand the recent multivariate method we have introduced in the field for the blind deconvolution of BOLD signals in both task-related and resting-state experiments [86].

While rather small networks have been employed so far on EEG data [83, 160] due to limited sets of annotations, the use of SSL tasks opens the possibility to work with much larger labeled datasets, and therefore many more overparametrized models. We aim to explore these directions, hoping to reach a state where pre-trained models could be available for EEG or MEG signals as is presently the case for images or for natural language processing (NLP) tasks.

3.4.3 Revealing spatio-temporal structures with convolutional sparse coding and driven point processes

Expected breakthrough: A novel way to study and quantify temporal dependencies between neural processes, going beyond connectomes based on spectral analysis.

Findings: Temporal pattern finding algorithms that scale to massive MEG/EEG datasets with parallel processing and point-process inference algorithms.

The convolutional sparse linear model is one established unsupervised learning framework designed for signals. Using algorithms known as convolutional sparse coding (CSC), this framework allows for the learning of shift-invariant patterns to sparsely reconstruct a time series. These patterns, also called atoms, correspond to recurrent structures present in the data. While some of our recent advances have improved the computational tractability of these methods [138, 137] and adapted them to neurophysiological data [117, 100, 86], there are still many shortcomings that make them unpractical for applications beyond denoising.

Model validation The main challenge for the evaluation of unsupervised convolutional models comes from current theoretical limitations: What can we guarantee statistically concerning the recovered atoms? Due to their non-convexity, existing algorithms can only guarantee convergence to local minima, which might be sub-optimal. In this setting, it is challenging to quantify if the model parameters are well estimated and if they are actually representative of the signals. In MIND, we aim to develop statistical quantification of the uncertainty associated with such models and in this regard, provide objective selection criteria for the model and its parameters. This topic of research will benefit from our other developments on bi-level optimization (cf. [subsection 3.1.2](#)) and on FDR control (cf. [subsection 3.3.2](#)) as well as the expertise of the team members on dictionary learning [138, 135, 137].

Capturing temporal dependencies with point processes Another shortcoming of these models is that they do not capture temporal dependencies between the occurrences of the different atoms. However, neural activity at level of the whole brain is highly distributed. Different brain regions form networks that are characterized by the presence of statistical dependencies in their activity [147]. An interesting question to formulate is how one can model and learn these time dependencies between brain areas from the MEG or EEG recordings using an unsupervised event-based approach such as CSC. One of the approaches considered is based on point processes (PP; [78, 111]). PP are classical tools to study event trains (e.g. sequence of spikes) and to model their dependency structure. We aim here to develop PP-based inference algorithms as a means to capture network effects in different brain areas, but also to quantify how experimental stimuli are affecting the temporal statistics of temporal patterns [147]. To model this latter scenario, we will develop the so-called driven PP. In a second stage, we aim to design fully unsupervised methods to capture the connections between different brain areas leveraging the full temporal resolution of non-invasive electrophysiological signals.

4 Application domains

The four research axes we presented earlier have been thought of in tight interaction with four main applications (large-scale predictive modeling, mapping cognition & brain networks, modeling clinical endpoints, from brain images and bio-signals to quantitative biology and physics).

4.1 Population modeling, large-scale predictive modeling

4.1.1 Unveiling Cognition Through Population Modeling

Linking the human brain's structure and function with cognitive abilities has been a research epicenter for the past 40 years. The sophistication of brain mapping machinery such as MRI, EEG and MEG, has produced a treasure trove of data. Nonetheless, the effect size of the phenomena leading to understanding cognition is often drowned out by noise and inter-individual variability. A main goal of MIND is to simultaneously harness the power of large-scale general purpose datasets, such as the Human Connectome Project (HCP) and the Adolescent Brain Cognitive Development Study (ABCD), as well as small scale high precision ones, such as the Individual Brain Charting (IBC) dataset [152], to understand the link between the human brain's architecture and function, and cognition. PARIETAL's expertise has already been demonstrated in this field. Examples of this include using diffusion MRI (dMRI) to link the brain's macrostructure with language comprehension [85], tissue microstructure with cognitive control [133], functional gradients on the cortical surface [98] to functional territory segregation [151].

MIND project will continue this task by seizing our core methodological developments, described in the previous section, and our global collaborative network of cognitive scientists.

4.1.2 Imaging for health in the general population

Individual differences in brain function and cognition have historically been investigated by studies carried out by individual laboratories having access mainly to small sample sizes. The growing availability of public large-scale data of epidemiological dimensions curated by dedicated consortia (e.g. UK Biobank) has enabled studying the relationship between cognition and the brain with unparalleled granularity and statistical power. These resources now allow researchers to relate brain signals/images to rich descriptions of the participants including behavioral and clinical assessments in addition to social and lifestyle factors. Machine learning has proven essential when modeling biomedical outcomes from the large-scale and high-dimensional data brought by consortia and biobanks. It is used to build predictive models of heterogeneous biomedical outcomes (cognitive, social, clinical) based on different neuroscientific modalities. Taken together, this facilitates the study of lifestyle and health-related behavior in the general population, potentially revealing risk factors leading to biomarker discovery.

MIND will greatly contribute to this effort by focusing on population modeling as a tool for enhancing the analysis of clinical data and mental health.

4.1.3 Proxy measures of brain health

Clinical datasets tend to be small as sharing of data is not incentivized or institutional and economic resources are missing. As a consequence, the capacity of machine learning to learn functions that relate complex-to-grasp biomedical outcomes to heterogeneous data cannot be fully exploited. This has stimulated growing interest in proxy measures of neurological conditions derived from the general population, such as individual biological aging. One counter-intuitive aspect of the methodology is that measures of biological aging (e.g. via brain imaging) can be obtained by focusing on the age of a person, which is known in advance and is, in itself not interesting as a target. However, by predicting the age, machine-learning can capture the relevant information about aging. Based on a population of brain images, it extracts the best guess for the age of a person, indirectly positioning that person within the population. Individual-specific prediction errors therefore reflect deviations from what is statistically expected [166]. The brain of a person can look similar to brains commonly seen in older (or younger) people. The resulting brain-predicted age reflects physical

and cognitive impairment in adults [165, 90, 99] and reveals neurodegenerative processes [126, 109], which could be overlooked without using machine learning.

MIND will extend this line of research in two directions: 1) Assessment of brain age using EEG and non-brain data such as health-records and 2) proxy measures of mental health beyond aging.

4.1.4 Studying brain age using electrophysiology

MRI is not yet available in all clinical situations and certain aspects of brain function are better understood using electrophysiological modalities (M/EEG). Until recently, it was unclear if brain age can be meaningfully estimated from M/EEG. In a recent study [104], we demonstrated, using the Cam-CAN cohort ($n = 650$), that combining MRI and MEG enhanced detection of cognitive dysfunction. The proposed approach not only achieved integration of brain signals from distinct modalities but explicitly handled the absence of MEG or MRI recordings, adapting ideas from [119]. This is key for clinical translation where one cannot afford excluding cases because one modality is missing. In the clinical setting, EEG is predominantly used (and not MEG). Clinical recordings are far noisier than lab EEG and gold-standard source modeling with MRI is rarely done outside the lab. Supported by theoretical analysis and simulations, we found through empirical benchmarks [163] that Riemannian embeddings 1) capture individual head geometry 2) bring robustness to extreme noise and, 3) enable good age prediction from clinical 20-channel EEG ($n=1300$) with performance close to 306-channel lab MEG.

MIND will extend this line of research by translating EEG-based brain age measures into the hospital setting and probe these in different patient populations in which ageing-related differences in brain structure and function are part of the clinical picture, e.g., neurodevelopmental disorders, postoperative cognitive decline and dementia (cf. subsection 4.3).

4.1.5 Proxy measures of mental health beyond brain aging

Quantitative measures of mental health remain challenging despite substantial research efforts [120]. Mental health, can only be probed indirectly through psychological constructs, e.g. intelligence or anxiety gauged by valid and statistically relevant questionnaires or structured examinations by a specialist. In practice, full neuropsychological evaluation is not an automated process but relies on expert judgment to confront multiple responses and interpret them in the context of a larger environmental context including the cultural background of the participant. Inspired by brain age, we set out to build empirical measures of mental health [93] by predicting traditional and broadly used psychological constructs such as fluid intelligence or neuroticism in the UK Biobank. Our results have shown that all proxies captured the target constructs and were more useful than the original measures for characterizing real-world health behavior (sleep, exercise, tobacco, alcohol consumption). In the long run, we anticipate that using proxies could complement psychometric assessments by corroborating data and potentially providing more accurate data faster and more efficiently for clinical populations.

MIND will expand this line of research by systematically searching for proxy measures of physical and mental health derived from large clinical population using electronic health records or transcripts from clinical interviews. We will propose a systematic causal analysis (treatment effect size and mediation) to provide a clearer understanding of the relationships between the many variables that characterize mental health. We will study more in detail the impact of general health markers on brain status, as this may well fit much of the *unexplained variance* on brain health.

4.2 Mapping cognition & brain networks

4.2.1 Problem statement

Cognitive science and psychiatry aim at describing mental operations: cognition, emotion, perception and their dysfunction. As an investigation device, they use functional brain imaging, that provides a unique window to bridge these mental concepts to the brain, neural firing and wiring. Yet aggregating results from experiments probing brain activity into a consistent description faces the roadblock that *cognitive concepts and brain pathologies are ill-defined*. Separation between them

is often blurry. In addition, these concepts (a.k.a. *psychological constructs*) may not correspond to actual brain structures or systems. To tackle this challenge, we propose to leverage rapidly increasing data sources: text and brain locations described in neuroscientific publications, brain images and their annotations taken from public data repositories, and several reference datasets.

4.2.2 What machine learning can do for neuroscience

Recent works in computer vision [96] or natural language processing [91, 97] have tackled predictions on a large number of classes, getting closer to open-ended knowledge. These approaches, that rely on uncovering some form of relational structure across these classes, in effect capture the semantics of the domain [91], including the similarity structure of the relevant classes and the ambiguities across classes or the multiple aspects of a class. Broadly speaking, these contributions converge to the concept of representation learning [74], i.e. estimating latent factors that *reformulate a learning problem into a new set of input features or output classes* that are more natural for the data and help further analysis. These new tools enable extraction of knowledge, for instance ontology induction, with statistical learning [144]. They are at the root of heterogeneous data integration, such as multi-modal machine learning [70]. The machine learning challenges that we aim to tackle are three-fold:

- Existing multi-modal machine learning techniques have been developed for relatively abundant data, with overall high SNR: text, natural images, videos, sound. These data are most often non-ambiguous, while brain data typically are, due to the low SNR per image and, more crucially, *poor annotation quality*. We propose to tackle this by adapting machine learning solutions to this low-SNR regime: introduction of priors, aggressive dimension reduction, aggregation approaches and data augmentation to reduce overfitting.
- *Leveraging implicit supervisory signals*: While data sources contain lots of implicit information that could be used as targets in supervised learning, there is most often no obvious way to extract it. We propose to tackle this by using additional, ill- or not-annotated data, relying on *self-supervision methods*.
- *Model interpretability*: Our goal is to provide clear assertions on the relationships between brain structures and cognition: the inference should always lead to an updated knowledge base, i.e. updated relationships between concepts pertaining to neuroscience on one hand, psychology on the other hand. Specifically, one should be able to reason about the information extracted within MIND. For this, we will develop dedicated statistical, causal and formal (ontology-based) data analysis schemes.

Associating knowledge engineering with statistical learning to boost cognitive neuroimaging, requires tackling the challenge of multimodal machine learning under noisy conditions with limited data. Doing so, it will capture links between behavior and brain activity, and enable aggregating the information carried by neuroimaging data to redefine and link concepts in psychology and psychiatry.

4.2.3 Perspective taken: combine distributional semantics with brain images

In natural language processing (NLP), *distributional semantics* capture meanings of words using similarities in the way they appear in their environment. We want to adapt these ideas to learn data-driven organizations of psychological concepts. Importantly, applying these techniques solely to the psychology literature merely captures the current status quo of the field. Including brain images is necessary to bring new information.

To link observed cognition to brain activity, two typical statistical learning problems arise: *encoding*, that seeks to describe brain activity from behavior; and *decoding*, that seeks the converse, predicting behavior from brain activity [121]. In addition, statistical modeling of each aspect of the data on its own generates knowledge, typically *spatial decompositions* from resting-state data, and *topic modeling* on descriptions of behavior. The research strategy followed in this proposal is to *combine the different statistical learning problems in a unified framework* to extract core structures

from the aggregation of neuroimaging data: on one side brain structures, and on the other side semantic relationships and concepts in psychological sciences.

MIND will in particular publish automated functional meta-analyses to give a systematic assessment of the publicly available data and question the limitations of the current conceptual framework of systems neuroscience as well as of these resources.

4.3 Modeling clinical endpoints

When sufficient data is available, machine learning can be employed to directly model various clinical endpoints (such as diagnosis, drug response, and neuropsychological scores) from brain signals without the need for proxy measures. This approach has the potential to significantly and meaningfully simplify statistical modeling in clinical research. Machine learning facilitates combining heterogeneous input data (different modalities) and does not need high confidence in underlying generative models linking the data to the clinical endpoint. As a consequence, the same class of models can be applied regardless of the endpoint. Its focus is on bounding the approximation error of the endpoint instead of correct parameter estimates. As such, it provides generalizing models that are more robust. Our team has pushed this type of research program through several important collaborations with our European clinical partners using EEG and MRI.

4.3.1 EEG-based modeling of clinical endpoints

Neurological and psychiatric disorders can show complex neurological patterns. Diagnosis is often performed clinically (based on cerebral signs and behavioral symptoms), leading to important variability across doctors. In clinical neuroscience, predicting diagnosis from *brain signals* is therefore a common application. In the clinical context, EEG is an economically viable option that can be applied in a wide array of circumstances. In collaboration with the Salpêtrière Hospital and the Paris Brain Institute (ICM) we have developed and validated an approach for an EEG-based modeling of diagnosis for severely brain injured patients suffering from consciousness disorders (DoC) [105]. Expert-defined features from consciousness studies were rigorously combined using random forest classification. Sensitivity analysis and benchmarks showed robustness across EEG-configurations (channels, time points), protocols (resting state vs evoked responses), label noise and differences between recording sites. When changes in the signal are more subtle than they are in DoC patients (average power turned out to be one of the strongest stand-alone features) more general approaches are needed.

Our future activities will focus on extending this line of research to other clinical populations and other endpoints. We have started a collaboration with the Institut Pasteur (GHFC team, T Bourgeron, R Delorme) and the University of Montreal (PPSP team, G Dumas), to characterize differences between normally developing children and children diagnosed with autism spectrum disorders. A wide array of EEG tasks will be used and endpoints (i.e. developmental timepoints) will go beyond the usually accurate diagnosis, focusing on symptom severity and social developmental scores. With the anesthesiology department at the Lariboisière hospital (A Mebazaa, E Gayat, F Vallée) and the cognitive neurology unit (C Paquet) we aim at developing EEG-based models of cognitive decline and dysfunction in two different settings. Postoperative cognitive decline is an important complication after general anesthesia and its antecedents must be better understood. As this might be an indicator for a latent neurodegenerative condition, we plan to use our EEG-based models of both Alzheimer’s Disease and Lewy body dementia in which disease progression is an important change over time.

This widening scope calls for a more general methodology as compared to our previous work on DoC. For example, in these conditions involving neurodegenerative problems, we have observed that both subtle and condition-specific spatial patterns matter more than strong and global amplitude changes. To approach these challenges we will draw on our latest M/EEG-methods that were recently developed for population-level modeling of brain health and brain aging [104]. We found that frequency band-specific spatial patterns of M/EEG power spectra conveyed important information of cognitive function (memory and cognitive performance) that were not explained by MRI or fMRI. This was implemented by predicting from a filter-bank of frequency-band-specific source power and

source connectivity features. Core challenges to enable clinical translation include lower SNR and absence of individual anatomical MRI scans needed for gold-standard source modeling. Through theoretical analysis, simulations and benchmarks we found [163, 162] that, in M/EEG sensor space, covariance matrices in combination with spatial filtering techniques and Riemannian embeddings provide good workarounds for absent anatomical MRI scans. This covariance-based approach allows to capture fine-grained spatial information related to power and connectivity without performing biophysics-based source localization. Moreover, Riemannian embeddings make predictive modeling from M/EEG covariance matrices more robust to noise, whereas their interpretability is more challenging than that of spatial filters, indicating a direction for further research. Another challenge is given by the limited numbers of labeled samples for supervised learning and EEG-devices with small channel numbers, such as monitoring or user-grade EEG with 2-4 electrodes for which random loss of electrodes can be frequent. In this context, we expect important enhancements from self-supervised learning approaches [71] and deep learning methods for data-augmentation for which we have obtained the first results on non-clinical data. In these settings, the previous elements from classical approaches such as Riemannian geometry or spatial filtering can be readily implemented alongside more involved computations and transformations.

4.3.2 MRI-based modeling of clinical endpoints

Image based biomarkers can be objectively measured and are a sign of normal or abnormal processes, of a condition or disease. Incorporating new potential imaging biomarkers requires several steps, often in parallel and complementary to each other, to be undertaken for translation into clinical practice. These can be divided into the following phases after identification: Development and evaluation, validation, implementation, qualification, and utilization. Our team aims to cross two main translational gaps, that is, the translation from patients first and then to practice. Our aim through our current and active projects is to ensure that potential biomarkers, like the clear delineation of subterritories of the subthalamic nucleus (STN) in pharmaco-resistant Parkinson's disease (PD) patients (i.e. candidates for implantation of a deep brain stimulator) are 'fit for purpose' and associated with the clinical endpoint of interest with the overarching goal being to demonstrated efficacy and health impact. This process is key to the translation into clinical practice and widespread utilization.

Through the ANR VLFMRI grant we aim to derive new MR imaging-based biomarkers related to prematurity and abnormal neurodevelopment of hospitalized neonates at low magnetic field (20 mTesla). In this setup, the objective is to perform an almost continuous monitoring to detect early signs of adverse events including ischemic stroke or encephalopathy (collaboration with Prof. V. Biran, APHP Robert Debré Hospital). An additional collaboration is already underway with the AP-HP Henri Mondor Hospital (neuroradiologist Dr B. Bapst, doing part of her PhD at NeuroSpin), to achieve high-resolution susceptibility weighted imaging (600 μ isotropic) in a scan time of 2m30s for an accurate delineation of the STN in PD patients prior to surgical planning. A database of 123 patients has already been collected using both the standard SWI imaging protocol and ours based on the SPARKLING technology. This annotated database will be key to compare the diagnosis power of our solution with that of the current care, analyse to what extent a higher image resolution is instrumental in providing a more accurate clinical diagnostic, and finally make our protocol more widely accepted in the clinical practice.

Our key contribution in these projects is to translate to the clinical realm both the SPARKLING technology on the acquisition side [124, 82] as well as our PySAP software [106] for MR image reconstruction. In this regard, the recently accepted CEA postdoc funding should help us move the technology to clinical 7T MR Systems (Magnetom Terra Siemens-Healthineers) in the University hospital of Poitiers through a nascent collaboration with Prof. Rémy Guillevin. Their interest is to use the high-resolution SPARKLING SWI protocol at 7T to better delineate the anomalies along the central vein for the diagnostic of multiple sclerosis as the number of anomalies predicts the grade/severity of this inflammatory pathology. On a longer perspective, we aim to generalize the use of our recently DL networks for MR image reconstruction [153, 154] to multiple acquisition setups and other downstream tasks (e.g. motion correction and correction of off-resonance artifacts related to B_0 inhomogeneities).

4.4 From brain images and bio-signals to quantitative biology and physics

Thanks to the developments in [subsection 3.1](#) and [subsection 3.4](#) we aim to approximate more accurately the biophysical models underlying MRI and electrophysiological signals. By estimating quantities grounded in the physics of the data (time, spatial localization, tissue properties) we ambition to offer more actionable outputs for cognitive, clinical and pharmacological applications.

Technologies like 4D SPARKLING should in the future allow us to carry out both fast high resolution multi-parametric quantitative imaging (e.g. T1, T2 and proton density mapping) and laminar (i.e. layer-based) functional imaging in BOLD-fMRI. First, in the mqMRI and fMRI setting, the fourth dimension is respectively the weighting contrast and time axis. mqMRI imaging enables a precise quantification of biomarkers such as iron stores in the pathological brain. Measuring these parameters intra-cortically in Parkinsonian patients defines one of the key challenges in the coming years, especially at 7 Tesla, to earlier stratify the PD patients and the evolution of their disease. Second, a particular attention will be paid to the impact of the developments performed in [subsection 3.1](#) on the statistical sensitivity of brain activity detection, which eventually defines the final validation metric of the data acquisition/image reconstruction pipeline. For this purpose, robust experimental activation protocols such as retinotopic mapping will be used for validation on the 7T scanner and eventually on the 11.7T Iseult MR system. The finest target resolution is 500 μm isotropic in 3D.

Novel development on bi-level optimization for hyper-parameter selection from [subsubsection 3.1.2](#) will bring state-of-the-art inverse methods to end users currently facing the difficulty of performing model selection on empirical data efficiently. This will lead to more accurate quantitative assessments, in sub-millimeters and milliseconds, of where neural activity occurs.

The line of work on inverse problems should also impact how non-invasive neuroimaging and electrophysiology, based on MRI, EEG and MEG, is considered by more traditional neurophysiologists working with animal data. By considering biophysical models of the data and aiming to estimate their parameters from empirical recordings our hope is to present estimates of physical quantities (tissue properties, neural interactions strengths, etc.). The line of work based on stochastic simulation based inference (SBI) can revolutionize the way MEG, EEG and MRI data are apprehended. For this line of work we will explore the inversion of the models as offered by major software such as The Virtual Brain (TVB) [164] or the Human Neocortical Neurosolver (HNN) [140]. A student from the group of Prof. S. Jones at the origin of the HNN software visited the team in 2022.

5 Social and environmental responsibility

The MIND team has not yet implemented specific guidelines for measuring carbon emission related to its research activities. Team members maximize the use of train for travelling across Europe and try to minimize the number of oversea flights per individual.

6 Highlights of the year

Philippe Ciuciu was plenary speaker at the [XXIX GRETSI](#) conference in Grenoble (Aug, 28-31). GRETSI is the French congress for signal and image processing and gathers approximately 500 people every two years.

6.1 Awards

Two PhD students from the MIND team received an award from the STIC Doctoral school in 2023. These prizes were jointly awarded by Paris-Saclay University and Polytechnique Paris Institute.

Two first prizes were awarded, notably one to Mathieu DAGREOU from Inria Saclay (MIND) & Paris-Saclay University for his paper entitled “A framework for bilevel optimization that enables stochastic and global variance reduction algorithms”. Mathieu DAGREOU is currently a third year PhD student under the supervision of Thomas Moreau.

Five runners-up prizes were awarded, including one to Charlotte CAUCHETEUX from Inria Saclay (MIND) & Paris-Saclay University, for her paper entitled “Evidence of a predictive coding hierarchy in the human brain listening to speech”. Charlotte CAUCHETEUX defended her PhD thesis on May, 10 2023 under the joint supervision of Alexandre GRAMFORT and Jean-Rémy KING.

7 New software, platforms, open data

7.1 New software

7.1.1 MNE

Name: MNE-Python

Keywords: Neurosciences, EEG, MEG, Signal processing, Machine learning

Functional Description: Open-source Python software for exploring, visualizing, and analyzing human neurophysiological data: MEG, EEG, sEEG, ECoG, and more.

Release Contributions: https://mne.tools/stable/whats_new.html

URL: <https://mne.tools/>

Contact: Alexandre Gramfort

Partners: HARVARD Medical School, New York University, University of Washington, CEA, Aalto university, Telecom Paris, Boston University, UC Berkeley, Macquarie University, University of Oregon, Aarhus University

7.1.2 NeuroLang

Name: NeuroLang

Keywords: Neurosciences, Probabilistic Programming, Logic programming

Functional Description: NeuroLang is a probabilistic logic programming system specialised in the analysis of neuroimaging data, but not exclusively determined by it.

Release Contributions: <https://neurolang.github.io/>

URL: <https://neurolang.github.io/#>

Contact: Demian Wassermann

7.1.3 Nilearn

Name: NeuroImaging with scikit learn

Keywords: Health, Neuroimaging, Medical imaging

Functional Description: NiLearn is the neuroimaging library that adapts the concepts and tools of scikit-learn to neuroimaging problems. As a pure Python library, it depends on scikit-learn and nibabel, the main Python library for neuroimaging I/O. It is an open-source project, available under BSD license. The two key components of NiLearn are i) the analysis of functional connectivity (spatial decompositions and covariance learning) and ii) the most common tools for multivariate pattern analysis. A great deal of efforts has been put on the efficiency of the procedures both in terms of memory cost and computation time.

Release Contributions: HIGHLIGHTS - Updated docs with a new theme using furo. - `permuted_ols` and `non_parametric_inference` now support TFCE statistic. - `permuted_ols` and `non_parametric_inference` now support cluster-level Family-wise error correction. - `save_glm_to_bids` has been added, which writes model outputs to disk according to BIDS convention.

NEW - `save_glm_to_bids` has been added, which writes model outputs to disk according to BIDS convention. - `permuted_ols` and `non_parametric_inference` now support TFCE statistic. - `permuted_ols` and `non_parametric_inference` now support cluster-level Family-wise error correction. - Updated docs with a new theme using furo.

See all details in https://nilearn.github.io/stable/changes/whats_new.html

URL: <http://nilearn.github.io/>

Contact: Bertrand Thirion

Participants: Alexandre Abraham, Alexandre Gramfort, Bertrand Thirion, Elvis Dohmatob, Fabian Pedregosa Izquierdo, Gael Varoquaux, Loic Esteve, Michael Eickenberg, Virgile Fritsch

7.1.4 Benchopt

Keywords: Mathematical Optimization, Benchmarking, Reproducibility

Functional Description: BenchOpt is a package to simplify, make more transparent and more reproducible the comparisons of optimization algorithms. It is written in Python but it is available with many programming languages. So far it has been tested with Python, R, Julia and compiled binaries written in C/C++ available via a terminal command. If it can be installed via conda, it should just work!

BenchOpt is used through a simple command line and ultimately running and replicating an optimization benchmark should be as easy as cloning a repo and launching the computation with a single command line. For now, BenchOpt features benchmarks for around 10 convex optimization problems and we are working on expanding this to feature more complex optimization problems. We are also developing a website to display the benchmark results easily.

Release Contributions: <https://github.com/benchopt/benchopt/releases/tag/1.5.1>

News of the Year: We organized in July 2023 a benchmarking sprint with benchopt with more than 40 participants.

During this sprint, we developed new benchmarks, gathered feedback, and saw which benchmarking tools were most needed. Most of the participants had never worked with benchopt. Their goal was to create new benchmarks using benchopt, ranging from optimization benchmarks – e.g. training a neural network with pytorch or jax on image classification – to more complex workflows – e.g. comparing different fMRI alignment or domain adaptation methods. The participants were all able to produce benchmarks within a few hours! Note that an important aspect of this benchmarking initiative is that the goal is not to re-code the various methods but to aggregate them from the different sources they are available from.

Take aways from this sprint have been discussed in a blog post accessible here: <https://notes.inria.fr/s/OuVJYf8bM>

Publication: [hal-03830604](https://hal.archives-ouvertes.fr/hal-03830604)

Contact: Thomas Moreau

Participants: Thomas Moreau, Alexandre Gramfort, Mathurin Massias, Badr Moufad

7.1.5 Scikit-learn

Keywords: Clustering, Classification, Regression, Machine learning

Scientific Description: Scikit-learn is a Python module integrating classic machine learning algorithms in the tightly-knit scientific Python world. It aims to provide simple and efficient solutions to learning problems, accessible to everybody and reusable in various contexts: machine-learning as a versatile tool for science and engineering.

Functional Description: Scikit-learn can be used as a middleware for prediction tasks. For example, many web startups adapt Scikitlearn to predict buying behavior of users, provide product recommendations, detect trends or abusive behavior (fraud, spam). Scikit-learn is used to extract the structure of complex data (text, images) and classify such data with techniques relevant to the state of the art.

Easy to use, efficient and accessible to non datascience experts, Scikit-learn is an increasingly popular machine learning library in Python. In a data exploration step, the user can enter a few lines on an interactive (but non-graphical) interface and immediately sees the results of his request. Scikitlearn is a prediction engine . Scikit-learn is developed in open source, and available under the BSD license.

URL: <http://scikit-learn.org>

Publications: [hal-00650905](#), [hal-00856511](#), [hal-01093971](#)

Contact: Olivier Grisel

Participants: Alexandre Gramfort, Bertrand Thirion, Gael Varoquaux, Loic Esteve, Olivier Grisel, Guillaume Lemaitre, Jeremie Du Boisberranger, Julien Jerphanion

Partners: Axa, BNP Parisbas Cardif, Dataiku, Nvidia, Chanel

7.1.6 joblib

Keywords: Parallel computing, Cache

Functional Description: Facilitate parallel computing and caching in Python.

News of the Year: We organized a dev sprint for joblib in February 2023, where we performed many maintenance changes and refactored a big part of the code necessary to provide asynchronous results collection in the library. This novel result collection paradigm was merged in March 2023 and released in the library.

See more info in this thread: <https://x.com/tomamoral/status/1648436595677331462>

URL: <https://joblib.readthedocs.io/en/latest/>

Contact: Gael Varoquaux

7.1.7 MRI-NUFFT

Keywords: MRI, Off-the-grid, Preconditioner, Brain MRI

Functional Description: MRI-NUFFT is a python package that extends various NUFFT (Non-Uniform Fast Fourier Transform) python bindings used for MRI reconstruction. It provides a unified interface with a large number of backends with implementations ranging from CPU to GPU.

In particular, it provides a unified interface for all the methods, with extra features such as coil sensitivity, density compensated adjoint and off-resonance corrections (for static B0 inhomogeneities). Additionally, useful IO tools like reading a k-space sampling trajectory and writing a binary file for run on MR scanner is also offered. Finally, it helps algorithmically speed up MR image reconstruction algorithms through fast ways to estimate preconditioning weights, also known as density compensators for a given sampling pattern.

URL: <https://mind-inria.github.io/mri-nufft/>

Contact: Philippe Ciuciu

7.1.8 SPARKLING

Name: Spreading Projection Algorithm for Rapid K-space sampLING

Keywords: Brain MRI, MRI, Optimization

Scientific Description: This python package allows us to generate "SPARKLING" curves as a new type of non-Cartesian trajectories to perform a more efficient sampling in 2D and 3D for anatomical imaging while using the same number of samples for a limited time budget. These segmented curves are obtained using a projection method on measure sets which offers three main advantages: i) generating segmented Non-Cartesian trajectories along a chosen density, ii) meeting the hardware constraints on the magnetic field gradients (magnitude, slew rate), iii) performing a fast coverage of k-space.

Functional Description: This python package implements "SPARKLING": an optimization driven method to obtain hardware compliant sampling curves that globally satisfy a user specified target sampling density. The resulting non-cartesian sampling curves can be used to efficiently undersample and speed up acquisitions on an MR scanner. This method is generic enough that it can be applied to any of the imaging modalities in MR.

Publications: [hal-01577200v1](#), [hal-02067080v1](#), [hal-03090471v2](#), [hal-04370475v1](#), [hal-02361265v1](#)

Contact: Chaithya Giliyar Radhkrishna

7.1.9 PySAP

Name: Python Sparse data Analysis Package

Keywords: Image reconstruction, Image compression

Functional Description: The PySAP (Python Sparse data Analysis Package, <https://github.com/CEA-COSMIC/pysap>) open-source image processing software package has been developed for the 3 years between the Compressed Sensing group at Inria-CEA Parietal team led by Philippe Ciuciu and the CosmoStat team (CEA/IRFU) led by Jean-Luc Starck. It has been developed for the Compressed Sensing for Magnetic resonance Imaging and Cosmology (COSMIC) project. This package provides a set of flexible tools that can be applied to a variety of compressed sensing and image reconstruction problems in various research domains. In particular, PySAP offers fast wavelet transforms and a range of integrated optimisation algorithms. It also offers a variety of plugins for specific application domains: on top of Pysap-MRI and PySAP-astro plugins, several complementary modules are now in development for electron tomography and electron microscopy for CEA colleagues. In October 2019, PySAP has been released on PyPi (<https://pypi.org/project/python-pysap/>, currently version 0.0.3) and in conda (<https://anaconda.org/agrigis/python-pysap>).

The Pysap-MRI has been advertised through a specific abstract accepted to the next workshop of ISMRM on Data Sampling & Image Reconstruction in late January 2020. It will be presented during a power pitch session together with an hands-on demo session using JuPyter notebooks.

Contact: Philippe Ciuciu

Partner: CEA

8 New results

8.1 Accelerated acquisition in MRI

Participants: Chaithya Giliyar Radhakrishna, Zaineb Amor, Philippe Ciuciu.

Main External Collaborators: Alexandre Vignaud (*CEA/NeuroSpin*), Aurélien Massire (*Siemens-Healthineers, France*), Guillaume Daval-Fr erot (*Chipiron, France*).

MRI is a widely used neuroimaging technique used to probe brain tissues, their structure and provide diagnostic insights on the functional organization as well as the layout of brain vessels. However, MRI relies on an inherently slow imaging process. Reducing acquisition time has been a major challenge in high-resolution MRI and has been successfully addressed by Compressed Sensing (CS) theory. However, most of the Fourier encoding schemes under-sample existing k-space trajectories which unfortunately will never adequately encode all the information necessary. Recently, the MIND team has addressed this crucial issue by proposing the Spreading Projection Algorithm for Rapid K-space sampLING (SPARKLING) for 2D/3D non-Cartesian T2* and susceptibility weighted imaging (SWI) at 3 and 7 Tesla (T) [123, 124], [107]. These advancements have interesting applications in cognitive and clinical neuroscience as we already have adapted this approach to address high-resolution functional and metabolic (Sodium 23Na) MR imaging at 7T – a very challenging feat [1]. However, the original SPARKLING trajectories are prone to off-resonance effects due to susceptibility artifacts. Therefore, we have extended the original SPARKLING methodology and developed the MORE-SPARKLING (Minimized Off-Resonance Effects) approach to correct for these artifacts. The fundamental idea implemented in MORE-SPARKLING is to make different k-space trajectories more homogeneous in time, in the sense that samples supported by different trajectories that are close in k-space must be collected at approximately the same time point. This allows us to mitigate the issue of off-resonance effects (signal void, geometric distortions) without increasing the scan time, as MORE-SPARKLING trajectories have exactly the same duration as their SPARKLING ancestor. This approach has been published [2] and is illustrated in Fig. 1. A patent application has been filed by the CEA for MORE-SPARKLING.

Complementary to that, we have also extended SPARKLING in another direction, namely the way we sample the center of k-space and proposed the GoLF-SPARKLING version in the same paper [2]. The core idea here is to reduce the over-sampling of the center of k-space and grid it to collect Cartesian data and make notably the estimation of sensitivity maps in multicoil acquisition easier. Similarly to MORE-SPARKLING, a patent application has been filed for GoLF-SPARKLING.

Additionally, we have shown that 3D-SPARKLING is a viable imaging technique and good alternative to Echo Planar Imaging for resting-state and task-based fMRI [4]. This is illustrated in Fig. 2 during a retinotopic mapping experiment which consists in mapping the retina to the primary visual cortex. These results have been obtained at a 1mm isotropic resolution both for EPI and SPARKLING acquisitions.

8.2 Deep learning for MR image reconstruction and artifact correction

Participants: Guillaume Daval-Fr erot, Chaithya Giliyar Radhakrishna, Philippe Ciuciu.

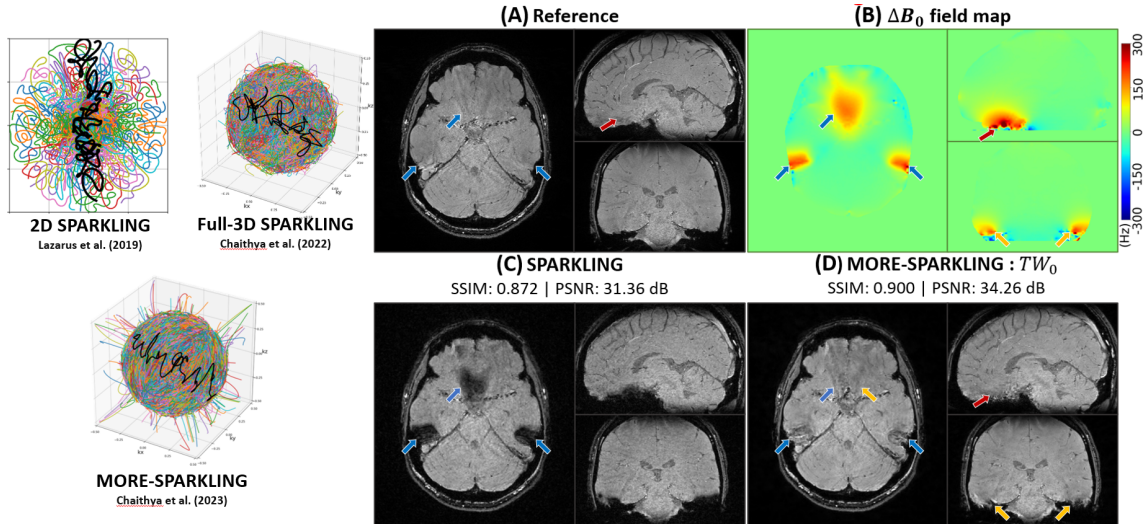


Figure 1: **Comparison between the original SPARKLING and the new MORE-SPARKLING 3D sampling patterns in k-space for accelerated MRI in presence of B_0 inhomogeneities.** The sampling patterns are shown on the left. (A): Cartesian reference acquisition. (B): ΔB_0 field map that captures the local variations in space of the static magnetic field B_0 . (C): Reconstructed 3D MR volume using the SPARKLING acquisition. Signal losses are depicted by blue arrows. (D): Reconstructed 3D MR volume using the MORE-SPARKLING version. The recovered signal is pointed with blue arrows. Minor artifacts are still there and depicted with orange/red arrows.

Main External Collaborators: Alexandre Vignaud (*CEA/NeuroSpin*), Mariappan Nadar (*Siemens-Healthineers, USA*), Boris Mailhé (*Siemens-Healthineers, USA*).

Although CS is used extensively, this approach suffers from a very slow image reconstruction process, which is detrimental to both patients and rapid diagnosis. To counteract this delay and improve image quality, as explained in Sec. 3.1 deep learning is used. In 2020 we secured the second spot in the 2020 brain fastMRI challenge (1.5 and 3T data) [139] with the XPDNet (Primal Dual Network where X plays the role of a magic card) deep learning architecture. Additionally, we assessed XPDNet’s transfer learning capacity on 7T NeuroSpin T2 images. However this DL reconstruction process was limited to Cartesian encoding, thus incompatible with our SPARKLING related technological push. In 2022, we went therefore further by proposing the NCPD-Net deep learning architecture for non-Cartesian imaging. NCPD-Net stands for Non-Cartesian Primal Dual Network and is able to handle both 2D and 3D non-Cartesian k-space data such as those collected with the full 3D SPARKLING encoding scheme [155]. This progress allowed us to make a significant leap in image quality when implementing high resolution imaging while maintaining a high acceleration rate.

In 2023, we published novel significant results based on the original NC-PDNet architecture. We actually combined with physics-driven model to speed up the correction of off-resonance effects induced by the inhomogeneities of the static magnetic field B_0 [6]. Fig. 3[left column] shows the signal void in the frontal region of the brain when not applying any correction. The CS correction yields a limited improvement when constraining its processing time to a little portion (actually 1/70) of the brute force correction shown in the top right column (Reference). Next, we show that the best correction of off-resonance artifacts is achieved by combining the NC-PDNet architecture (Network, 4th column in Fig. 3) with non Fourier encoding model in a 70-fold faster process compared to the reference correction (left column). In contrast, using a standard NC-PDNet architecture that is not physically informed by the degradation process causing these off-resonance artifacts leads to

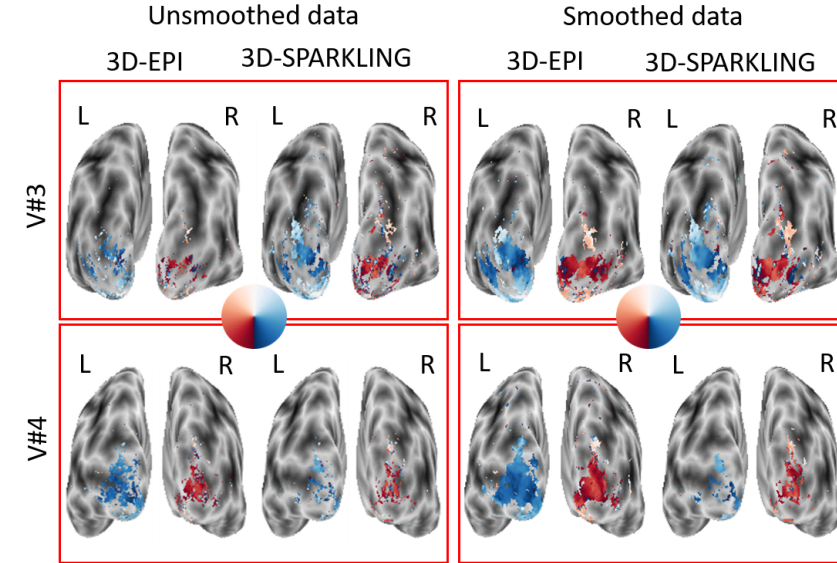


Figure 2: **Projection of the BOLD phase maps on the pial surface visualized on the inflated surface for participants V#3 (3D-SPARKLING run first) and V#4 (3D-EPI run first).** 3D-SPARKLING yields improved projected BOLD phase maps for V#3 in comparison with 3D-EPI both on raw and spatially smoothed data. Opposite results were found in favor of 3D-EPI in V#4, notably on spatially smoothed data.

oversmoothed correction (cf. middle column in Fig. 3). Overall, this work has demonstrated how investigating into the combination of physics-informed deep learning architectures was instrumental in obtaining high image quality in clinically viable processing time.

MRI magnetic resonance imaging essentially involves the optimization of (1) the sampling pattern in k-space under MR hardware constraints and (2) image reconstruction from undersampled k-space data. Recently, deep learning methods have allowed the community to address both problems simultaneously, especially in the non-Cartesian acquisition setting. In 2023, the MIND has made major contribution [9] to this field by tackling some major concerns in existing approaches. Particularly, current state-of-the-art learning methods seek hardware compliant k-space sampling trajectories by enforcing the hardware constraints through additional penalty terms in the training loss. Through ablation studies, we rather show the benefit of using a projection step to enforce these constraints and demonstrate that the resulting k-space trajectories are more flexible under a projection-based scheme, which results in superior performance in reconstructed image quality. In 2D studies, our novel PROjection for Jointly LEarning non-Cartesian Trajectories while Optimizing Reconstructor (PROJeCTOR) trajectories present an improved image reconstruction quality at a 20-fold acceleration factor on the fastMRI data set with SSIM scores of nearly 0.92–0.95 in our retrospective studies as compared to the corresponding Cartesian reference and also see a 3–4 dB gain in PSNR as compared to earlier state-of-the-art methods. Finally, we extend the algorithm to 3D and by comparing optimization as learning-based projection schemes in Fig. 4, we show that data-driven joint learning-based PROJeCTOR trajectories outperform model-based methods such as SPARKLING through a 2 dB gain in PSNR and 0.02 gain in SSIM.

8.3 Large Scale Bayesian Network Resolution with Applications to Neuroimaging

Participants: Demian Wassermann, Louis Rouillard, Alexandre Le Bris, Thomas Moreau.

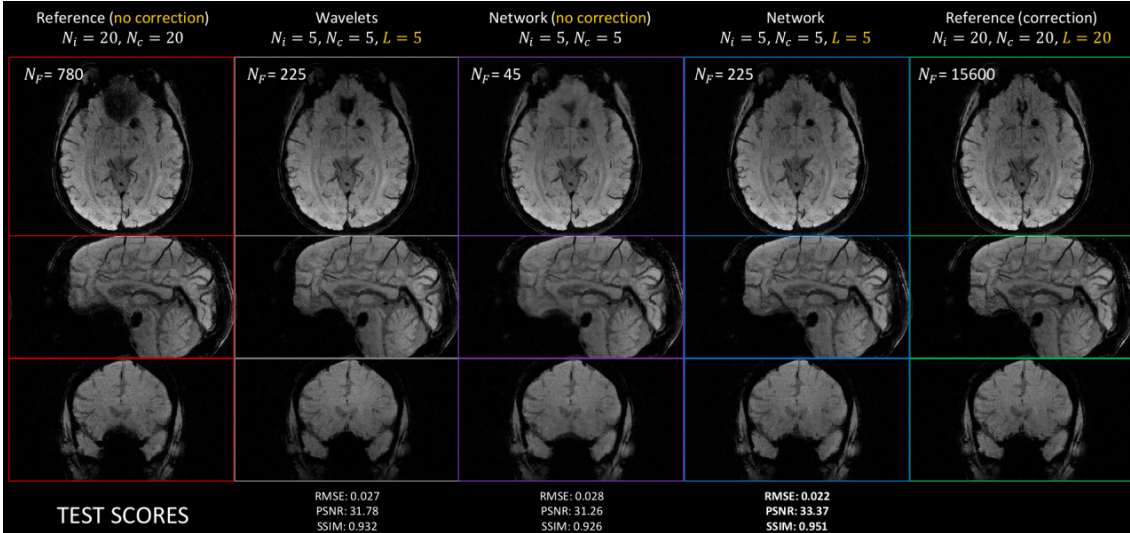


Figure 3: **Deep learning physics-informed correction of off-resonance artifacts during MR image reconstruction using the NC-PDnet architecture.** Illustration on a single SWI volume (high resolution: $600 \mu\text{m}$). **Left** (red): Compressed Sensing (CS) reconstruction with no artifact correction, computed in 25min. **Center left**: CS reconstruction using a reduced non-Fourier forward model to correct for B_0 inhomogeneities in approximately 10min. **Middle** (purple): Network or NC-PDnet based reconstruction without physics based knowledge to correct for B_0 inhomogeneities (approx. 1min of computation). **Center right** (blue): NC-PDnet based reconstruction without physics based knowledge to correct for B_0 inhomogeneities (7min of computation). **Right** (green): Classical CS reconstruction and off-resonance artifact correction based on an extended non-Fourier model, which costs 8 hours of computation. The best result is that in the blue frame.

Bayesian networks (BNs) have emerged as a powerful tool for modeling complex relationships among variables in neuroimaging data generatively. Their ability to capture causal and probabilistic dependencies makes them well-suited for representing the intricate and multifaceted nature of brain activity. However, the large scale of neuroimaging data presents a significant challenge for BNs. This data in a large database can scale to millions of random variables, if we consider 1,000 subjects with at least 32,000 measurements on the brain cortex per subject. As the number of variables increases, the complexity of the BN grows exponentially, making it computationally intractable to fit these models using existing generic algorithms. This computational bottleneck impedes the widespread application of BNs in neuroimaging research and hinders our ability to fully understand the intricate workings of the brain.

To address this problem we have proposed the PAVI method (Plate Amortized Variational Inference) [158] as a follow up of our previously proposed Automatic Dual Amortized Variational Inference (ADAVI) [159]. These methods harness the symmetry of large neuroimaging models, specifically considering each cortical measurement and each subject as independent identically distributed realizations of the same random variables. In complement with stochastic optimization techniques, the PAVI algorithm is able to produce individualized parcellations of 1,000 of subjects at a time. Thus, we are now able to harness the descriptive and interpretable power of BNs to produce individualized cortical parcellations which we then test through the prediction of cognitive abilities.

8.4 Generalized parametric models for temporal point processes

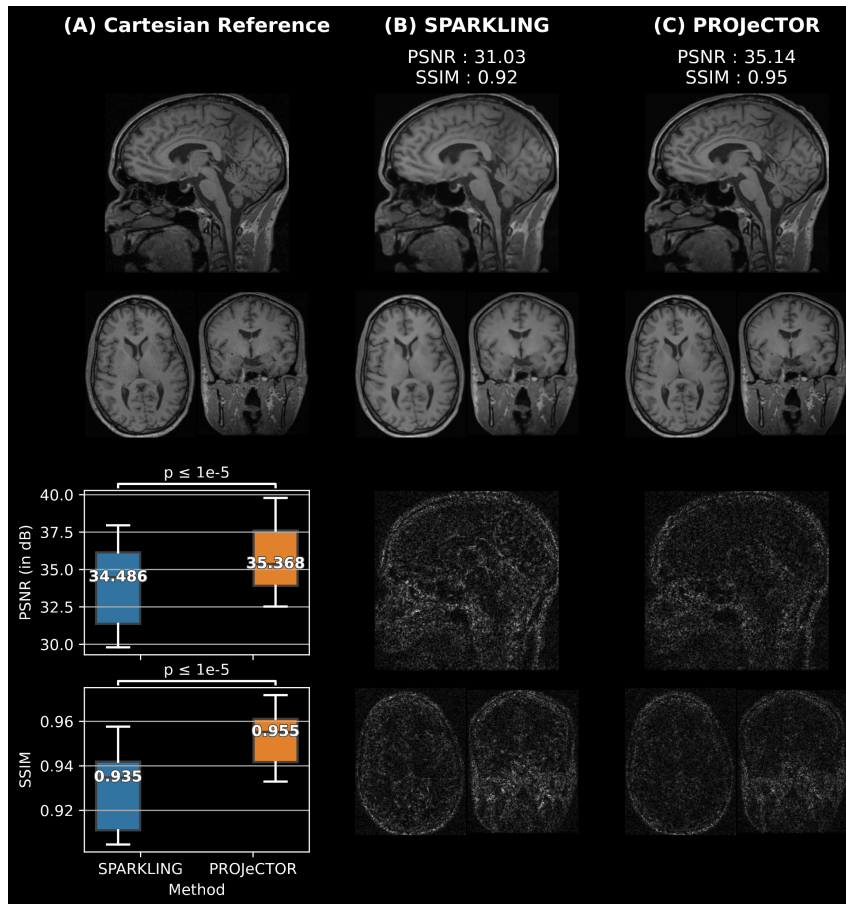


Figure 4: **A generic learning-based framework for joint optimization of the MRI acquisition and reconstruction models.** Qualitative and quantitative comparisons of reconstructed images from 3D (B) SPARKLING and (C) PROJeCTOR trajectories at an acceleration factor $AF = 20$ as compared to (A) Cartesian reference. The reconstructed images are shown in the top row, while the residuals are shown in the bottom. Further, box plots of the SSIM and PSNR scores on 20 test data sets are shown in the bottom-left. The significance levels are marked through a paired samples Wilcoxon test.

Participants: Cedric Allain, Guillaume Staerman, Virginie Loison, Thomas Moreau.

Main External Collaborators: Alexandre Gramfort (*Meta*).

Temporal point processes (TPP) are a natural tool for modeling event-based data. Among all TPP models, Hawkes processes have proven to be the most widely used, mainly due to their adequate modeling for various applications, particularly when considering exponential or non-parametric kernels. Although non-parametric kernels are an option, such models require large datasets. While exponential kernels are more data efficient and relevant for specific applications where events immediately trigger more events, they are ill-suited for applications where latencies need to be estimated, such as in neuroscience. We developed an efficient solution to TPP inference using general parametric kernels with finite support. The developed solution consists of a fast ℓ_2

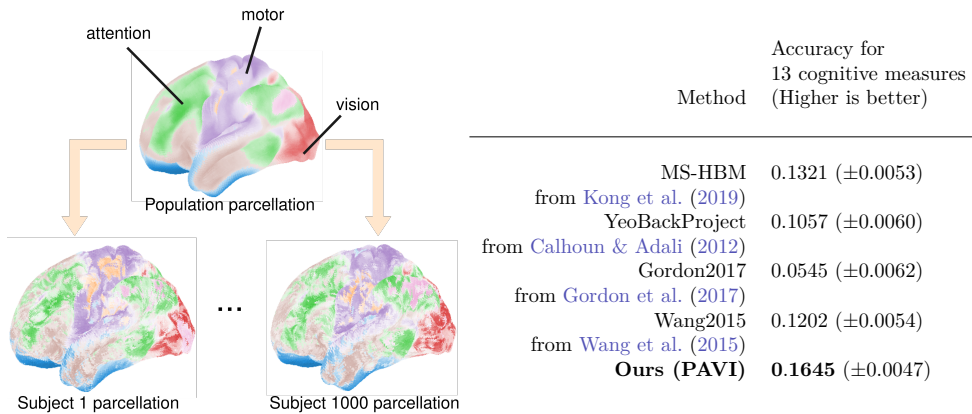


Figure 5: Results from individualized parcellation and cognitive function production using our method PAVI [158]. On the left the population parcellation along with two individualized ones. On the right the aggregated correlation of cognitive score predictions for 1,000 subjects along with those currently in literature

gradient-based solver leveraging a discretized version of the events. After theoretically supporting the use of discretization, the statistical and computational efficiency of the novel approach has been demonstrated through various numerical experiments. Finally, the method’s effectiveness is evaluated by modeling the occurrence of stimuli-induced patterns from brain signals recorded with magnetoencephalography (MEG), as reported in Fig. 6. This result was presented in Staerman et al. [34]. These results are prerequisites to scale the resolution of bi-level optimization problems to larger applications such as the one in neurosciences.

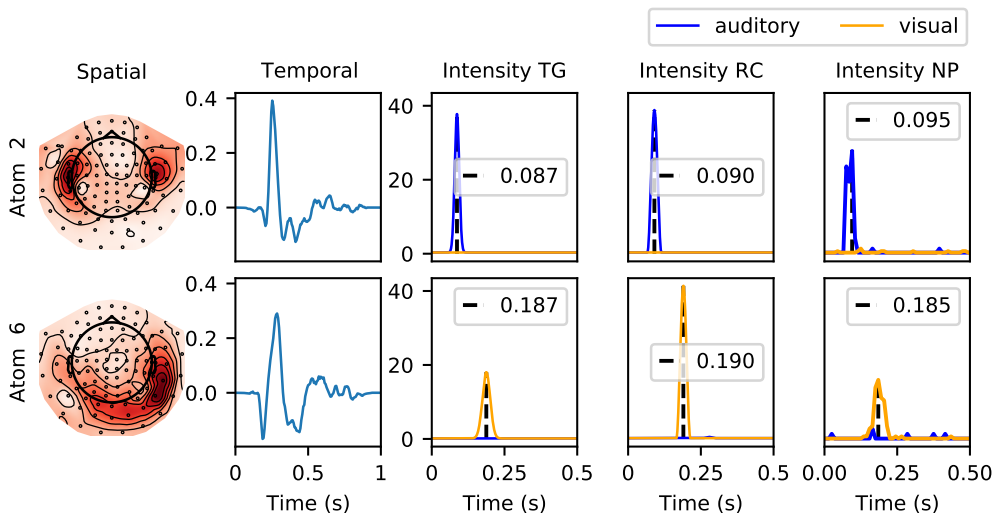


Figure 6: Spatial and temporal patterns of 2 atoms from *sample* MEG dataset, and their respective estimated intensity functions after a stimulus (cue at time = 0 s), for auditory and visual stimuli with non-parametric (NP), Truncated Gaussian (TG) and Raised Cosine (RC) kernels. The parametric kernels recover cleaner estimates of the brain response to the stimuli compare to NP, and both estimate correctly the link between the stimuli and the response.

8.5 Statistically Valid Variable Importance Assessment through Conditional Permutations

Participants: Bertrand Thirion, Ahmad Chamma.

Main External Collaborators: Denis Engemann (*Roche*).

Variable importance assessment has become a crucial step in machine-learning applications when using complex learners, such as deep neural networks, on large-scale data. Removal-based importance assessment is currently the reference approach, particularly when statistical guarantees are sought to justify variable inclusion. It is often implemented with variable permutation schemes. On the flip side, these approaches risk misidentifying unimportant variables as important in the presence of correlations among covariates. Here we develop a systematic approach for studying Conditional Permutation Importance (CPI) that is model agnostic and computationally lean, as well as reusable benchmarks of state-of-the-art variable importance estimators. We show theoretically and empirically that CPI overcomes the limitations of standard permutation importance by providing accurate type-I error control. When used with a deep neural network, CPI consistently showed top accuracy across benchmarks. An experiment on real-world data analysis in a largescale medical dataset showed that CPI provides a more parsimonious selection of statistically significant variables. Our results suggest that CPI can be readily used as drop-in replacement for permutation-based methods.

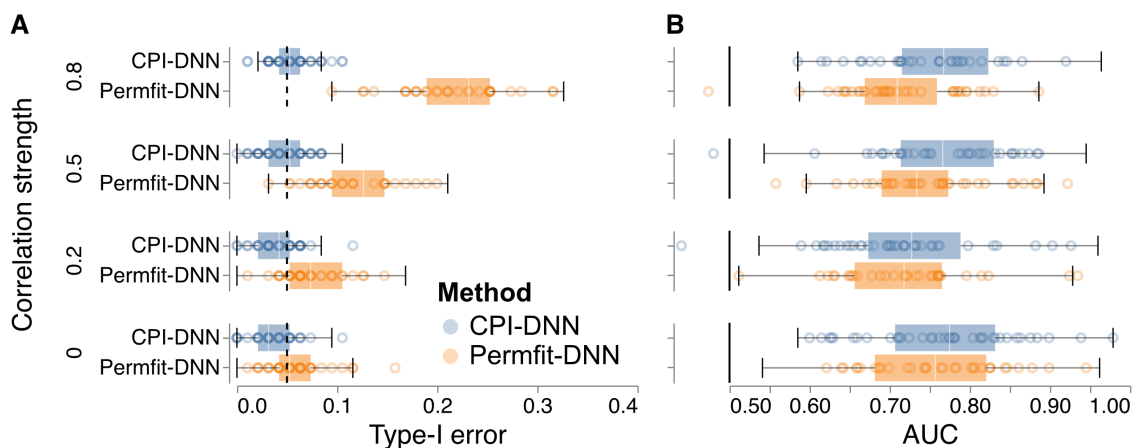


Figure 7: **Performance of Conditional permutation-based vs standard permutation-based variable importance:** Performance at detecting important variables on simulated data with n 300 samples and p 100 features. **(A)**: The type-I error quantifies to which extent the rate of low p -values (p 0.05) exceeds the nominal false positive rate. **(B)**: The AUC score measures to which extent variables are ranked consistently with the ground truth. Dashed line: targeted type-I error rate. Solid line: chance level.

8.6 False Discovery Proportion control for aggregated Knockoffs

Participants: Bertrand Thirion, Alexandre Blain.

Main External Collaborators: Pierre Neuvial (*IMT, Univ. Toulouse*), Olivier Grisel (*Inria, Soda team*).

Controlled variable selection is an important analytical step in various scientific fields, such as brain imaging or genomics. In these high-dimensional data settings, considering too many variables leads to poor models and high costs, hence the need for statistical guarantees on false positives. Knockoffs are a popular statistical tool for conditional variable selection in high dimension. However, they control for the expected proportion of false discoveries (FDR) and not their actual proportion (FDP). We present a new method, KOPI, that controls the proportion of false discoveries for Knockoff-based inference. The proposed method also relies on a new type of aggregation to address the undesirable randomness associated with classical Knockoff inference. We demonstrate FDP control and substantial power gains over existing Knockoff-based methods in various simulation settings and achieve good sensitivity/specificity tradeoffs on brain imaging and genomic data.

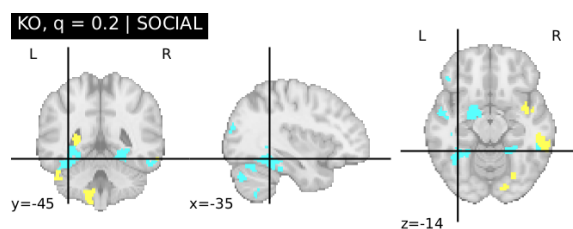


Figure 8: **Application of Kopia to cognitive brain imaging.** We have employed KOPI on fMRI and genomics data. The aim of fMRI data analysis is to recover relevant brain regions for a given cognitive task as shown below. Here we display brain regions whose activity predicts that the participant is attending to stimuli with social motion.

9 Bilateral contracts and grants with industry

Participants: Philippe Ciuciu, Guillaume Daval-Fr erot, Alexandre Gramfort, Charlotte Caucheteux, Thomas Moreau.

9.1 Bilateral contracts with industry

9.1.1 Siemens Healthineers & AI lab (Princeton, USA)

Since Fall 2019, Philippe Ciuciu has actively collaborated with the Siemens-Healthineers AI lab, led by Mariappan Nadar in the context of the joint supervision of Guillaume Daval-Fr erot’s CIFRE PhD thesis dedicated to Deep learning for off-resonance artifact correction in MR image reconstruction in the specific application of susceptibility weighted imaging at 3 Tesla. On top of the PhD funding, this contract has generated 45k  for MIND and was managed by CEA/NeuroSpin. G. Daval-Fr erot’s PhD defense was held on December, 16 2022. As this first collaboration was successful, we engaged strategic discussions with the Siemens-Healthineers headquarters (Erlangen, Germany) during Spring 2022 to pursue this partnership and eventually set up a new one in 2023. Finally, a new CIFRE PhD thesis will start in January 2024 where Mrs. Asma Tanabene will be working on self-supervised 3D MR image reconstruction using deep learning models.

9.1.2 Facebook AI Research (FAIR)

There is currently a CIFRE PhD between FAIR and MIND (Alexandre Gramfort) to investigate the differences between deep learning models and the brain, especially considering NLP machine

learning models. As the collaboration is led by Alexandre Gramfort in the team, it is therefore financially managed by Inria.

9.1.3 Saint Gobain Research (SGR)

There is currently a consulting contract between SGR and MIND (Thomas Moreau) to provide an expertise in machine learning to process temporal data, numerical optimization and scientific computing. The expertise is provided one half-day per month, in SGR offices, and it consists in scientific discussion sessions on the ML projects led by SGR data scientists.

9.2 Bilateral Grants with Industry

9.2.1 Google

MIND (Thomas Moreau) received a 30k€ donation from Google to support its open source activity around `benchopt`. In particular, the grant aims to support the organization of coding and benchmarking sprints around `benchopt`, the development of visualization tools, and the benchmarking of bilevel solvers, in particular the ones using `jaxopt`.

Participants: Demian Wassermann, Bertrand Thirion, Philippe Ciuciu, Thomas Moreau, Chaithya Giliyar Radhakrishna.

10 Partnerships and cooperations

10.1 International initiatives

10.1.1 Inria associate team not involved in an IIL or an international program

NeuroMind

Title: Precision mapping of the Brain by Neuromod & Mind

Duration: 2022 ->

Coordinator: Pierre BELLEC (pierre.bellec@criugm.qc.ca)

Partners:

- Université de Montréal Montréal (Canada)

Inria contact: Bertrand Thirion

Summary: Among the main advances of the last decade, the development of powerful AI systems for vision, language processing, as well as reinforcement learning, have led to sophisticated cognitive systems that can be compared to the human brain, and sometimes surpass human performance. Brain/AI system comparison is a great opportunity for AI and for neuroscience. One of the most urgent tasks for cognitive neuroscience is thus to put together datasets that probe the brain system and are comprehensive enough to allow a reliable comparison of brain activity to the representations generated by AI systems. To address this endeavor, Parietal and NeuroMod have launched ambitious data acquisitions initiative (individual Brain CHarting and Courtois Neuromod), that consist in collecting huge amounts of brain data in few participants. These unprecedented data collection efforts bring novel challenges for data analysis: handling TB-scale data, automation, and better integration of analysis pipeline. Software such as Nilearn and MNE increasingly face the challenge of scaling up to larger datasets. Addressing this challenge in the context of IBC and Courtois Neuromod is thus a unique opportunity.

10.2 International research visitors

10.2.1 Visits of international scientists

Other international visits to the team

David Degras

Status Associate Professor in the Department of Mathematics

Institution of origin: University of Massachusetts Boston

Country: USA

Dates: from 01/09/2023 to 30/06/2024

Context of the visit: David is financially supported by the DataIA program and the Inria Saclay Ile-de-France center. His research projects in the team will revolve around machine learning and optimization for computational neuroimaging. For a smooth integration in the team, he is currently involved in dynamic functional connectivity analysis from fMRI data. Next he will be contributing to two ongoing research projects, namely (i) robustness in multifractal analysis of MEG/EEG signals and (ii) functional alignment of brain images. The first project will crucially engage with issues of robustness in learning. The second will largely revolve around optimization (including combinatorial optimization for the choice of barycenter and optimization of hyperparameters). Both projects will investigate the reproducibility of the obtained results as well as out-of-sample validation with independent data. Together, these aspects address the following points of the subject area:

- Automatic learning and hyper-optimization
- Optimization for learning, e.g., improvements in stochastic gradient methods, Bayesian optimization), combinatorial optimization
- Reproducibility and robust learning
- Statistical Inference and Validation.

The proposed projects both contain: (i) an important methodological component of general interest to the statistical and machine learning community, and (ii) an applied neuroimaging component that serves the long-term goal of promoting health (for example, by better understanding the neural foundations of psychological/neurodegenerative pathologies and by better predicting therapeutic/surgical outcomes for people based on their brain function and anatomy).

Mobility program/type of mobility: sabbatical, i.e. invited Professor.

10.3 European initiatives

10.3.1 H2020 projects

EBRAIN HEALTH

Title: EBRAIN-HEALTH

Duration: 2023 -> 2026

Coordinator: Petra Ritter (Charité, Berlin)

Partners:

- CHARITE - UNIVERSITAETSMEDIZIN BERLIN
- EBRAINS

- FORSCHUNGSZENTRUM JULICH GMBH
- STICHTING RADBOUD UNIVERSITEIT
- UNIVERSIDAD POMPEU FABRA
- OSLO UNIVERSITETSSYKEHUS HF
- TP21 GMBH
- FRAUNHOFER GESELLSCHAFT ZUR FORDERUNG DER ANGEWANDTEN FORSCHUNG EV
- INDOC RESEARCH EUROPE GGMBH
- UNIVERSITAT WIEN
- UNIVERSIDAD COMPLUTENSE DE MADRID
- EODYNE SYSTEMS SL
- ATHINA-EREVNITIKO KENTRO KAINOTOMIAS STIS TECHNOLOGIES TIS PLIROFORIAS, TON EPIKOINONION KAI TIS GNOSIS
- UNIVERSITETET I OSLO
- STICHTING VUMC
- UNIVERSITA DEGLI STUDI DI ROMA LA SAPIENZA
- ALZHEIMER EUROPE
- INSTITUT NATIONAL DE RECHERCHE EN INFORMATIQUE ET AUTOMATIQUE

Inria contact: Bertrand Thirion

Summary: The project aims to develop a decentralized, data protection-compliant research platform capable of simulating some of the brain’s complex neurobiological phenomena. As part of the project, researchers will collate an array of different types of information, including data from PET and MRI scans, EEG tests, behavioral studies and lifestyle surveys, as well as clinical data from thousands of patients and healthy controls. These will be combined with biological information from knowledge databases and made available for research purposes. The resultant digital ‘brain twins’ will enable large numbers of researchers to conduct innovative research within a powerful digital infrastructure.

Thanks to its transparent analytical pipelines, the new research infrastructure will also help to promote reproducible research.

Furthermore, complex, personalized brain simulations which take into account large quantities of data may be able to provide a better understanding of the mechanisms underlying brain function and disorders. Virtual brain modeling may also improve diagnostics and disease prediction, in addition to enabling the optimization of treatment plans. The project consortium comprises 20 partners and operates in cooperation with EBRAINS AISBL, the coordinating entity of the EU-funded flagship ‘Human Brain Project’.

10.4 National initiatives

CEA BlueSky project

Title: Brain & Computers

Duration: 2023 ->

Coordinator: Philippe Ciuciu (CEA/DRF/JOLIOT/NEUROSPIN/MIND), Saclay

Partners:

- CEA/DRF/JOLIOT/NEUROSPIN (BAOBAB, UNICOG), Saclay
- CEA/DRT/LETI/CLIMATEC, Grenoble

- CEA/DRT/LIST/DSCIN, Grenoble

Inria contact: Philippe Ciuciu

Summary: Artificial Intelligence (AI) is now capable of approaching human performance in tasks such as visual recognition, classification (i.e., decision-making), and even textual or visual production (e.g., GPT-4). Understanding the human brain mechanisms of learning and decision-making in an uncertain environment remains a major scientific challenge in neuroscience. This understanding will enable the development of AI architectures that replicate brain circuits. Additionally, in clinical applications, it can lead to a generational leap in the design of neuroprostheses. These neuroprostheses hold great promise for improving the quality of life for individuals affected by spinal cord injuries (approximately 30% of cases). The two main objectives of this BlueSky project complement each other. On one hand, in healthy subjects, the goal is to design computational models based on AI that encode these cerebral functions to gain a more precise understanding of the associated brain activity. On the other hand, the objective is to enable a greater number of patients to control neuroprostheses autonomously through AI, making these medical devices more widely accepted as a therapeutic solution for motor rehabilitation. Tackling such a challenge is not without risks and requires expanding knowledge in neuroscience, surpassing current technological and clinical limits. It also calls for strong synergies among the various CEA institutes involved (Joliot, LETI, and LIST) and their academic (Inserm, Inria, Universities Paris-Saclay, and Grenoble Alpes) and clinical partners (CHU Grenoble-Alpes).

This project has received a funding of 1.5M€ for the 2023-2025 period.

ANR DARLING

Title: DARLING: Distributed adaptation and learning over graph signals

Duration: 2020 -> 2025 (extended)

Coordinator: Cédric Richard (cedric.richard@unice.fr), Professor 3IA Senior Chair in UCA

Partners:

- Université Côte d'Azur Nice, France
- CNRS, École Normale Supérieure, Lyon, France
- Gipsa-lab, UMR 5216, CNRS, UGA, Grenoble, France
- CentraleSupélec, University of Paris-Saclay, Gif-sur-yvette, France

Inria contact: Philippe Ciuciu

Summary: The DARLING project will aim to propose new adaptive learning methods, distributed and collaborative on large dynamic graphs in order to extract structured information of the data flows generated and/or transiting at the nodes of these graphs. In order to obtain performance guarantees, these methods will be systematically accompanied by an in-depth study of random matrix theory. This powerful tool, never exploited so far in this context although perfectly suited for inference on random graphs, will thereby provide even avenues for improvement. Finally, in addition to their evaluation on public data sets, the methods will be compared with each other using two advanced imaging techniques in which two of the partners are involved: radio astronomy with the giant SKA instrument (Obs. Côte d'Azur) and MEG brain imaging (Inria MIND at NeuroSpin, CEA Saclay). Sheng Wang as a postdoc in MIND and Merlin Dumeur as a MIND PhD student in co-tutelle with Matias Palva from Aalto University, Finland are actually involved in the processing of MEG and S/EEG time series on graphs, notably to analyze scale-free (i.e. critical and bistability) phenomena across these graphs and extract potentially new biomarkers for characterizing the pathophysiology of epileptogenic zone (EZ) in drug resistant epilepsy.

ANR VLFMRI**Title:** VLFMRI: Very low field MRI for babies**Duration:** 2021 -> 2025**Coordinator:** Claude Fermon (CEA Saclay, DRF/IRAMIS/SPECT)**Partners:**

- CEA/SHFJ/BIOMAPS, Orsay, France
- CEA/NeuroSpin, Gif-sur-Yvette, France
- APHP Robert Debré hospital, Paris, France
- APHP Bicêtre hospital, Kremlin-Bicêtre, France

Inria contact: Philippe Ciuciu

Summary: VLFMRI aims at developing a very low-field Magnetic Resonance Imaging (MRI) system as an alternative to conventional high-field MRI for continuous imaging of premature newborns to detect hemorrhages or ischemia. This system is based on a combination of a new generation of magnetic sensors based on spin electronics, optimized MR acquisition sequences (based on the SPARKLING patent, Inria-CEA MIND team at NeuroSpin) and a open and compatible system with an incubator that will allow to achieve an image resolution of 1mm^3 on a whole baby body in a short scan time. This project is a partnership of three academic partners and two hospital departments. The different stages of the project are the finalization of the hardware development and software system, preclinical validation on small animals and clinical validation. Kumari Pooja has been hired in January 2022 as research engineer in MIND to interact with the coordinator of this ANR project, Claude Fermon and design new accelerated acquisition methods for verly low field MRI. Preliminary encouraging results allow us to retrospectively accelerate MRI acquisition by a factor of 10 without degrading image quality at 2mm isotropic resolution.

KARAIB AI CHAIR**Title:** KARAIB: Knowledge And RepresentAtion Integration on the Brain**Duration:** 2020 -> 2024**Coordinator:** Bertrand Thirion**Partners:**

- INRIA MIND, Gif-sur-Yvette, France

Inria contact: Bertrand Thirion

Summary: Cognitive science describes mental operations, and functional brain imaging provides a unique window into the brain systems that support these operations. A growing body of neuroimaging research has provided significant insight into the relations between psychological functions and brain activity. However, the aggregation of cognitive neuroscience results to obtain a systematic mapping between structure and function faces the roadblock that cognitive concepts are ill-defined and may not map cleanly onto the computational architecture of the brain.

To tackle this challenge, we propose to leverage rapidly increasing data sources: text and brain locations described in neuroscientific publications, brain images and their annotations taken from public data repositories, and several reference datasets. Our aim here is to develop multi-modal machine learning techniques to bridge these data sources.

- Aim 1 develops representation techniques for noisy data to couple brain data with descriptions of behavior or diseases, in order to extract semantic structure.
- Aim 2 challenges these representations to provide explanations to the observed relationships, based on two frameworks: i) a statistical analysis framework; ii) integration into a domain-specific language.
- Aim 3 outputs readily-usable products for neuroimaging: atlases and ontologies and focuses on implementation, with contributions to neuroimaging web-based data sharing tools.site.

BrAIN AI CHAIR

Title: BrAIN: Bridging Artificial Intelligence and Neuroscience

Duration: 2020 -> 2024

Coordinator: Alexandre Gramfort

Partners:

- INRIA MIND, Gif-sur-Yvette, France

Inria contact: Alexandre Gramfort

Summary: The BrAIN project investigates learning tasks from multivariate EEG and MEG time series. In clinical or cognitive neuroscience, electromagnetic signals emitted by synchronously firing neurons are collected by electroencephalography (EEG) or magnetoencephalography (MEG). Such data, typically sampled at millisecond resolution, are routinely used for clinical applications such as anesthesia monitoring, sleep medicine, epilepsy or disorders of consciousness. Low cost EEG devices are also becoming commodities with hardware startups such as DREEM in France or InteraXon in Canada that have collected hundred of thousands of neural recordings. The field of neuroscience urgently needs algorithms that can learn from such large and poorly labeled datasets. The general objectives of BrAIN is to develop ML algorithms that can learn with weak or no supervision on neural time series. It requires contributions to self-supervised learning, domain adaptation and data augmentation techniques, exploiting the known underlying physical mechanisms that govern the data generating process of neurophysiological signals.

The BrAIN project is organized around four objectives:

- Learn with no-supervision on noisy and complex multivariate signals
- Learn end-to-end predictive systems from limited data exploiting physical constraints
- Learn from data coming from many different source domains
- Develop high-quality software tools that can reach clinical research

ANR MICBrainPres

Title: MicBrainPres: Distributed adaptation and learning over graph signals

Duration: 2023 -> 2026

Coordinator: Demian Wassermann

Partners:

- Brain and Spine Institute, Paris, France
- CNRS, Université de Paris, Lyon, France

Inria contact: Demian Wassermann

Summary: The main goal of this project is to harness the latest advances on machine learning-based neuroimage processing technologies to improve function-preserving brain tumour resection. Identifying eloquent brain regions is fundamental to performing tumour resection while preserving a maximum level of cognitive function. Despite the sustained advance in predicting subject-level cognitive abilities from neuroimaging data, current approaches lack sensitivity and specificity in identifying eloquent brain regions. This hinders neuroimaging’s usefulness for pre-surgical planning as a tool to predict the preservation of cognitive function after tumour resection. In this project, we propose that using subject-specific parcellations, derived from functional and diffusion MRI through deep-learning technologies, will achieve the needed sensitivity and specificity to locate eloquent areas pre-surgically and to predict cortical reshaping after tumour resection.

ANR EBUL

Title: EBUL: Event-based Unsupervised Learning for Physiological Signals

Duration: 2023 -> 2027

Coordinator: Thomas Moreau

Partners:

- INRIA MIND, Gif-sur-Yvette, France

Inria contact: Thomas Moreau

Summary: Sensor-based body monitoring is now routine clinical care. The resulting records are called physiological signals. While enormous quantities of signals are collected every day, the cost and time necessary to clean and annotate them is prohibitive to constitute large labeled databases. When working with physiological signals, extra sources of information are the events surrounding the recordings. Events are external phenomena that impact the signal and can correlate with the prediction task considered. EBUL propose to develop novel unsupervised learning techniques to process such records based on the notion of events, and to apply them to process general anesthesia records collected in Paris hospital Lariboisière. The methodology of the project relies on the development of novel point process models adapted to capture the distribution of physiological events, and their coupling with event detection algorithms. This will provide novel signal representations based on the distribution of events inside them, which are simpler to analyze and fine tune to derive predictive bio-markers.

The EBUL project is organized around 3 objectives:

- Develop novel point process models for physiological signals
- Learn joint models for signals and events
- Develop high-quality models for general anesthesia that can reach clinical research

11 Dissemination

Participants: Demian Wassermann, Bertrand Thirion, Philippe Ciuciu, Thomas Moreau, Chaithya Giliyar Radhakrishna.

11.1 Promoting scientific activities

11.1.1 Scientific events: organisation

T. Moreau 2019-2023: Co-organizer of the *Séminaire Palaisien*, a monthly seminar in the Saclay ecosystem around statistics and machine learning (40 people).

Member of the organizing committees

- P. Ciuciu** July 2023: Co-organizer of the [Harmonic and Multifractal analysis summer school](#) (50 people), 2 weeks, Montreal, Canada.
- B. Thirion** organized a Statistics workshop in Paris, on Oct 19th, see [FastBig](#).
- B. Thirion, D. Wassermann** co-organized the CogBases Workshop in Paris, Pasteur, on Oct 10-11th, see [CogBases 2023](#).
- D. Wassermann** June 2023: Co-organizer as program chair the [28th biennial International Conference on Information Processing in Medical Imaging \(IPMI\)](#) (200 people), 1 weeks, Bariloche, Argentina.

Member of the conference program committees

- P. Ciuciu** October 2023: Member of the congress planning committee of [ESMRMB 2023](#), Basel, Switzerland.
- B. Thirion** PCMember for IABM conference.
- B. Thirion** Area chair for NeurIPS 2023.

Reviewer

- T. Moreau** Reviewer for ICML and NeurIPS 2023.

11.1.2 Journal

Member of the editorial boards

- P. Ciuciu** Associate Editor (AE) for [IEEE Transactions on Medical Imaging \(TMI\)](#), Senior Area Editor for [IEEE Open Journal on Signal Processing](#), AE for Frontiers in Neuroscience, section Brain Imaging Methods.
- B. Thirion** Associate Editor (AE) for [Medical Image Analysis \(MIA\)](#) and [Transactions on Machine Learning Research](#).

Reviewer - reviewing activities

- P. Ciuciu** IEEE Trans on Medical Imaging, IEEE Signal Processing Magazine, Magnetic Resonance in Medicine, iScience, Medical Image Analysis, Computers in Biology and Medicine, Developmental Cognitive Neuroscience.
- B. Thirion** NeuroImage, MEdIA, IEEE Transactions on Medical Imaging, Brain Structure and Function, Human Brain Mapping, Nature Communications.
- T. Moreau** Transactions on Biomedical Engineering.
- D. Wassermann** reviewed for several conferences and journals including Nature Communications, Medical Image Analysis, NeurIPS.
- C. Giliyar Radhakrishna** reviewed for Magnetic Resonance in Medicine and IEEE Transactions on Medical Imaging.

11.1.3 Invited talks

P. Ciuciu

- August 2023: Keynote speaker at the [2023 GRETSI](#) conference, Grenoble, France.
- October 2023: Invited speaker at the [Minnesota Workshop on high and ultra-high field imaging](#) (Minneapolis, MI, USA).
- October 2023: Invited speaker at the [2023 AMU Biomedical Imaging school](#) in Cargese (Corsica, France).

B.Thirion

- March 2023: Data science Institute, Oxford: "How to remove or Control Confounds in predictive models, with application to brain biomarkers"
- April 2023: Conference at CYCERON imaging center, CEA/CNRS, Caen, France
- April 2023: Conference at the Brain Matters symposium "Synthesizing brain images from the neuroscientific literature"
- June 2023: HBP WP2 final conference, 2 presentations; Barcelona, Spain
- June 2023: One health day, Université Paris Saclay "Dealing with the data deluge: identifying important variables from multimodal health data".

T. Moreau

- June 2023: Invited speaker at the [SIAM OP 2023](#) conference, Seattle, USA.
- August 2023: Invited speaker at the [ICIAM 2023](#) conference, Tokyo, Japan.

D.Wassermann

- October 2023: NeuroLang Tutorial at [Cogbases](#): Boosting Specificity in Cognitive Neuroimaging
- October 2023: Keynote at [Computational Diffusion MRI Workshop](#): How do we link diffusion MRI with brain structure and cognition? Breaching the gap between classical neuroanatomy and machine learning.
- May 2023: [Neural 2023](#): Specificity in Cognitive Neuroimaging: Pushing the Envelope in Meta-Analyses by Harnessing Rich Probabilistic Logical Models
- March 2023: Neurosynth 2.0 group meeting: Specificity in Cognitive Neuroimaging: Pushing the Envelope in Meta-Analyses by Harnessing Rich Probabilistic Logical Models

11.1.4 Scientific expertise

P. Ciuciu :

- European expert reviewer for the European Innovation Council Accelerator actions (main track: AI and health).
- External reviewer for the European Research Council (ERC) Synergy grant.

11.1.5 Research administration

P. Ciuciu

- Member of the Board of Directors at NeuroSpin (CEA).
- Member of the steering committee of the CEA cross-disciplinary research program on numerical simulation and AI.

B. Thirion

- Délégué Scientifique of Inria Saclay Center
- Member of ENS Paris-Saclay Scientific Council
- Member of Telecom Sud Paris Scientific Council
- Member of Inria Commission évaluation

11.2 Teaching - Supervision - Juries

11.2.1 Teaching

P. Ciuciu

- Tutorial presenter at the **2023 IEEE ISBI: Computational MRI in the Deep Learning Era**.
- Instructor at the **Harmonic and Multifractal analysis** summer school.
- October 2023: Invited speaker at the **2023 AMU Biomedical Imaging school** in Cargese (Corsica, France).
- Lecturer at the Institut d'Optique Graduate School (3rd year, Signal & Images major).
- Lecturer at the M2 ATSI (CentraleSupélec, ENS Paris-Saclay): Medical imaging course.

D. Wassermann

- Master MVA (École Polytechnique, École Normale Supérieure, Centrale Supélec): Graphical Models
- Master in Biomedical Engineering (Université Paris Descartes): Quantification in NeuroImaging.

T. Moreau

- Master Data Science (IPP/UP Saclay): Datacamp.
- Executive Master Big Data (Université Dauphine): Introduction to Python.

B. Thirion

- MVA Master (École Polytechnique, École Normale Supérieure, Centrale Supélec): Brain Function ; 12h
- NeuroEngineering Master (UPSAclay): fMRI data analysis; 2h
- Instructor at the HBP/Ebrains conference, March 2023: tutorial on fMRI data analysis on Ebrains ; 2h
- Instructor at ESMRMB conference, Oct 2023, Basel. Two courses taught: "When does the use of statistics make sense ?" and "Help ! My sample is too small."

11.2.2 Supervision

P. Ciuciu

- C. Giliyar Radhakrishna, PhD 2020-2023
- M. Dumeur (with M. Palva, Aalto Univ), PhD in cotutelle (4y), 2020-2024
- Z. Amor (with A. Vignaud, CEA) PhD 2020-2024
- P.-A. Comby (with A. Vignaud, CEA), PhD 2021-2024
- S. Brosset, (with Z. Saghi, CEA) PhD 2022-2025
- D. Nuñez-Fernandez (with A. Vignaud, CEA), PhD 2023-2026
- M. Marzulli, M1 BME Paris, (June - Sep 2023)
- L. Oudjman, work-study professional master's degree at EpiTech (Oct 2023 - Jul 2025)

B. Thirion

- Alexandre Pasquiou, PhD 2020-2023 (with C.Pallier)
- Alexis Thual, PhD 2020-2024 (with S. Dehaene)
- Ahmad Chamma, PhD 2021-2023 (with D.Engemann)
- Raphael Meudec, PhD 2021-2024 (with D.Wassermann)

- Thomas Chapalain, PhD 2021-2024 (with E.Eger)
- Alexandre Balin, PhD 2021-2024 (with P.Neuviat)
- Nicolas Salvy, PhD 2023-2026 (with H.Talbot)

D. Wassermann

- Gaston Zanitti, PhD 2020-2023
- Louis Rouillard, PhD 2021-2024
- Raphael Meudec, PhD 2021-2024 (with B. Thirion)
- Alexandre Le Bris, PhD 2022-2025
- Gabriela Gomez Jimenez, PhD 2023-2026 (with J. Valette CEA)

T. Moreau

- B. Malézieux (with M. Kowalski, UP Saclay), PhD 2020-2023
- C. Allain (with A. Gramfort, Meta), PhD 2021-2024
- M. Dagréou (with S. Vaiter, Université Cote d'Azur and P. Ablin, Apple), PhD 2021-2024
- F. Michel (with M. Kowalski, UP Saclay), PhD 2022-2025
- V. Loison (with J. Cartailier, APHP), PhD 2023-

11.2.3 Juries

- P. Ciuciu** : External reviewer of the PhD thesis defended by Clément Poiret (Univ Paris-Cité), Paris, France.
- P. Ciuciu** : PhD committee president of the PhD thesis defended by Pierre Barbot (Univ Paris-Saclay), L2S, Gif-sur-Yvette, France.
- B. Thirion** External reviewer of the PhD thesis defended by Lucrezia Carboni (Grenoble Université), October 2023
- B. Thirion** External reviewer of the PhD thesis defended by Etrit Haxholli (Université Nice Côte d'Azur), October 2023
- B. Thirion** PhD committee president for the PhD thesis defended by Adrien Pavao (Université Paris-Saclay), in Dec 2023.
- B. Thirion** PhD committee president for the PhD thesis defended by Sydnez Krystal (Université Paris-Saclay), in Dec 2023.

11.3 Popularization

- P.Ciuciu, B. Thirion** Le 13-14 broadcasted on France Inter radio, April, 12. Round table around AI progress for health and neuroscience.
- B.Thirion** CPGE Saint Benoit, December 2023 *Où va l'intelligence artificielle ?*
- B.Thirion** Plenary conference at NeuroPlanet, Marc 2023 *Cartographie Cérébrale Individualisée*
- D. Wassermann** A Pint of Beer, talk on AI and Human Brain Function, June 2023

11.3.1 Internal or external Inria responsibilities

- D. Wassermann** COERLE Scientific representative for Inria Saclay Île-de-France; Representative at the Graduate School in Computer Science of Université Paris-Saclay for Inria Saclay Île-de-France.
- T. Moreau** President of the Inria Saclay CUMI; Representative for Inria Saclay in the commission for the development of the national computational resources.

11.3.2 Education

P.Ciuciu Talk given at the 3rd Doctoral Students day organized by DataIA for PhD students in AI/Data Science at the Paris-Saclay University, December 7.

12 Scientific production

12.1 Major publications

- [1] Z. Amor, C. Le Ster, C. Gr, G. Daval-Fr erot, N. Boulant, F. Mauconduit, B. Thirion, P. Ciuciu and A. Vignaud. ‘Impact of B0 field imperfections correction on BOLD sensitivity in 3D-SPARKLING fMRI data’. In: *Magnetic Resonance in Medicine* (29th Dec. 2023). DOI: [10.1002/mrm.29943](https://doi.org/10.1002/mrm.29943). URL: <https://hal.science/hal-04363381>.
- [2] C. Giliyar Radhakrishna, G. Daval-Fr erot, A. Massire, A. Vignaud and P. Ciuciu. ‘Improving spreading projection algorithm for rapid k-space sampling trajectories through minimized off-resonance effects and gridding of low frequencies’. In: *Magnetic Resonance in Medicine* 90.3 (22nd May 2023), pp. 1069–1085. DOI: [10.1002/mrm.29702](https://doi.org/10.1002/mrm.29702). URL: <https://inria.hal.science/hal-04370475>.
- [3] G. Staerman, C. Allain, A. Gramfort and T. Moreau. ‘FaDIn: Fast Discretized Inference for Hawkes Processes with General Parametric Kernels’. In: *PMLR*. International Conference on Machine Learning. Vol. 202. Honolulu, Hawaii, United States, 25th July 2023, pp. 32575–32597. URL: <https://hal.science/hal-03811810>.

12.2 Publications of the year

International journals

- [4] Z. Amor, C. Le Ster, C. Gr, G. Daval-Fr erot, N. Boulant, F. Mauconduit, B. Thirion, P. Ciuciu and A. Vignaud. ‘Impact of B0 field imperfections correction on BOLD sensitivity in 3D-SPARKLING fMRI data’. In: *Magnetic Resonance in Medicine* (29th Dec. 2023). DOI: [10.1002/mrm.29943](https://doi.org/10.1002/mrm.29943). URL: <https://hal.science/hal-04363381>.
- [5] C. Caucheteux, A. Gramfort and J.-R. King. ‘Evidence of a predictive coding hierarchy in the human brain listening to speech’. In: *Nature Human Behaviour* (2nd Mar. 2023). DOI: [10.1038/s41562-022-01516-2](https://doi.org/10.1038/s41562-022-01516-2). URL: <https://hal.science/hal-04036331>.
- [6] G. Daval-Fr erot, A. Massire, B. Mailh e, M. Nadar, B. Bapst, A. Luciani, A. Vignaud and P. Ciuciu. ‘Deep learning-assisted model-based off-resonance correction for non-Cartesian SWI’. In: *Magnetic Resonance in Medicine* 90.4 (22nd June 2023), pp. 1431–1445. DOI: [10.1002/mrm.29738](https://doi.org/10.1002/mrm.29738). URL: <https://inria.hal.science/hal-04391871>.
- [7] C. Fang, D. Wassermann and J.-R. Li. ‘Fourier representation of the diffusion MRI signal using layer potentials’. In: *SIAM Journal on Applied Mathematics* 83.1 (28th Feb. 2023), pp. 99–121. DOI: [10.1137/21M1439572](https://doi.org/10.1137/21M1439572). URL: <https://hal.science/hal-03940100>.
- [8] C. Fang, Z. Yang, D. Wassermann and J.-R. Li. ‘A simulation-driven supervised learning framework to estimate brain microstructure using diffusion MRI’. In: *Medical Image Analysis* 90 (Dec. 2023), p. 102979. DOI: [10.1016/j.media.2023.102979](https://doi.org/10.1016/j.media.2023.102979). URL: <https://hal.science/hal-04254343>.
- [9] C. Giliyar Radhakrishna and P. Ciuciu. ‘Jointly Learning Non-Cartesian k-Space Trajectories and Reconstruction Networks for 2D and 3D MR Imaging through Projection’. In: *Bioengineering* 10.2 (24th Jan. 2023), p. 158. DOI: [10.3390/bioengineering10020158](https://doi.org/10.3390/bioengineering10020158). URL: <https://inria.hal.science/hal-04370490>.
- [10] C. Giliyar Radhakrishna, G. Daval-Fr erot, A. Massire, A. Vignaud and P. Ciuciu. ‘Improving spreading projection algorithm for rapid k-space sampling trajectories through minimized off-resonance effects and gridding of low frequencies’. In: *Magnetic Resonance in Medicine* 90.3 (22nd May 2023), pp. 1069–1085. DOI: [10.1002/mrm.29702](https://doi.org/10.1002/mrm.29702). URL: <https://inria.hal.science/hal-04370475>.

- [11] A.-S. Hamy, J. Abécassis, K. Driouch, L. Darrigues, M. Vandenberghe, C. Laurent, F. Zaccarini, B. Sadacca, M. Delomenie, E. Laas, O. Mariani, T. Lam, B. Grandal, M. Laé, I. Bieche, S. Vacher, J.-Y. Pierga, E. Brain, C. Vallot, J. Hotton, W. Richer, D. Rocha, Z. Tariq, V. Becette, D. Meseure, L. Lesage, A. Vincent-Salomon, N. Filmann, J. Furlanetto, S. Loibl, E. Dumas, J. Waterfall and F. Reyat. ‘Evolution of synchronous female bilateral breast cancers and response to treatment’. In: *Nature Medicine* (6th Mar. 2023). DOI: [10.1038/s41591-023-02216-8](https://doi.org/10.1038/s41591-023-02216-8). URL: <https://hal.science/hal-04020231>.
- [12] A. Mellot, A. Collas, P. L. Coelho Rodrigues, D. Engemann and A. Gramfort. ‘Harmonizing and aligning M/EEG datasets with covariance-based techniques to enhance predictive regression modeling’. In: *Neuroscience Imaging* (20th Nov. 2023), pp. 1–26. DOI: [10.1162/iimag_a_00040](https://doi.org/10.1162/iimag_a_00040). URL: <https://hal.science/hal-04328670>.
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