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# Un voyage en électroencéphalographie : entre héritage centenaire et modernité

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# Habilitation à Diriger des Recherches

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## *A journey in Electroencephalography: between century-old heritage and modernity*

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*A Aude et à nos enfants, Vadim et Yaël*

*Aux doctorants qui ont largement contribué à ces travaux, et à tous ceux qui  
avec moi les ont accompagnés*

*A journey in Electroencephalography: between century-old heritage and modernity ©*

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# Résumé

Cette année nous célébrons un siècle d'électroencéphalographie (EEG), une technique pionnière qui permet de mesurer l'activité cérébrale *in vivo* et de manière non-invasive. Aujourd'hui, l'EEG est devenue un outil incontournable, notamment dans les services dédiés à l'épilepsie, aux troubles du sommeil et en réanimation. Au fil des décennies, cette méthode a captivé l'imaginaire des scientifiques, mais aussi des artistes et du grand public. Il y a cinquante ans, en pleine guerre froide, le cinéma la présentait comme un détecteur de mensonge. Au même moment, les premiers capteurs de magnétoencéphalographie (MEG) ont vu le jour, et les premiers dispositifs tête entière ont émergé un quart de siècle plus tard. Plutôt que de supplanter l'EEG, la MEG a ouvert la voie à de nouveaux développements, notamment en matière de localisation des sources corticales des signaux mesurés à la surface du crâne. Et l'EEG s'est modernisée pour aller vers des systèmes haute-densité, à électrodes actives.

Je suis entré en Electroencéphalographie par le chemin ouvert aux ingénieurs et physiciens. Loin des questions de Neurosciences, j'ai d'abord travaillé à développer des méthodes de résolution de ce problème inverse dit mal posé, qui visent à estimer les générateurs corticaux des faibles fluctuations de potentiel électrique (et de champ magnétique, en MEG) mesurables sur le scalp.

A travers mes travaux de doctorat, à Paris, puis de post-doctorat, à Londres, j'ai abordé les principaux éléments de ces méthodes de résolution : (i) le problème direct, autrement dit le modèle biophysique qui à partir de l'activité des réseaux de neurones corticaux prédit leur expression électromagnétique sur le scalp ; (ii) les informations de différentes natures (biophysiques mais aussi anatomiques et fonctionnelles) que l'on peut exploiter pour contraindre la reconstruction de l'activité corticale ; (iii) les méthodes d'inférence probabiliste ou Bayésienne, qui permettent de combiner ces contraintes de manière optimale, et même d'interroger les données pour évaluer leur pertinence respective. Ces travaux font l'objet de la première partie (**Chapter I – Estimating cortical activity from EEG and MEG data**).

Mon post-doctorat m'a aussi permis de me familiariser avec les questions de neurosciences cognitives et les approches computationnelles pour aborder notamment les fonctions de perception, d'apprentissage, et de prise de décision, avec pour objectif de faire le lien entre psychologie expérimentale (l'observation du comportement) et neurophysiologie (l'observation de l'activité cérébrale). Là encore les approches Bayésiennes se révèlent particulièrement puissantes, et notamment comme analogie des calculs réalisés par le cerveau lui-même, pour faire sens de son observation du monde et mettre à jour ses connaissances.

J'ai eu la chance d'être recruté comme chercheur à l'INSERM, à Lyon, où j'ai essentiellement contribué à faire progresser deux axes de recherche, qui sont de plus en plus amenés à se nourrir l'un l'autre. L'un porte sur l'interprétation fonctionnelle des signaux EEG et plus particulièrement des réponses évoquées. C'est l'objet de la deuxième partie (**Chapter II – Interpreting and modeling evoked responses**). L'autre porte sur l'utilisation de l'EEG pour des applications de type interfaces cerveau machine à visée clinique. C'est l'objet de la troisième partie (**Chapter III – Brain-Computer Interfaces, theoretical and applied works**). L'enjeu ici est d'analyser les signaux EEG en temps réel et de les interpréter en termes cognitifs (l'intention, la commande ou l'état mental qu'ils reflètent).

La dernière partie évoque brièvement des projets s'inscrivant dans la continuité de mes travaux, tant en recherche fondamentale qu'appliquée. L'un de mes objectifs est de participer à l'avènement du deuxième centenaire de l'EEG, en œuvrant à sa démocratisation et son expansion vers de nouvelles applications cliniques (**Chapter IV – Conclusion and perspectives**).

# CHAPTER I

## Estimating cortical activity from EEG and MEG data<sup>1</sup>

*“Will the day come when mathematicians know enough about brain physiology, and neurophysiologists enough about mathematical discoveries, for effective cooperation to be possible?”*

*Jacques Hadamard (Mathematician, 1865-1963)*

### Introduction

EEG and MEG directly measure the electrical activity of neuronal populations. They provide a fairly distant observation of this activity, but millisecond by millisecond. On the scalp, sensors capture a mixture of cortical and subcortical activities [1], [2]. EEG has long been used with few electrodes and signal time series analysed visually. Nevertheless, pioneering works from the 50s up to the 70s have developed the conceptual advances and first methods to try to localize the brain sources of EEG measures. First computational approaches became really mature in the 90s and 00s, also greatly stimulated by the recent advent of whole head MEG systems. Indeed, magnetic fields are much less distorted by head tissues than electric potentials and subjects can be easily and quickly equipped with hundreds of sensors. Everything seemed to be in place for EEG and MEG to become genuine high-resolution neuroimaging techniques.

This chapter briefly reviews the main ingredients and hypothesis behind modern methods to estimate cortical activity from EEG or MEG data. It briefly covers forward modelling [3], [4], [5] and inverse solutions with a focus on my own (collaborative) contributions to this effort. The application of a Bayesian approach in this context proved decisive, as it is the parent of most existing inverse methods, uses mandatory *a priori* in an optimal and data-informed fashion, and provides a formal way of combining information (e.g., from other neuroimaging data) and evaluating direct and inverse solutions.

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<sup>1</sup> Suggestion d'écoute pendant la lecture de ce chapitre : [Elégie, Op. 24 \(Version for Cello & Piano\) \(youtube.com\)](https://www.youtube.com/watch?v=...)

## EEG/MEG forward models

### *The biophysics of EEG and MEG*

Neuronal activity generates measurable electric potentials and magnetic fields. Precisely, neurons produce transmembrane electric currents that contribute to macroscopic signals. Pyramidal cells are the main contributors due to their orientation and synchronous activity. A detectable signal is typically obtained when a few tens of neurons from the same population are simultaneously active. Among this activity, post-synaptic potentials are the primary source of EEG/MEG signals, while action potentials contribute minimally.

EEG and MEG are not inherently limited to low frequencies, but several factors make it challenging to measure and analyse high-frequency neuronal activity with these techniques. Synchronized neural activity across large populations of neurons is more likely to occur at lower frequencies. Higher frequency signals are also more susceptible to spatial smearing due to volume conduction through the head tissues. Neuronal signals naturally exhibit a  $1/f$  power spectrum, meaning power decreases as frequency increases, which means that higher frequency activity is typically associated with a lower signal-to-noise ratio. Finally, higher frequency ranges are more susceptible to contamination by muscle artifacts and other high-frequency noise sources.

The biophysical relationship between cortical electromagnetic sources and the measurable electric and magnetic fields at the scalp level is governed by the four Maxwell's equations established in the second part of the 19th century. Importantly, under quasi-static approximation that holds for EEG/MEG frequencies, these equations greatly simplify, allowing calculation of electric potentials and magnetic fields from neuronal currents. What makes this computation challenging in this context though, are the various head tissue types (brain, cerebrospinal fluid, skull, skin) whose structures, shapes and physical properties (electrical conductivities) are complex and inhomogeneous. This suggests that the forward problem will ultimately be solved optimally, at the single subject level, i.e., by taking into account individual anatomy and physical properties.

A forward model consists in three main elements.

- **The source model:** it typically rests on equivalent current dipoles (ECDs) to represent neuronal activity from a cortical macrocolumn. First approaches have consisted in using a few ECDs to model the activity of large brain regions. Localizing or reconstructing this activity then amounts to estimating the position, the orientation and the intensity of each ECD vector. I personally focused on distributed approaches which aim at producing images of brain activity by using several thousands to several tens of thousands ECDs with fixed location and orientation to cover the whole source space (usually the cortical surface).
- **The head model:** it ranges from simple, spherical models to more complex and realistic ones. While spherical models offer simple analytical but less accurate solutions, realistic models account for individual anatomy. The latter call for numerical, approximate solutions, as realistic head models imply several layers with different electromagnetic properties and complex shape boundaries between layers. Most frequently implemented methods include the Boundary Element Method (BEM) [6], the Finite Element Method (FEM) [7] or the Finite Difference Method (FDM) [8]. My first encounter with this field was during my Master 2 internship in Physics, when I developed an FDM C++ algorithm to solve the EEG/MEG forward problem (unpublished). Refining these head models and their computation is still an active area of research, e.g., see [9].
- **The sensor model:** this is simply the type (EEG, MEG magnetometer or gradiometer), the location and, for MEG only, the orientation. For EEG, one also needs to define a reference electrode.

### The distributed source model

Importantly, when relying on a distributed source model, i.e., using many dipoles with fixed location and orientation, the forward model becomes linear. It writes:

$$Y = G.J + \varepsilon \quad (1)$$

where  $Y$  and  $\varepsilon$  are  $[N \times T]$  matrices representing the data and additive noise, respectively,  $N$  being the number of sensors and  $T$  the number of data time samples.  $\varepsilon$  can be viewed as the part of measurement that the forward model cannot (and likely should not) explain (e.g., measurement noise, non-physiological signal...).  $J$  is the  $[P \times T]$  matrix of source intensities, to be estimated, where  $P$  is the number of distributed dipoles, which is generally several tens or hundreds of times greater than the number  $N$  of sensors. This linear system is therefore underdetermined and its solution is non-trivial. Finally,  $G$  is the so-called lead-field matrix. Of size  $[N \times P]$ , it embodies all the assumptions of the predictive model based on the above-mentioned main elements, and in particular the degree of realism with which the anatomical and biophysical properties of the head's tissues are transcribed. Each column of this matrix (a forward field) predicts how each source expresses onto the sensors.

This means that  $G$  contains all the information on sources that express themselves in a similar way on the scalp or, on the contrary, that have very different expressions.

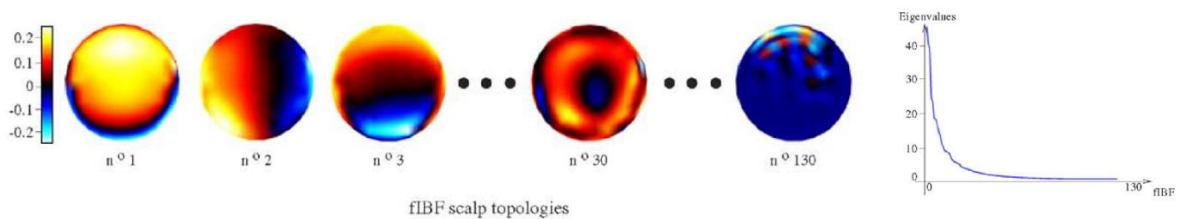
### functionally Informed Basis Functions

During my PhD, I proposed to uniquely summarize potential brain activity contributions by deriving functionally informed basis functions (fIBF) from the forward model [10]. fIBF are simply derived from the singular value decomposition (SVD) of the normalized forward matrix  $\bar{G}$ , such that:

$$\bar{G} = B\Lambda^{1/2}C^T \quad (2)$$

where  $B$  is the  $[N \times N]$  fIBF matrix,  $C$  is the  $[P \times N]$  matrix made of the coordinates of each forward field on each basis function, and  $\Lambda$  is the  $[N \times N]$  diagonal matrix made of the eigenvalues associated with each fIBF. Note that this SVD is equivalent to applying Principal Component Analysis (PCA) to covariance matrix  $X = \bar{G}\bar{G}^T$ , hence eigenvalues in  $\Lambda$  reflect and are ordered according to the part of variance in  $X$  explained by each fIBF. The normalization of the forward matrix ensures that each source contribution or forward field is given the same weight, regardless of its distance or orientation with respect to sensors.

Figure 1 shows typical fIBF and associated eigenvalues for an MEG forward matrix. Note that as a consequence of PCA or SVD, fIBF with higher variance also correspond to the ones with lower spatial frequencies, which supports the usefulness of fIBF to separate between data part of interest from noise.



**Figure 1:** fIBF and associated eigenvalues for an MEG forward matrix with  $N = 130$  sensors and  $P = 7205$  dipolar sources. They are ranked from highest to lowest explained variance (adapted from [10]).

I could show that one can compare these fIBF scalp topographies with the actual (normalized) data topographies, and derive a correlation coefficient that, for each source location, can be viewed as an activation probability. This yields a dissociation between source localization and source amplitude estimation, as these coefficients can then be used as data-driven information to better condition the inversion of linear system (1). It can be used in different ways to constraint or initialize inverse methods, as we illustrated in [10], [11] and [12]. It has also been used by other teams in different contexts, namely epilepsy [13], [14] and more recently with fNIRS<sup>2</sup> [15] or for Brain-Computer Interfaces [16].

However, Bayesian inference is arguably the most rational way of combining prior information and EEG/MEG observations to solve the ill-posed inverse problem. This was the main focus of my postdoctoral work. The following two sections briefly summarize the main aspects of Bayesian inference in this context, and how it can be usefully applied to EEG/MEG source localization. Two features of Bayesian inference are particularly relevant here: inference about model parameters (to estimate the source amplitudes) and inference about model itself (for model comparison and selection).

## Key elements of Bayesian inference for EEG/MEG source localization

### *A probabilistic forward model*

In the case of a distributed source model as described in equation (1), source localization amounts to solving or inverting this equation to estimate source amplitudes over time (matrix  $\mathbf{J}$ ). This problem is known as the ill-posed EEG/MEG inverse problem, because it contradicts the requirements defined by Jacques Hadamard for well-posed inverse problems. In particular, it has no unique solution and its solutions may be unstable<sup>3</sup>. Importantly, the ill-posed nature of this inverse problem is not only due to the under-determined and badly conditioned nature of equation (1). It is inherent to our aim of reconstructing brain activity from scalp data only<sup>4</sup>. Additional or prior information is required to constrain the inversion. The Bayesian framework offers a generic and optimal means of achieving this.

In the Bayesian framework, unknown parameters are treated as random variables. This is a way of quantifying both our knowledge and our uncertainty concerning the parameters of a given problem or system.

In this context, it is therefore necessary to make two additional assumptions as part of our forward model to be inverted: one about the distribution of source amplitudes  $\mathbf{J}$ , and the other about the distribution of the noise  $\boldsymbol{\varepsilon}$ .

Without loss of generality, one usually assumes gaussian distributions for both.

$$\mathbf{J} \sim N(\mathbf{0}, \mathbf{C}_J) \quad (3)$$

where  $\mathbf{J}$  is the vector of source amplitudes, i.e., the vectorized matrix  $\mathbf{J}$  (a column vector of length  $N.T$ ) and  $\mathbf{C}_J$  is the associated spatiotemporal prior source covariance matrix (of dimension  $[N.T \times N.T]$ ). Under stationarity assumptions, i.e., assuming that sources remain the same over the short period of time considered for inversion, this matrix usually writes:

$$\mathbf{C}_J = \mathbf{C}_{J_s} \otimes \mathbf{C}_{J_t} \quad (4)$$

---

<sup>2</sup> Functional Near-Infrared Spectroscopy.

<sup>3</sup> A small change in the data, due to noise, can produce very different inverse solutions.

<sup>4</sup> A challenge similar to that of deducing the nature of a 3D object from the mere observation of its shadow.

where  $\otimes$  is the tensor product and  $C_{J_s}$  (resp.  $C_{J_t}$ ) is the  $[N \times N]$  spatial (resp.  $[T \times T]$  temporal) source covariance matrix. Most often,  $C_{J_t}$  is set to the identity matrix, while  $C_{J_s}$  is where spatial constraints on the estimated solution will be introduced (see below).

Note that the prior mean in equation (3) is set to 0. This is a conservative choice and favours sparse solutions. In other words, only sources for which the data speak against their inactivity will be given a non-zero intensity. Besides, *a priori* distinctions between sources can be introduced through diagonal elements in  $C_{J_s}$  with different values.

Similarly for the noise term in equation (1),

$$\varepsilon \sim N(0, C_\varepsilon) \quad (5)$$

For simplicity, the identity matrix is typically assumed for  $C_\varepsilon$  but it could also include prior knowledge about the spatial distribution of the noise in sensor space. For instance, in MEG, it could be inferred empirically, from recordings when the room is empty, without any subject beneath the sensor helmet.

Given all the above assumptions or hypothesis  $H$  (including what enters the computation of the forward matrix  $\mathbf{G}$ ), the posterior distribution over source intensities can be derived from Bayes rule and will be gaussian such that:

$$p(\mathbf{J}|\mathbf{Y}, H) = \frac{p(\mathbf{Y}|\mathbf{J}, H) \cdot p(\mathbf{J}|H)}{p(\mathbf{Y}|H)} \propto p(\mathbf{Y}|\mathbf{J}, H) \cdot p(\mathbf{J}|H) \quad (6)$$

where

$$p(\mathbf{J}|\mathbf{Y}, H) = N(\hat{\mathbf{J}}, \widehat{C}_{\mathbf{J}}) \quad (7)$$

Solving equation (6) yields the following inverse solution, which corresponds to the maximum a posteriori (MAP) estimate:

$$\hat{\mathbf{J}} = [\mathbf{G}^T \mathbf{G} + C_{J_s}^{-1}]^{-1} \mathbf{G}^T \mathbf{Y} \quad (8)$$

Equation (8) provides nothing but the pseudo-inverse or regularized solution for source intensities. It is also known as the weighted minimum (L2) norm solution, where the prior spatial covariance matrix is rewritten as:

$$C_{J_s} = \lambda \cdot \mathbf{W}^T \mathbf{W} \quad (9)$$

where  $\lambda$  is a so-called hyperparameter. Note that if the prior source covariance matrix is well defined, that is definite positive, it is thus symmetrical and can always write as in equation (9).

### ***From single to multiple priors***

It turns out that most inverse solutions that have been proposed in the literature for solving the EEG/MEG inverse problem, although not all formulated within the Bayesian formalism, boils down to setting a particular form to matrix  $C_{J_s}$  or  $\mathbf{W}$ . This is the case for the weighted minimum-norm [17], the LORETA [18] as well as the LCMV beamformer [19] solutions, which are among the most used ones until today.

What those methods often do not make very much explicit is how the hyperparameter  $\lambda$  is set. This hyperparameter is important because it sets the relative importance of previous information and current observations in the calculation of the inverse solution. In the Bayesian framework, this hyperparameter can be considered unknown and treated as a random variable, with a prior

distribution, and be estimated as part of the inference process. This approach is also referred to as parametric empirical Bayes. In practice, the twofold inference process that consists in computing both  $\hat{\mathbf{J}}$  and  $\lambda$  is iterative and is solved using an Expectation-Maximization (EM) algorithm.

Together with my collaborators, using simulated data, we have shown that this approach surpasses heuristics such as the *L-curve* to estimate the hyperparameter and yields more accurate inverse solutions [20].

But most importantly, this approach can be generalized to combine several priors in an independent fashion, and to optimize their relative influence in constraining the inverse solution [21], [22], [23]. This is particularly relevant in this context as one may combine prior information of different nature, namely anatomical (e.g., spatial smoothness) [21] and functional (e.g., fMRI-derived prior) [24], [25].

As we proposed in [21], extending the EEG/MEG inversion to the combination of multiple constraints simply consists in formulating the source covariance matrix as a weighted sum of prior covariance matrices:

$$\mathbf{C}_{J_s} = \sum_{k=1:K} \lambda_k \cdot \mathbf{Q}_k \quad (10)$$

where the  $\mathbf{Q}_k$ 's are the  $[P \times P]$  prior covariance matrices (expressed in source space) and the  $\lambda_k$ 's are their associated, unknown hyperparameters. The latter control the relative influence of each independent prior, such that the higher the hyperparameter, the higher the weight of the corresponding prior in guiding the inverse solution. Using our EM-based empirical Bayes approach, they are inferred as well as the source amplitudes, within the same iterative inference process. In other words, one further considers prior over the hyperparameters, yielding a hierarchical generative model of the data.

This framework can be used with different strategies.

In [20], we used synthetic EEG data to show that this flexible hierarchical model and EM inversion outperforms conventional weighted minimum-norm or maximum smoothness solutions ; that when noise level increases, the hyperparameter estimates are adjusted accordingly ; and that when inaccurate priors are included in the model, they are assigned a low hyperparameter value.

In [21], we confirmed and extended these results to MEG simulated data by showing that valid spatial priors do improve the source localization accuracy ; that invalid spatial priors do not significantly hamper inversion performance, simply because data-driven hyperparameter estimation allows these unsuitable constraints to be discarded ; and that Bayesian model comparison (see below) can be used to formally select the best set of priors.

Finally, in [23], we generalized this approach to the use of a large set of sparse priors, where each component corresponds to a patch or cluster of dipoles on the cortical manifold. We used a hierarchical linear model with hyperpriors that favour sparsity by setting all hyperparameters to zero *a priori*. This yields sparse solutions closer to those sought with ECD models (see also [26] for a modelling work bringing together ECD and distributed EEG/MEG inverse solutions). This approach rests on the principle of Automatic Relevance Determination (ARD), which automatically prunes unnecessary prior components, in a computationally efficient manner, even when dealing with a large number of components.

### Bayesian model comparison

As shown before, Bayesian inference on source intensities rests on computing the posterior densities of  $\mathbf{J}$  and then estimating its maximum, that is the most likely source amplitudes given the data. The same rational applies to make inference on models or hypothesis  $H$ . If alternative models are envisaged,  $H$  becomes a random variable to be optimized and Bayes rule in model space writes:

$$p(H|Y) = \frac{p(Y|H) \cdot p(H)}{p(Y)} \propto p(Y|H) \cdot p(H) \quad (11)$$

Bayesian model selection involves choosing the hypothesis  $H$  with the highest posterior probability [27].

We can then compute the *a posteriori* estimate of the parameters and hyperparameters for this winning model<sup>5</sup>. In practice, it is generally assumed that all models are *a priori* equiprobable, so that selecting the best model boils down to selecting the one with the highest model evidence  $p(Y|H)$ .

The problem is that the exact calculation of the evidence of the model, which is the integral of the likelihood function and the prior over the entire parameter space, is most often intractable. However, it can be approached by the maximized free energy  $F$ , which is a lower bound of the log-model evidence.

$$\log p(Y|H) = F + KL(q(\boldsymbol{\theta})||p(\boldsymbol{\theta}|Y, H)) \quad (12)$$

since the *KL-divergence*<sup>6</sup> is always non-negative.

Here  $p(\boldsymbol{\theta}|Y, H)$  indicates the true posterior that we aim at approximating with an analytical and simple distribution  $q(\boldsymbol{\theta})$  over all model parameters  $\boldsymbol{\theta}$  (in our case  $\boldsymbol{\theta} = \{\mathbf{J}, \boldsymbol{\lambda}\}$ ).

$F$  is known as the negative variational free energy and writes [29]:

$$F = \int q(\boldsymbol{\theta}) \log(Y|\boldsymbol{\theta}, H) d\boldsymbol{\theta} - KL(q(\boldsymbol{\theta})||p(\boldsymbol{\theta}|H)) \quad (13)$$

This formulation highlights that  $F$  computes a compromise between model accuracy (first right-hand term) and model complexity (second right-hand term). Under the Laplace approximation and using variational methods,  $F$  becomes tractable and at convergence,  $q(\boldsymbol{\theta})$  approximates the true posterior (for parameter estimation) and  $F$  approximates the model log-evidence (for model comparison).

When comparing two models  $H_1$  and  $H_2$ , one typically follows the same reasoning as for classical statistical tests where a typical 5% threshold is applied on the probability for a type I error (the probability of incorrectly rejecting the null hypothesis). To conclude in favour of  $H_1$ , we expect a Bayes factor ( $BF$ ) greater than 20 [30], i.e.,

$$BF_{12} = \frac{p(Y|H_1)}{p(Y|H_2)} > 20 \quad \text{or} \quad \log BF_{12} > 3 \quad (14)$$

---

<sup>5</sup> Note that an alternative to model selection is model averaging, where the parameter estimates are derived from the weighted sum of the *a posteriori* maximum of each model considered. And for each model, its weight corresponds to its posterior probability [28].

<sup>6</sup> KL stands for Kullback-Leibler.

Note that several very different models can be compared, provided that the data to which they are fitted remain the same. Model comparison is always conditional on the available observations. This may seem restrictive, but it also means that, over and above traditional, compulsory simulation studies where we know the ground truth, Bayesian model comparison provides a formal, quantitative means of evaluating model assumptions on real data, where we do not know the actual solution.

When the model space becomes large, one can often organize it along few relevant dimensions (factors) and apply family model comparison [31]. In the general context of Neuroimaging and Cognitive Neurosciences, Bayesian model comparison has been used quite extensively, with the advantage of encouraging hypothesis to be made explicit and framed in a quantitative manner [32]. Further important developments for broader application have included extension to group studies [33], [34].

The next sections illustrate how model comparison can be used to formally address important questions regarding the estimation of EEG and MEG cortical sources.

## Applications

### *How accurate should the forward model be?*

A faithful forward model will account for individual anatomy, a fine description of the source space as well as of the head tissues' geometry and conduction properties. However, this comes at a cost in terms of finance, time and computational resources since it requires the individual anatomical MR images. Typically, the latter are used to compute meshes of the different tissue interfaces (namely the white/grey matters boundary, the CSF/skull and the scalp surface). Based on these meshes, a BEM forward matrix can be derived. Meshes computation is quite tedious. It relies on several fine steps such as segmentation, surface extraction, smoothing and surface tessellation. It often requires manual intervention and is subject to errors depending on the quality of the MR images.

In [35], we introduced a method that eschews the need for individual cortical surface extraction. It uses a canonical cortical mesh defined in a standard (common) space, which is then warped to match the subject's anatomy using nonlinear transformation derived from spatial normalization of the individual subject's MRI [36]. This offers two main advantages: (i) it provides a fast, simple and automated way to derive individual cortical meshes; (ii) individual source estimates can be readily mapped back to standard stereotactic coordinates without additional spatial normalization, for group level inference. The latter is particularly important as group level inference is standard procedure in Neuroimaging and pooling data across subjects as well as reporting in standard space (e.g., Talairach coordinates) is very useful but challenging for EEG and MEG.

Using formal Bayesian model selection and real MEG data from a face perception study [37], we compared three forward models based on: (i) standard anatomy; (ii) automatically derived individual meshes from a standard mesh (the proposed automatic method); (iii) individual meshes finely computed from each subject's own MR images. **We could show that the two models proved significantly better than the one based on a cortical template, confirming the need to rely on individual anatomical information for MEG source reconstruction. But importantly, we showed no significant difference between the last two models, suggesting that an automatic wrapping of a template mesh can be sufficient [35].**

In a subsequent paper, we used the same data and a factorial design approach to assess the relevance of different choices along key dimensions of the forward model. We compared again individualized MRI-derived meshes with inverse-normalized template meshes, but also meshes of different resolution (3000 vs. 7000 dipoles), the use of a single-sphere, overlapping spheres or a BEM head model, the use of orientation free or constrained dipolar sources, and the use of various spatial prior types. **To make a long story short, we concluded, at the group level, that a canonical cortical mesh with individually-adjusted skull and scalp meshes, along with a BEM head model and multiple sparse priors [23], may provide optimal results for many applications [38].**

### ***Should we use fMRI-derived priors for EEG/MEG source reconstruction?***

Given the high spatial resolution obtained with fMRI to describe cortical activity, it is a potentially very useful source of information for constraining the EEG/MEG inverse problem. However, the validity of such an a priori is questionable, as fMRI measures slow metabolic changes rather than rapid fluctuations in neuronal activity. In [24], we formally assessed fMRI-derived empirical priors on real EEG and MEG data within our empirical Bayesian framework. We used group fMRI activation clusters mapped onto 2D cortical meshes to define spatial priors (one per cluster). We used canonical cortical meshes [35] allowing fMRI priors from group analyses to be applied to individual EEG/MEG data. This pragmatic Bayesian approach allows fMRI data to inform source reconstruction in a flexible way, without requiring direct correspondence between fMRI and EEG/MEG data. **We showed that, driven by the EEG/MEG data, some fMRI-derived priors (invalid ones) were discarded during the inversion process, while others (valid ones) were given significant weight [24].**

### **Is it worth combining EEG and MEG data?**

More recently, we have used an empirical Bayesian approach to formally compare EEG, MEG and fused EEG/MEG data for source reconstruction<sup>7</sup>. It is widely accepted that MEG offers better spatial resolution than EEG. However, this point has rarely been quantified and, beyond that, what has rarely been addressed is the usefulness of combining simultaneous EEG and MEG recordings. In fact, EEG and MEG are complementary, as they respectively measure the electrical and magnetic parts of the same electromagnetic phenomenon. They are also differently sensitive to the location and orientation of the sources. But the addition of EEG to an MEG experiment comes at the price of discomfort for the subject, a significantly longer set-up time, and also a lower quality of MEG recordings due to the increased distance between the squids and the scalp.

In [40], we used data from a simultaneous EEG/MEG experiment with healthy adults passively listening to auditory oddball sequences [41]. We used a two-step procedure. First, we derived group-level solutions using both EEG and MEG data, EEG data only or MEG data only. We then used these solutions as three different sets of priors for individual source reconstruction. Here again, we considered individual source reconstruction based on EEG, MEG or both EEG and MEG data. This way, we could formally assess on all subjects together, using group-level model comparison, whether EEG, MEG or fused EEG/MEG data could distinguish between the three sets of priors.

**MEG showed greater sensitivity compared to EEG. However, multimodal inference proved superior to unimodal ones and revealed detailed spatiotemporal activity within the supratemporal plane for Mismatch-Negativity (MMN) responses.**

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<sup>7</sup> As part of Françoise Lecaigard's PhD work [39] (co-supervised with Anne Caclin)

## Conclusion

I significantly contributed to develop the first version of SPM<sup>8</sup> for EEG and MEG data, making available the above mentioned methods through a user friendly interface [42]. The toolbox has evolved since then and is mostly maintained by Vladimir Litvak and collaborators in London. It has been conveniently coupled with the fieldtrip Matlab open toolbox developed by the Donders institute in the Netherlands [43]. Inverse methods have also been complemented with for instance an empirical Bayes beamformer [44].

I also worked on extending the Bayesian inverse approach to reconstructing induced (non-stimulus locked, frequency specific) activity [45].

However, the most salient extension of this work is arguably, in the time domain, the Dynamic Causal Model (DCM) framework which extends the EEG/MEG source model with temporal constraints in the form of realistic mesoscopic descriptions of neuronal subpopulation dynamics and both their short- and long-range interactions [46]. Importantly, DCM enables to interpret experimental modulations of electrophysiological responses in terms of changes in connection strengths, within and between cortical or subcortical areas.

Most recently, in the space domain, MEG has proven to be able to reach laminar resolution [47], [48], namely using head-casts in order to minimize within and between session head movements, so as to guarantee a fixed position with respect to sensors over time, enabling the pooling of many data trials for source reconstruction.

In the near future, adaptation of these methods to the new generation of MEG systems (based on Optically Pumped Magnetometers (OPM)) will highly contribute to make MEG cheaper, portable and available for on field acquisitions (including at patient's bedside) [49]. This will include extending the forward model to predicting the full magnetic field vector on scalp.

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<sup>8</sup> SPM stands for Statistical Parametric Mapping. It is an open Matlab toolbox initially developed by the group of Prof. Karl Friston at UCL (UK) but with contributions from a large worldwide community. It was first developed for the analysis of Neuroimaging (PET, MRI) data and later extended to EEG and MEG.

# CHAPTER II

## Interpreting and modelling evoked responses<sup>9</sup>

*“The true logic for this world is the calculus of Probabilities [...] which is, or ought to be, in a reasonable man's mind.”*

*James Clerk Maxwell (Physicist and Mathematicians, 1831 - 1879)*

### Introduction

EEG and MEG are used and praised for their high temporal resolution. They are unique for observing finely and non-invasively the dynamics of brain activity. However, the complexity, the high variability and the low signal-to-noise ratio of the measured signals have led to methods that average data over trials to reveal robust and interpretable brain responses. Evoked responses, that is evoked potentials (in EEG) and evoked fields (in MEG) are defined as the averaged transient responses to sensory stimuli. Peaks and troughs of those wavy responses, also referred to as components, are known for decades and have been shown to be highly reproducible. They occur between a few tens to a few hundred milliseconds after stimulation onset. Initially described in EEG, they are named after their sign and latency. Famous components include the visual P1 [50], the auditory N1 [51], [52], the N170 associated with face perception [53], the P2 [54], the N2 and the P300 [55], [56] or the N400 [57], [58] associated with language processing. They do not always have clear equivalent in MEG, due to the difference in its sensitivity to source locations and orientations.

Early components are rather associated with low level sensory processing. They are characterized by sharp peaks, at highly reproducible latencies. Latest components are associated with more advanced cognitive processes, meaning that they are modulated in a context-dependent fashion, by attention, emotion, learning, decision-making... In other words, they are impacted by subjective processes. As a consequence, they are more variable over time and across subjects. But the distinction in time between pure sensory processes and cognitive ones is obviously not clear cut. The two are rather intermingled, and even quite early components are affected by cognitive states [51].

Although variations of evoked responses with trial types (experimental conditions) have long been studied, their variations over time, over trials, hence their dependence upon recent past experience, have been largely overlooked. Fully interpreting those responses requires freeing oneself from averaging the data across trials to study brain responses at the single trial level. It is thus a question of going against the original definition of these responses, of deconstructing them [59].

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<sup>9</sup> Conseil d'écoute pour la lecture de ce chapitre : [Pavane, Op. 50 \(Arr. for Cello & Piano\) \(youtube.com\)](https://www.youtube.com/watch?v=...)

This chapter deals with a hypothesis-driven attempt to deconstruct evoked responses. Note that it differs from the study of non-time-locked stimulus induced responses, typically rhythms which may occur on each trial but with a variable phase [60]. It focuses on rather time-locked evoked responses, but at the level of single trials. It is hypothesis-driven in the sense that it approaches those responses as a window on perceptual processes viewed as probabilistic or Bayesian inference implemented by the brain. This chapter briefly introduces the so-called Bayesian brain hypothesis and summarizes a few studies that we conducted in order to test the hypothesis that evoked responses reflect prediction errors, and hence that their modulations over trials partly reveal individual (implicit) learning processes.

## **Evoked responses through the lenses of predictive coding and the Bayesian brain hypothesis**

The Bayesian brain hypothesis has become quite influential over the last two decades in computational neurosciences [61], [62]. The broad formulation and scope of Bayesian computation has made it a compelling framework to address Marr's three levels of analysis [63]: what function, what algorithm to perform this function, what neural implementation to run this algorithm ? These three levels focus on the elements that fully characterise an information processing system such as the brain, and Marr insisted on the need to approach them concomitantly, taking into account the mutual constraints they exert on each other.

In an attempt to develop a general theory of brain function, the Bayesian brain hypothesis emerged from the initial idea that human agents (and beyond, any living organism) have to make sense of the external world they perceive and interact with. Therefore, they need to infer and integrate relevant information, and hence represent and manage uncertainty. Encoding information in the form of probabilistic distributions and up-dating those representations according to Bayes rule then appear as a sensible if not optimal thing to do. This idea was backed up by empirical behavioural observations from experiments studying multisensory integration [64] or sensorimotor learning [65].

From a neurophysiological perspective, this implies that neuronal populations encode probabilistic distributions and that message passing within neural networks implement Bayesian computations [66]. A seminal modelling work in that respect has been the one by Rao and Ballard at the end of the last century, proposing predictive coding as an efficient, principled way to implement perception as inference [67]. Predictive coding represents a fundamental shift from the traditional bottom-up model of perception. It posits that perception is primarily driven by prior predictions, with sensory input modulating perception through prediction errors. The brain maintains internal representations of the environment, which it uses to generate predictions about incoming sensory information. These predictions are subsequently compared to actual sensory inputs, and any discrepancies result in prediction errors.

Predictive coding operates across multiple levels of the brain's hierarchical structure. Higher-level generates predictions about lower-level neural activity, while lower-level compares incoming data with these top-down predictions. When mismatches occur, prediction errors are propagated back up the hierarchy to update the internal model.

Learning in the predictive coding model occurs through the continuous refinement of these internal representations. Persistent prediction errors lead to adjustments in the brain's internal models, allowing for increasingly accurate predictions over time. This adaptive process enables the brain to optimize its predictive capabilities and enhance its understanding of the environment.

Building on this emerging unifying theory of brain function, Karl Friston proposed that the brain updates hierarchical probabilistic models of the world by optimising free energy [68], just as the observational and computational scientist does when solving, for example, the inverse EEG/MEG problem (see Chapter 1). It follows that neural dynamics should reflect inference and learning processes, which boil down to minimising prediction error. It also attributes particular functions to feedforward (bottom-up) and feedback (top-down) connections, namely a purely driving role and a driving or modulatory role, respectively.

The Bayesian brain theory is also widely debated [69]. It has been argued that it is so broad and vague as to be both attractive and somewhat useless, and that it is difficult, if not impossible, to dismiss. Indeed, despite empirical evidence in favour (or say not contradicting) the theory, several studies have also reported non-Bayesian or suboptimal behaviour. However, such behaviours can also be described as optimal (Bayesian) inference based on suboptimal models of the world. Since there is an indeterminacy when trying to infer the model (the likelihood and priors) that a particular subject or patient is entertaining. In other words, given a likelihood function, there will always be a prior distribution that can explain a particular behaviour (or posterior outcome) as the result of optimal Bayesian inference. It follows that what matters is not to identify the exact or true model at play, but to select a model or model family that is useful in capturing part of the processes of interest, in order to predict some current and future observable behavioural and/or neurophysiological responses.

In sum, the Bayesian brain computational theory and its neurophysiological counterpart, predictive coding, constitute a powerful general framework to develop explicit, quantitative, generative and biologically plausible models of brain functions in order to interpret and predict behaviour and brain activity.

In particular, this framework, which postulates that evoked responses reflect prediction errors, suggests that these responses should be deconstructed and not averaged over all trials, as they are expected to evolve over the course of trials (i.e., over the course of sensory exposure to the environment), due to model updating, i.e., learning.

The next two sections intend to illustrate this rationale. They summarize a few original studies I conducted with PhD students, other colleagues and collaborators to shed light on the processes underlying two well-known EEG components which, by nature, can readily be associated with the notion of prediction error:

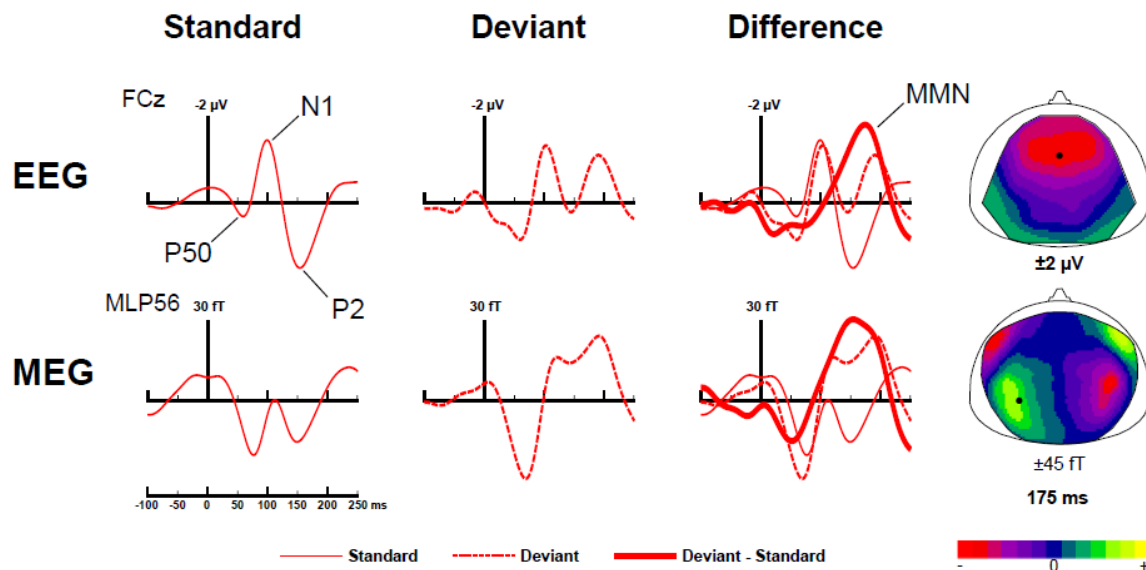
- the mismatch negativity (MMN) associated with sensory prediction error,
- the feedback related negativity (FRN) associated with reward prediction error.

### ***Deconstructing the Mismatch Negativity (MMN)***

The Mismatch Negativity (MMN) is an electrophysiological measure of surprise, elicited when a change occurs in a regular stream of sensory events, reflecting the brain's detection of this mismatch. The MMN has been observed in auditory, visual, and tactile modalities, with auditory stimuli being the most commonly studied [70]. The typical method for measuring the MMN is the oddball paradigm, which involves sequences of repeating standard sounds interspersed with infrequent deviant sounds. Deviants can differ from standards by their physical attributes (e.g., location, duration, intensity, or frequency) or by their temporal and statistical regularities. An MMN also occurs at the omission of a stimulus and with contextual changes (as shown in our study).

The MMN is a robust, automated response, although with a low signal-to-noise ratio which makes it sometimes difficult to detect at the individual level, even in healthy volunteers. The MMN appears after only few standards and does not habituate over time. It is calculated by subtracting the standard evoked response from the deviant response. It peaks between 130 and 210ms after stimulus onset. Mostly described in EEG, using a nose-reference, its topography exhibits a negativity on frontal sensors and a polarity inversion at temporal sensors (see Figure 2).

Importantly, the MMN has proven to be an index of cognitive function and dysfunction [71] in various neurological and psychiatric conditions such as disorders of consciousness [72], schizophrenia [73] or autism spectrum disorder [74].



**Figure 2:** Typical standard, deviant and auditory MMN responses obtained with frequency deviants in EEG and MEG, with their topographies at the peak latency of the MMN (from [39]).

In an original passive listening study<sup>10</sup>, we recorded 27 healthy adult participants using EEG and MEG data simultaneously, for optimal source reconstruction. Datasets from 7 participants were excluded, either because of poor data quality or because they did not respect the instruction of not attending the sound sequences but to focus on a silent movie with subtitles. We thus ended up with a group of 20 subjects, recorded with a CTF-275 sensor device and a CTF-supplied EEG cap with 63 electrodes.

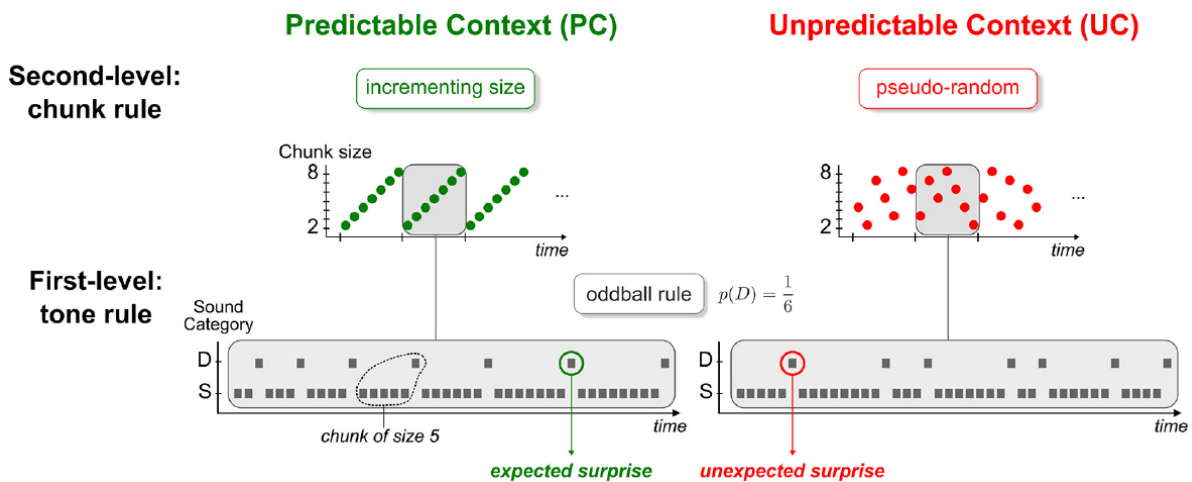
We used predictable and unpredictable sound sequences embedding a typical frequency oddball rule, presented in blocks. Predictable sound sequences comprised 16 cycles that were each made of a repeating 42-tone pattern following the deterministic incrementing rule depicted in Figure 3. Unpredictable sequences corresponded to pseudo-random oddball sequences typically used in oddball paradigms, with specific controls for the number of standards in between two deviants to mirror the predictable sequences (see Figure 3).

This way, we could contrast the MMN that represents an unexpected surprise, in the Unpredictable Condition (UC), with the MMN that reflects an expected surprise, in the Predictable Condition (PC).

We used this design to address the following questions in relation to predictive coding and Bayesian inference:

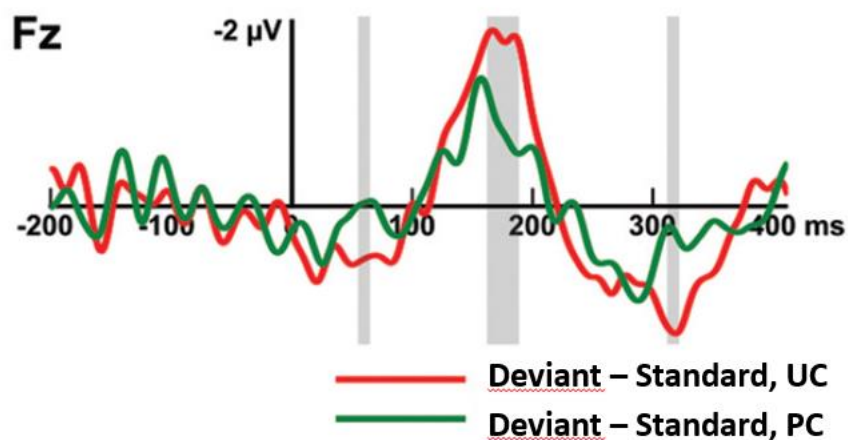
<sup>10</sup> As part of Françoise Lecaigard's PhD work [39] (co-supervised with Anne Caclin).

- Although automated and quite low-level, does the MMN exhibit modulations with implicit learning, that is differences between a predictable and an unpredictable context?
- If so, what kind of modulation do we observe? Does predictability induce a reduction of the MMN, as expected if the MMN encodes the sensory prediction error? Or does the MMN also encode the relevance (or precision) of prediction error for learning, which is higher in the predictable context?
- Then, through trial-by-trial deconstruction of the evoked responses leading to the MMN, and using cognitive computational modelling, can we reveal the learning mechanisms at play?
- Finally, using Dynamic Causal Modelling (DCM), can we shed light on the message passing within the cortical network underlying the MMN, in relation to the contextual modulation?



**Figure 3:** Experimental design of the EEG/MEG MMN study: schematic view of the predictability manipulation. The Predictable Condition (PC, left/green) involves cycles with ordered transitions between segments of repeating standards (chunks), which become shuffled in the Unpredictable Condition (UC, right/red). Importantly, the deviant probability remains the same in both context (adapted from [75]).

Figure 4 shows the MMN for the UC (red) and PC (green) conditions as well as the time window at which the difference between the two was significant, at the group level.

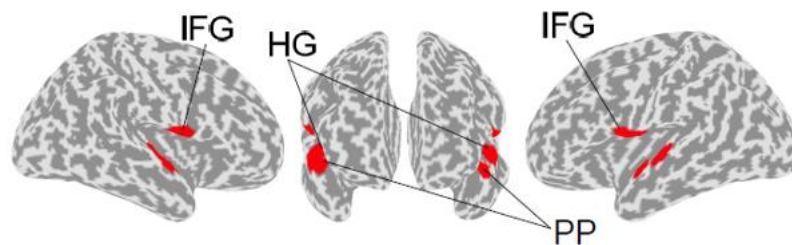


**Figure 4:** Group-level MMN at fronto-central electrode Fz for conditions UC (red) and PC (green). Shaded areas indicate windows of statistical significance (adapted from [41]).

We observed a strong decrease of the MMN for the predictable condition compared to the unpredictable one, but also a decrease of the early deviance response around 50ms, and a decrease of the P3a component around 300ms associated with attentional capture. This finding strongly suggests that although the subjects did not pay attention to the sounds, they implicitly learned about the statistics of the two sequences. Now the larger MMN in the case of the unpredictable sequence suggests that indeed, the MMN reflects surprise or prediction error, since in essence, all other things being equal, unexpected surprise is larger than expected surprise.

However, at this stage, one cannot characterize this learning process and how it differs between the two conditions. To do so, we need to deconstruct the evoked responses and consider, for each subject, the sequence of single trial responses. We hypothesized that their variations over time (trials) should reflect learning and should thus be partly predicted by a probabilistic learning model.

In order to maximize our sensitivity, we fitted these models at the source level. Therefore, we combined EEG and MEG data to identify the fronto-temporal cortical network underlying the MMN. As shown in Figure 5, we identified a network including on both hemispheres, the Planum Polare (PP), Heschl's Gyrus (HG) and the Inferior Frontal Gyrus (IFG).



**Figure 5:** MMN source cortical network estimated at the group-level from both EEG and MEG recordings (adapted from [39]).

For each individual, we estimated each single trial response, in each of the above six cortical sources. Then, for each peri-stimulus latency (between -50ms to 350ms, by steps of 10ms), we fitted each of our computational models to the time series made of the amplitudes of the single trial responses at a given source. Hence for each subject, each model was fitted to 41 (latencies) x 6 (sources) data time series. Group level model comparison was then performed for each data time series to select the winning model family.

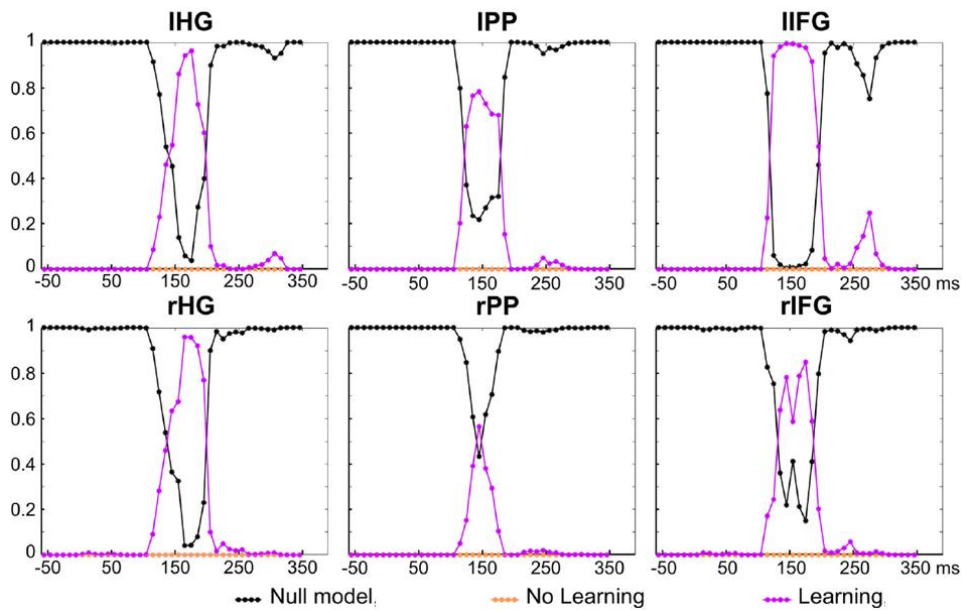
We considered three model families:

- The null model **M0**, which stipulates that between trial fluctuations just correspond to random noise;
- The static or non-learning model **M1**, which assumes that evoked responses distinguish between standard and deviant sounds but do not reflect any dynamic learning process;
- The learning model **M2**, which assumes that the subject implicitly updates over trials an estimate of the probability of observing a deviant sound.

Importantly, the latter implement an exponential forgetting. In other words, it rests on one free parameter  $\tau$ , which characterizes the memory span of the model, such that the larger  $\tau$ , the larger the number of past stimuli that are accounted for to predict the future stimulus. Interestingly, one can easily show that  $\tau$  equivalently reflect the precision (or inverse-variance) assigned to the prediction-error. In other words,  $\tau$  acts as a learning rate.

From our experimental manipulation, considering unpredictable and predictable sequences, we not only predicted that the learning model would prove better than the other two models, to predict the fluctuations of evoked responses over trials. We further predicted that the learning rate would be higher in the predictable condition. Simply because in a predictable context, prediction errors (or equivalently past stimuli) are more informative and should be given more weight.

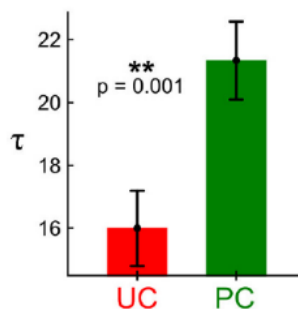
Results of the group model comparison are summarized in Figure 6, which represents the exceedance probability for each of the three models, for each of the six cortical sources of the MMN network, at each peri-stimulus latency. Exceedance probability represents the posterior belief that a given model is more likely than any other model in the comparison set. It provides an intuitive way to assess model superiority [76].



**Figure 6:** For each source, each peri-stimulus latency, each model, group-level Bayesian model comparison provides a posterior exceedance probability (**M0**: black, **M1**: orange, **M2**: magenta), (adapted from [75]).

Exceedance probabilities clearly reveal that for most if not all sources of the MMN network, the null model best explain the data at the group level, except on a time window around 150ms (the typical latency of the MMN), where the learning model prevails. This shows that **the trial-by-trial fluctuations of cortical responses around 150ms post-stimulus, are best explained by a learning process.**

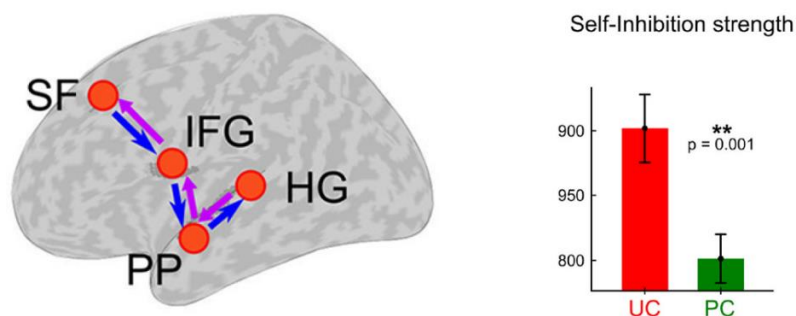
Then, based on data from all sources, around 150ms, we estimated the value of parameter  $\tau$  for each condition (UC and PC), and each subject. As shown on Figure 7, we found that **the learning rate was significantly higher in the predictable condition (PC).**



**Figure 7:** Effect of predictability on the learning rate (adapted from [75]).

Finally, we used a dynamic causal modelling approach to assess the modulations of effective connectivity (message passing) within the MMN cortical network that would best explain the reduction of the evoked response in PC compared to UC. Combining EEG and MEG data again, in each subject, we first identified the most likely bilateral hierarchical network at the group level. It corresponded to the same six sources mentioned above plus a superior frontal region (see Figure 8).

Given this cortical network, we assessed the most likely modulated connections and compared their strengths between conditions. Crucially, predictability appears to reduce the self-inhibition of superficial pyramidal cells, suggesting a direct mapping between precision weighting and this inhibitory parameter. This nicely dissociates the encoding of precision and prediction-error. It is in line with what is expected under predictive coding, when prediction error (bottom-up messages), under higher predictability, should be afforded higher weights (akin to increased cortical excitability) [77], [78].



**Figure 8:** Left: most likely Dynamic Causal Model (DCM) at the group level, explaining the MMN responses, with forward (bottom-up) connections in magenta, and feedback (top-down) ones in blue. Right: group comparison of the self-inhibitory connection strengths averaged over all sources, for each condition (UC in red, and PC in green), (adapted from [75]).

### **The case of the feedback related negativity (FRN)**

In another study<sup>11</sup>, using a completely different paradigm, we assessed the modulations of another evoked component known as the feedback related negativity (FRN), but under the same hypothesis that it could be interpreted as a prediction error signal reflecting an ongoing learning process.

The FRN is a centrally distributed, stimulus-locked waveform, generated about 250-300ms after an external negative feedback [80], and usually followed by a P300-like component. Such responses to feedbacks are known to reflect performance monitoring, hence learning [81].

A strong originality of this study is that it was not based on a classical behavioural task but on a Brain-Computer Interface (BCI) task: the P300-speller [82]. In short (but see Chapter 3), this task consists in focusing visual spatial attention onto a relevant stimulus (e.g., a letter) and select it by eliciting a P300 response following its short visual enhancement. Like in this study, letters and digits are typically displayed on a 6x6 matrix. They are flashed rapidly and repeatedly in groups (e.g., rows and columns), in a pseudo-random fashion.

The task requires the subject to maintain attention on their target, while ignoring the other flashing items. The subject is usually instructed to be proactive, for example by mentally counting each time the target flashes (repetitions are used to obtain more data and increase the probability of identifying the target). At the end of the sequence of flashes and after online signal processing, the machine displays the most likely target letter as feedback.

<sup>11</sup> As part of Margaux Perrin's PhD work [79] (co-supervised with Emmanuel Maby).

Nine-teen healthy adult participants were involved in our study. After a short individual calibration of the BCI classifier, each subject performed 3 online spelling sessions, each made of 24 5-letter words. Importantly, although the subjects believed they were actually controlling the BCI, the feedback was simulated and fully controlled, so the overall error rate was 20%. Precisely, the feedback was faked and such that there was zero, one or two errors per word, with no consecutive errors within a word. Furthermore, error predictability was manipulated such that 50% of the words contained 1 error (“expected” condition), while another 25% had 2 errors and the remaining 25% showed no error (“unexpected” conditions). We therefore had a 2-by-2 design to study feedback related evoked responses: (good vs. bad) x (expected vs. unexpected) feedback.

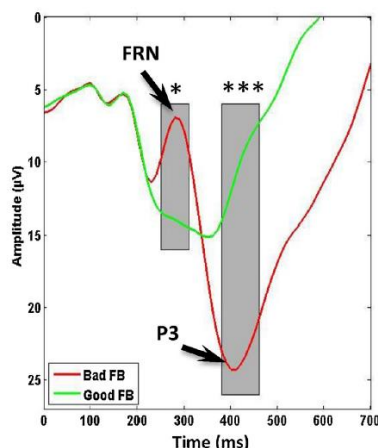
Note that the overall error rate of 20% was chosen so as to match the average expected true performance, as predicted by a preceding pilot experiment with other naïve BCI users. In this way, we ensured that the subjects were convinced that the BCI was working and effectively reflecting their true performance, as confirmed by their responses to a questionnaire completed at the end of the experiment.

For each subject, using a 32-sensor EEG headset, we extracted the cortical responses evoked by the feedback for each of the four conditions of interest. Interestingly, we also calculated (offline) for each trial the BCI's true spelling performance (correct vs. incorrect), which we used as an indicator of attentional effort (high vs. low).

In this study, we could thus address the following questions:

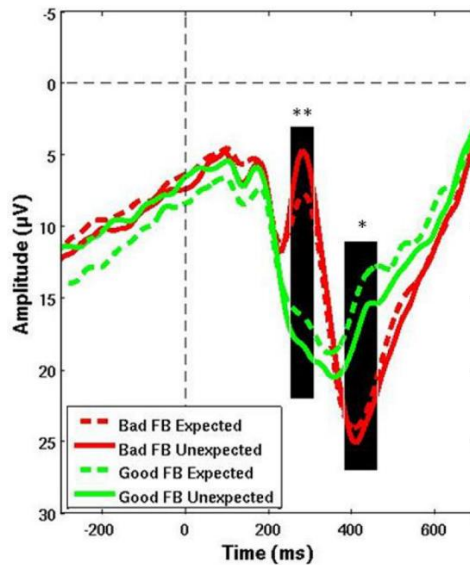
- First, does such a BCI task elicit a feedback related negativity, in case of an error, that contrasts with the evoked response to a correct spelling? (**Valence effect**)
- If so, are those responses to feedback modulated by its predictability? (**Learning or predictability effect**)
- Finally, are those responses modulated by the (hidden) true BCI performance? (**Attentional effect**).

As reported in [83], **we found a clear distinction between the response to good and bad feedback, with an FRN component in the latter case**, peaking slightly before 300ms and followed by a P300-type component peaking at 400ms (see Figure 9). This confirms that **an FRN can be observed during a brain-computer interaction**. It was already known that the FRN can be elicited, even in the absence of a motor action or a choice [84], although it is larger when the subjects believe they do have an influence on the feedback (see also [85]).



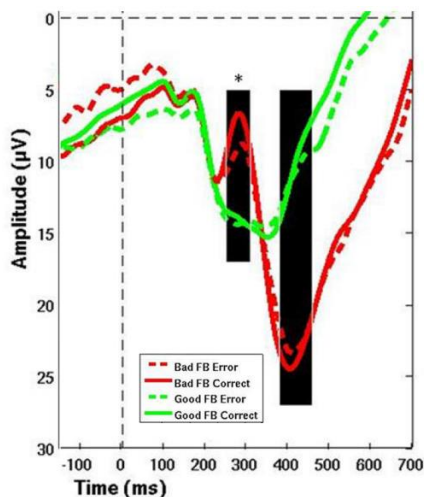
**Figure 9: Valence effect** - Group-averaged EEG evoked responses observed on central sensors, to good (green) and bad (red) feedback, respectively (adapted from [86]).

Interestingly, when contrasting more or less predictable responses to feedback, **we found that both responses (to good and bad feedback) were reduced when expected, at the latency of the FRN.** We also found an effect, although weaker, at the latency of the P300, mostly driven by responses to good feedback (see Figure 10). **This is perfectly in line with what we observed with the MMN. The FRN, which can also be seen as a mismatch or prediction error signal, is partly reduced when the discrepancy is rather expected.**



**Figure 10: Predictability effect** - Group-averaged EEG evoked responses for good (green) and bad (red) feedback, associated with an unexpected (solid lines) or expected (dashed lines) outcome (adapted from [79]).

Finally, by comparing the same responses to good and bad feedback, as a function of the underlying actual BCI performance (correct vs. incorrect), we found a significant difference in amplitude, at the latency of the FRN (see Figure 11). Specifically, **we observed that when attention is low or diverted (incorrect BCI performance), the FRN and its positive counterpart are smaller.** Again, this is consistent with predictive coding and the Bayesian view of attention as a (precision) gain weighting the prediction error. In other words, attention alters the signal-to-noise ratio of evoked responses, so that higher attention produces a larger response. This is of practical importance for BCI, as it means that a high level of attention could facilitate online feature extraction, and therefore improve classification (see Chapter 3).



**Figure 11: Attention effect** - Group-averaged EEG evoked responses to good (green) and bad (red) feedback, associated with a true correct (high attention, solid lines) or true mistaken (low attention, dashed lines) spelling (adapted from [79]).

To sum up, **these findings further support the view of evoked responses as (precision-weighted) prediction errors, both in the case of sensory or reward stimuli.** Here we found that **responses to feedback were modulated by both learning and attention.** The amplitude difference between good and bad feedback responses proved higher for less probable feedback. This suggests that **participants implicitly learned the underlying probabilities of errors, even though this knowledge had no direct benefit for them.** Besides, higher attention had a further enhancing effect on those responses, at the same (FRN) latency.

**From a BCI perspective, these findings speak in favour of adaptive approaches that would account for such individual feedback responses and their modulations in order to improve the performance along the course of the interaction [87]** (see Chapter 3). From a neuroscience perspective, this nicely illustrates that BCI could be a useful paradigm to deepen our understanding of feedback-related and other brain responses, namely to refine the neural correlates and computational underpinnings of learning and attention [88].

From now on, whether to deconstruct evoked responses, as illustrated here for the MMN, or to improve BCI performance by detecting the FRN online (see Chapter 3), it appears necessary to deal with single trial responses of single subjects, and no longer with averaged responses and group-level effects. This clearly represents a major signal processing and modelling challenge. And the scope of potential applications of these results in EEG depends on our ability to meet this challenge.

To help achieve this, we have developed a principled online approach to make the most of the noisy and highly variable single trial responses in each individual. This work is summarised in the next section.

### **Towards real-time hypothesis testing through single-trial evoked responses**

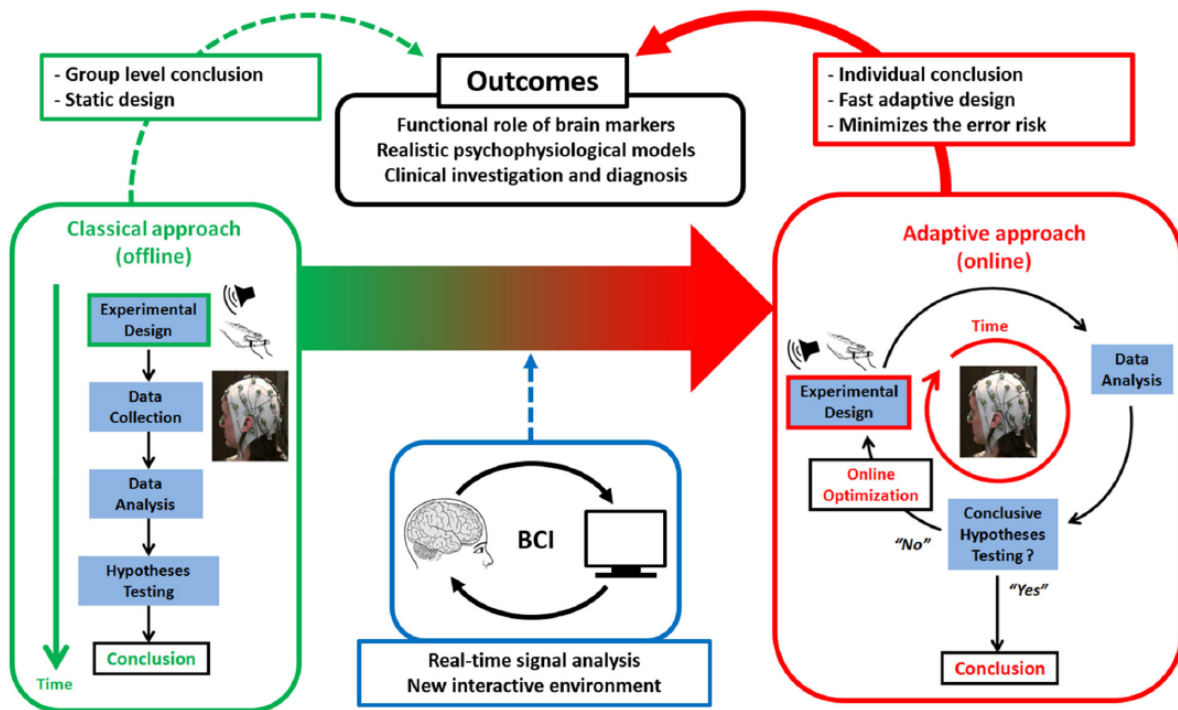
As illustrated in the previous section, it is possible to extract and interpret single-trial responses measured by non-invasive recordings such as EEG or MEG. This method is also essential for going beyond average responses and group effects. We could show that it is also very useful for finely characterising individual perception and learning dynamics, since the MMN component, for example, reflects prediction error, hence context-dependent or adaptive perceptual inference. Similarly, the FRN reflects reward prediction error and associated learning processes, while being also modulated by attention. These results provide a strong incentive to make full use of the fluctuations in evoked responses over trials, at the individual level, whether to test hypotheses about perceptual and learning processes at play in each subject, or to control a BCI. In fact, these two objectives are closely related. Indeed, although the first involves testing subtle and fundamental questions and the second concerns very pragmatic and applied objectives, both converge in trying to push back the limits of decoding single-trial responses. The challenge is to do this despite the very low signal-to-noise ratio of those responses.

In fact, in our study on cognitive modelling of the MMN [75], although carefully combining EEG and MEG and operating at the source level, the (winning) learning model explained only a small part of the between-trial variance. In addition, the comparison of the alternative cognitive models was mostly inconclusive at the individual level. Yet the potential clinical applications of EEG tests require reliable conclusions to be drawn at the single patient level. In autism, for example, adaptation to context is known to be a fundamental difficulty [89], [90], [91], and identification of these processes in a given individual is therefore crucial. Similarly, in patients with disorders of consciousness, where the MMN has been shown to be a good predictor of awakening [72], it is also imperative to be able to probe these processes at the individual level.

Finally, the alternative models that we will have to compare for each individual, in a process akin to that of a differential diagnosis, are likely to be numerous. In addition, as with learning processes, most of them will be dynamic and highly non-linear, and therefore involve non-trivial predictions.

**Consequently, and for all the reasons mentioned above, optimising this type of model comparison, i.e., maximising our chances of concluding and selecting the best model for a given subject, requires the experimental design to be optimised adaptively, online.**

The principle of the approach we proposed<sup>12</sup> is illustrated in Figure 12. In contrast with a classical, offline experiment, it implements adaptive design optimisation (ADO) [93]. This principle is quite intuitive. The basic idea is to choose the best stimulation to present next, based on the data acquired so far and a given optimization criterion. In our context, we want to optimize hypothesis testing. In other words, one wants to minimize the model selection error. In a nutshell, this is implemented as follows [94].



**Figure 12: Online vs. Offline experiments** – Conventional, serial experiment (left, green) versus ADO (also called ASAP for Active SAmping Protocol; right, red), which optimizes experimental design on the fly and therefore requires experimental data to be processed in real-time, as in the case of BCI. ADO also allows the experiment to be stopped prematurely, as soon as a conclusion can be drawn (adapted from [94]).

Let us consider a model space made of  $K$  alternative hypothesis to be compared. After each trial  $t$ , having delivered stimulation  $u_t$  and observed data  $y_t$ , Bayes rule for model  $M_k$ 's posterior writes:

$$p(M_k | y_t, u_t) \propto p(y_t | M_k, u_t) p_t(M_k) \quad (15)$$

where  $p_t(M_k)$  is the prior over model  $M_k$  after having observed trials 1 to  $t - 1$ .

<sup>12</sup> As part of Gaëtan Sanchez's PhD work [92].

It is simply given by the posterior over  $M_k$  after trial  $t - 1$ :

$$p_t(M_k) = p(M_k|y_{t-1}, u_{t-1}) \quad (16)$$

Usually, prior to any data observation, the a priori over the whole model space is equiprobable, which means that for each model  $M_k$ :

$$p_0(M_k) = \frac{1}{K} \quad (17)$$

Then equation 15 applies under the constraint that:

$$\sum_{All\ k} p(M_k|y_t, u_t) = 1 \quad (18)$$

In practice, the log-evidence  $\log p(y_t|M_k, u_t)$  is approximated by the variational free energy, which computes a trade-off between model accuracy and complexity and can be used for model comparison (see Chapter 1). Importantly, it depends on the design variable  $u_t$ . This implies that one can choose stimulation  $u_t$  so as to optimize model comparison, which is equivalent to minimizing the risk of model selection error. For non-linear dynamic models, it has been shown that minimizing that risk with respect to  $u_t$  can be approximated by maximizing Jensen-Shannon divergence, also referred to as the design efficiency [95]:

$$D_{JS}(u_t) = H\left(\sum_{All\ k} p(y_t|M_k, u_t)p_t(M_k)\right) - \sum_{All\ k} p_t(M_k)H(p(y_t|M_k, u_t)) \quad (19)$$

where  $H$  is Shannon's entropy.

At any trial  $t$  the design efficiency is also equivalent to the mutual information between the data space and the model space, given experimental design  $u_t$  [93]. This means that choosing design parameter  $u_t$  in such a way as to minimize the risk of model selection error is equivalent to maximizing design efficiency, which is also equivalent to maximizing the mutual information between the data and the models. In other words, we seek to perform the next short experiment  $u_t$  (i.e., ask the question or present the stimulation  $u_t$ ) that will maximize the information gain about our hypothesis and their comparison.

It is interesting to note that ADO allows the ongoing experiment to be stopped as soon as a conclusion can be drawn, typically when the winning model reaches a posterior probability greater than 0.95.

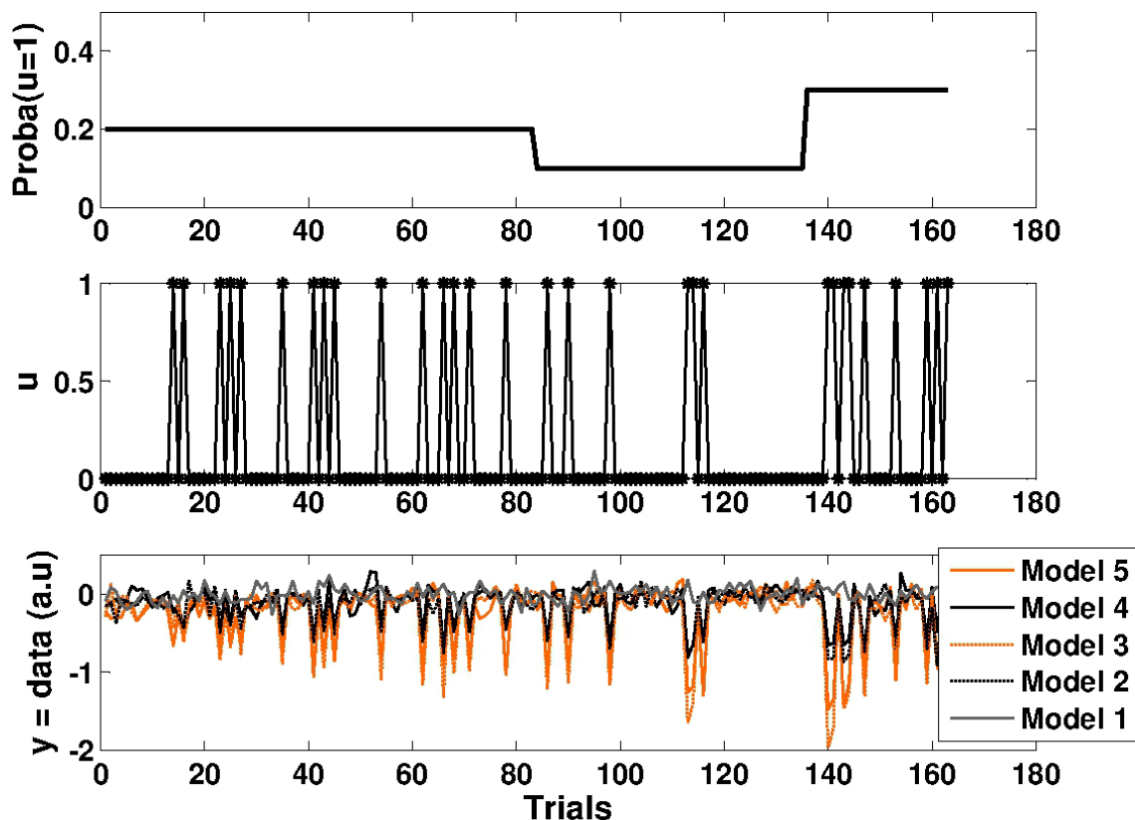
Hence ADO simply implements a sequential hypothesis testing procedure [96]. It is very similar to the empirical scientific approach whereby scientists carry out a study, make observations, draw conclusions about their initial hypothesis and plan their next experiment in order to increase their knowledge by testing new, refined hypotheses. Except that ADO implements this approach in real-time, as if each trial were a new experiment. It also extends the approach to a wide range of model types, including non-linear dynamic models that are particularly relevant in cognitive neuroscience, for optimal hypothesis testing at the level of the individual subject.

To establish the face validity of this approach, we first carried out realistic simulations [93] and reproduced previous results from a similar approach developed to optimise behavioural psychology experiments. [97].

Next, we simulated an EEG oddball experiment (see Chapter 1) in which, at each trial, ADO had to choose the next stimulus (either a standard tone or a deviant tone) in order to disentangle the different perceptual models. In echo to our work on deconstructing the MMN, trial by trial, we considered five alternative hypotheses:

- Model  $M_1$ : the null model which assumes that EEG responses do not contain any information about the incoming stimulations, but noise.
- Models  $M_2$  and  $M_3$ : Learning models that update their beliefs about the probability of observing a deviant after each trial. These models were simple in the sense that they assumed a constant learning rate over the whole experiment, either low or high, respectively. A low learning rate means that precision or confidence in any new unique information is low and beliefs are slowly updated.
- Models  $M_4$  and  $M_5$ : Learning models that can adapt their learning rate to the volatility of the environment, i.e., to changes in the underlying probability of hearing a deviant tone. These two more complex hierarchical models are distinguished by the speed with which they update their beliefs, either slowly ( $M_4$ ) or rapidly ( $M_5$ ).

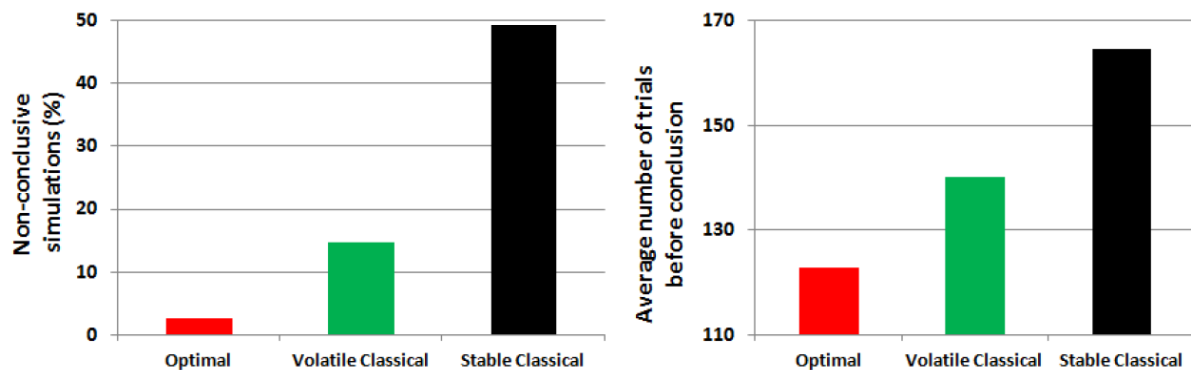
Figure 13 illustrates the predictions of each model when exposed to a static (non-adaptive) but volatile (with changes over time of the deviant probability) experimental design. Differences in the predicted data are subtle.



**Figure 13: Model predictions** – The top panel shows the design parameter over time (the probability of a deviant); the middle panel shows the actual stimulus delivered on each trial (0: standard, 1: deviant); the bottom panel shows each model prediction on each trial, equivalent to the predicted amplitude of the evoked response at sMMN latency (adapted from [93]).

We then performed 75 simulations, equivalent to 75 different subjects corresponding to 5 groups of 25, each group being associated with a different true underlying model.

For each synthetic subject, we ran 3 different experiments: one with a static design and fixed deviant probability; one with a static design but volatile probability (as in Figure 13); and the last one implementing ADO. As shown on Figure 14, **ADO yields both more accurate conclusions and faster experiments.**



**Figure 14: ADO assessment through realistic simulations** – Comparison of the three design strategies: optimal or ADO (red), static but volatile (green), static and fixed (black). While the stable classical (offline) design is very often inconclusive and terminates at the maximum number of trials, ADO outperforms the volatile classical design in both being more conclusive and shorter (adapted from [93]).

Although the results obtained from these simulations have been very promising, our various attempts to demonstrate the usefulness of ADO in real experiments have so far been unsuccessful. Several factors may explain this failure, one being clearly the difficulty to pre-process EEG data online compared to offline. At the individual level and when comparing different models with subtle differences, it is particularly important to efficiently reject bad trials and correct for artefacts **whenever possible**. Therefore, we have been assessing a few algorithms dedicated to online artefact correction for EEG-based BCI<sup>13</sup>, namely: Artifact Subspace Reconstruction (ASR) [98], Fully Online and automated artifact Removal for brain-Computer interfacing (FORCe) [99], online Empirical Model Decomposition (EMD) [100], and online Independent Component Analysis (ICA). Using simulations of the online process with real data previously acquired in the Lab, **we observed that both ASR and EMD can provide accurate online artifact correction and data quality, and even exhibit more sensitive results compared to traditional offline analysis, in identifying the most likely perceptual process underlying trial-by-trial variations in evoked responses [101].** This now needs to be implemented and assessed in online experiments.

Note that the principle of ADO has attracted much interest over the recent years, in the field of human electrophysiology as well as in neuroimaging [102], [103]. It still raises technical challenges and also requires further advances in identifying fine neurocomputational models of perception and other brain functions to become an effective clinical tool.

<sup>13</sup> As part of Amanda Medeiros de Freitas's PhD work (co-supervised with Alcimar Barbosa Soares, Universidad Federal De Uberlândia, Brazil).

## **Conclusion**

Our hypothesis-driven approach within the framework of predictive coding and the Bayesian brain hypothesis has led us to deconstruct EEG and MEG evoked responses in order to fully characterise the dynamics of perception, in particular implicit perceptual learning in various contexts. We have shown that this can help shed light on the cognitive processes underlying well-known components such as the MMN (see also [104]).

**In a way, this approach extends the high temporal resolution of EEG even further.**

In addition, we have shown that this modelling approach, combined with online data processing (as in BCI, see Chapter 3) and adaptive design optimisation, opens up great prospects, including possible personalised and quantitative diagnostic approaches in various brain pathologies.

# CHAPTER III

## Brain-Computer Interfaces, theoretical and applied works<sup>14</sup>

*“The first principle is that you must not fool yourself and you are the easiest person to fool.”*

*Richard Feynman (Physicist and Mathematicians, 1918 - 1988)*

### Introduction

EEG has emerged as a highly advantageous neuroimaging technique for non-invasive Brain-Computer Interfaces (BCIs). Its appeal stems from several key factors. Firstly, EEG technology has undergone significant advancements, resulting in robust and wireless devices equipped with active sensors. This evolution has facilitated the swift deployment of many sensors when necessary. Secondly, EEG's inherent portability and cost-effectiveness make it particularly attractive for widespread use. Furthermore, as illustrated in previous Chapters, methods have been developed to maximize the utility of EEG data. These combined attributes position EEG as the preeminent choice for implementing non-invasive BCIs, not only in clinical settings but also in a broad range of applications beyond healthcare.

Approximately a decade and a half ago, invasive BCIs, which require surgical implantation of electrodes directly into the brain, were still in their nascent stages. Their potential was recognized, but the technology was not at all mature yet. Only very few patients had been implanted, for research purposes only, and barely no actors from the private sector had massively invested in this endeavour. At the time, EEG-based systems were considered to be viable contenders to their invasive counterparts [105]. In particular, I remember the keynote lecture given by Jonathan Wolpaw, a pioneer of EEG-based BCI [106], at the international conference in Graz, Austria (the main European BCI meeting), in 2011, extolling not only their advantages in terms of accessibility and security but also in terms of performance.

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<sup>14</sup> Suggestion d'écoute pendant la lecture de ce chapitre [Kol Nidrei, Op. 47 \(Version for Cello & Piano\) \(youtube.com\)](https://www.youtube.com/watch?v=K0lNidrei)

Things have come a long way since then. There have been ground-breaking demonstrations of invasive BCIs to control a robotic arm [107] or restore speech [108]. Although very few carefully selected patients have been implanted, and even those who have, do not yet benefit from these systems in their daily lives, it has become clear that EEG-based BCIs can hardly compete with implants in terms of decoding performance. In fact, the benefit/risk ratio of BCIs remains low, both for invasive BCIs (higher benefit/higher risk) and for non-invasive BCIs (lower benefit/lower risk). Non-invasive BCI are also having a hard time to find their way out of the lab. Beyond the notion of the benefit/risk ratio, the use of EEG can be restrictive: it is non-invasive but intrusive in the sense that it is impractical, and even a little painful, to put on and then wear an EEG cap for up to several hours at a time. In addition, EEG BCIs often require the system to be calibrated for a given user before it is used again.

However, there is room for improvement in EEG-based BCIs, which show promise in many other areas of non-clinical and clinical applications, including for rehabilitation of patients with neurological disorders (e.g., stroke [109]) or in psychiatric conditions [110].

The key question for the coming years of research is therefore how to turn EEG BCIs into real solutions for such applications. There are a number of important avenues and challenges, including:

- Providing the computer or machine in the loop with adaptive capabilities, in order to optimise cooperation with the subject or patient and therefore improve performance.
- Keeping abreast of the latest advances in neurophysiology in order to use the most relevant EEG biomarkers to decode mental commands and states.
- Targeting appropriate applicative objectives, which seems obvious but is not so simple in practice.

This chapter summarises some of the research we have carried out to contribute to these objectives of maturing EEG BCIs.

## **Of adaptive humans and adaptive machines**

Conant and Ashby, pioneers of cybernetics, devised the so-called good regulator theorem, which states that *“every good regulator of a system must be a model of that system”* [111]. In the context of BCI, the machine aims to collaborate with the user. Therefore, it can be said that to be effective, it must be a good regulator, both of the interaction with the user and of the user's brain activity, to enable it to control the BCI.

A BCI, whose aim is to restore or issue a command, will have to adapt and regulate both the way in which it infers intentions and mental states from neural signals, and the decisions and actions on the environment that result from this inference. A BCI whose aim is to rehabilitate (typically a neurofeedback system) will need to adapt in order to regulate brain activity itself, encouraging neuronal plasticity and learning.

Therefore, to be a good regulator, the machine must include a model of the system it aims to regulate, i.e., the user. In other words, just as the human in the loop tries to learn and build a model of the BCI it seeks to control, the machine in this (BCI) dyadic system should ideally incorporate a model of the user in order to cooperate and optimally regulate the interaction with the user [112].

This objective or principle has guided several methodological and empirical studies that we have carried out to improve the performance of the emblematic P300 speller, which is designed to help patients suffering from global paralysis (locked-in patients) to communicate with or regain control of their environment.

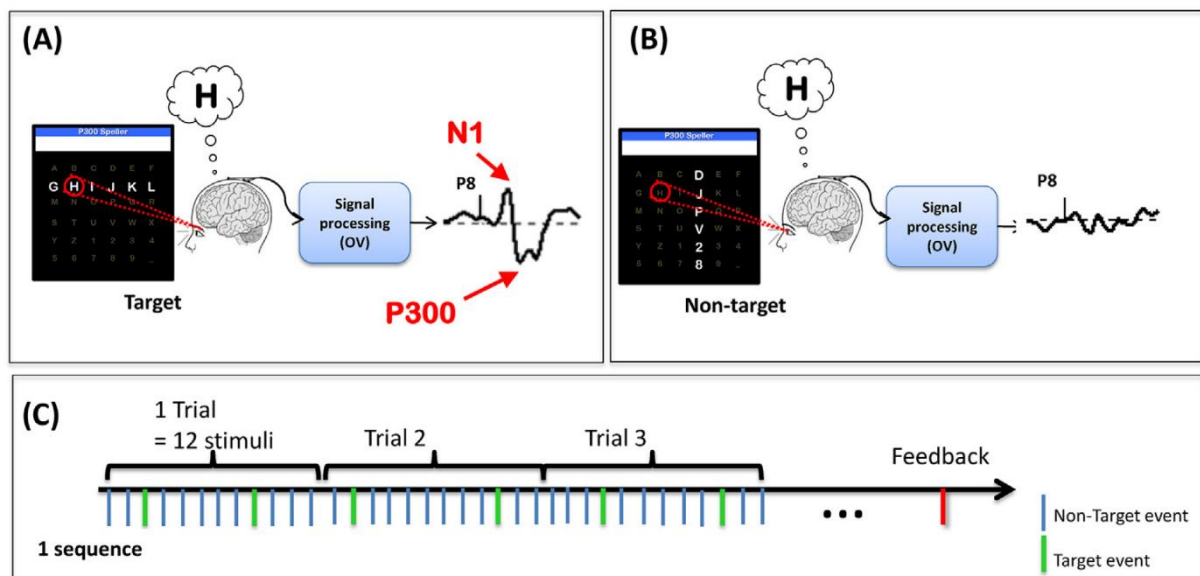
Specifically, we have equipped the classic P300 speller with additional knowledge, i.e., the ability to extract more information from the EEG data available online. The result is smoother interaction and improved performance [86].

### Exploiting error signals

The general principle of the P300 speller BCI and the type of interface we used are illustrated in Figure 15. With this BCI, and especially with naive users, we know that performance never reaches 100% accuracy. Furthermore, the faster the spelling (i.e., the lower the number of flashing sequences, see Figure 15), the lower the performance.

In this study involving 16 healthy adult volunteers<sup>15</sup>, we implemented and evaluated automated online error detection and correction. To do this, we measured and classified feedback-evoked responses (i.e., the EEG response evoked by the display of the identified target letter at the end of each spelling trial). If an FRN was detected (see Chapter 2) with a sufficiently high probability, the spelled letter was considered erroneous and was automatically replaced by the second most likely target letter, according to our P300 component classifier [87].

At the end of the experiment, we also asked the participants to complete a short questionnaire on their feelings about the difficulty of the task, their control performance, the usefulness of automatic error correction, etc.

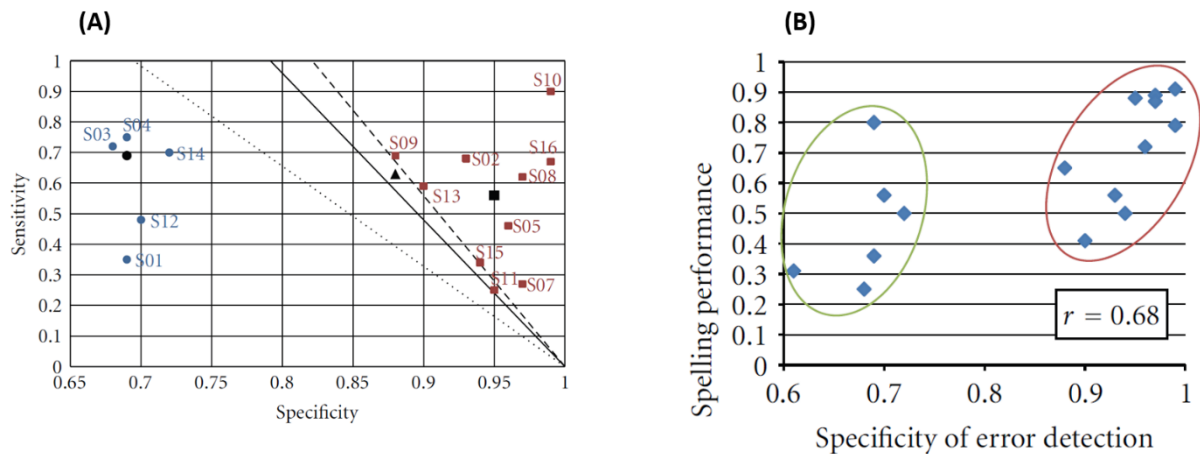


**Figure 15: General principle of the P300 speller** – when the user focuses on the target and the target is flashed (e.g., letter H), the typical EEG evoked response will exhibit a strong N1 component followed by a P300 waveform (A); when the user focuses on the target but the target is not flashed, the typical EEG evoked response should be weaker with a smaller N1 component and no P300 waveform (B). Each group of letters is flashed, one after the other. One sequence is obtained as soon as every group has been flashed once. One trial or item spelling may consist in several sequences (C) (adapted from [86]).

At the group level, we observed that automatic correction did not improve, nor deteriorate the spelling accuracy compared to no correction. However, automatic correction yielded a higher information transfer rate than a respelling strategy. Interestingly, we observed a high variability in participants' performance, which contributed to the variability in the effectiveness of error correction.

<sup>15</sup> As part of Margaux Perrin's PhD work [79] (co-supervised with Emmanuel Maby).

The participants clearly split into two distinct groups based on their individual efficiency in automated error detection (see Figure 16). The high specificity group (10 participants) had larger evoked responses, made fewer errors, and had their errors corrected more efficiently, leading to a 4% improvement in spelling accuracy and a higher bit rate compared to the low specificity group (6 participants) for whom error correction proved detrimental. Accordingly, participants in the high specificity group preferred spelling with automatic correction, while those in the low specificity group preferred spelling without correction.



**Figure 16:** (A) Error detection sensitivity as a function of error detection specificity. All subjects are represented as well as the global metasubject (triangle) and the two metasubjects for the low specificity (circle) and high specificity (square) groups, respectively. The lines are the boundaries above which the automatic correction becomes fruitful, for the three groups (plain, dotted, and dashed, resp.). (B) Correlation between the spelling accuracy (rate of correctly spelled letters, in the absence of correction) and the specificity of error detection (adapted from [87]).

**These results clearly show that the effectiveness of automatic error detection and correction depends on the subject. Specifically, we observe a ‘The rich get richer’ effect, since automated correction only benefited participants who already had fairly good spelling accuracy before any correction.** This makes sense if we recall the effects presented in Chapter 2, namely that the FRN is reinforced both by a higher level of attention (measured by a higher baseline spelling accuracy) and by greater surprise (for example, the scarcity of errors). A higher FRN will then be more easily detected, after which a higher level of attention predicts a higher probability of accurate automatic correction (i.e., a higher probability that, in the rare situation of an error, the second-best guess is likely to be the correct letter).

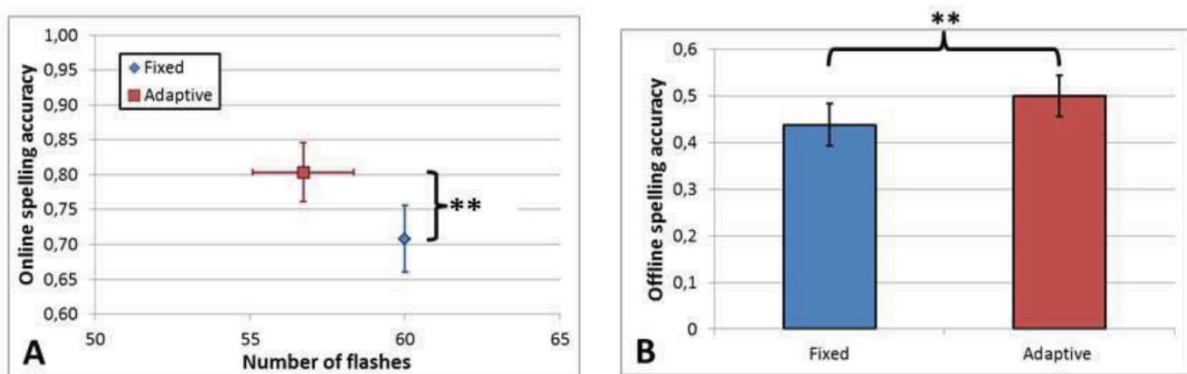
### Optimal stopping

All animals, and humans in particular, are highly adaptive by nature. Their flexible behaviour includes important features such as balancing speed and accuracy according to context. Why not endow the P300 speller with a similar capability?

We conducted an experiment with 11 healthy adult participants, who completed two spelling sessions, one with a fixed number of stimulus sequences (i.e., a fixed ‘reaction time’), and the other with an optimal stop (i.e., a ‘reaction time’ that depended on the quality of incoming evidence). For the latter, we implemented a probabilistic classifier that updates the posterior probability of each letter being the target, after each new observation/flash. And we used an arbitrary threshold on an entropic measure in order to stop the spelling as soon as enough information had been gathered in favour of one item (the alleged target).

As shown on Figure 17 (A), our results showed that **the adaptive approach significantly improved both spelling accuracy and bit rate compared to a fixed, time-based decision criterion**. In the adaptive condition, the average spelling accuracy was 80% with an average of 57 flashes, corresponding to 24.1 bits/minute. In contrast, the fixed condition achieved 71% accuracy with 60 flashes, resulting in 18.8 bits/minute.

**Importantly, we found an additional positive effect of the adaptive approach on user motivation.** When the data from both conditions were reanalysed offline using the same number of flashes (24), the spelling accuracy was still significantly higher in the adaptive condition (see Figure 17 (B)). This suggests that **the adaptive optimization of the speed-accuracy trade-off creates a ‘virtuous circle’ where higher spelling accuracy leads to increased user engagement and motivation, further improving BCI performance.**



**Figure 17:** (A) Online spelling accuracy as a function of the average number of flashes for each condition: fixed (blue diamond), adaptive (red square). (B) Offline spelling accuracies obtained with the same datasets reanalysed using a time-based criterion (decision made after 24 flashes). P-value: \*\*  $p < 0.01$  (adapted from [113]).

### Active sampling

Active sampling or active inference is another adaptive feature available to the P300 speller. In conventional P300 spelling, flashing sequences are pseudo-random, but within a sequence, each group of elements is flashed once, meaning that in total, by the end of the flashing, every element has been flashed in the same way. In contrast, active sampling allows the machine to choose which group of letters to flash next, based on the evidence accumulated so far. In other words, the machine acts on the basis of its current knowledge and, in particular, it can decide to flash the elements whose associated evoked response will be the most informative about the target.

Active sampling is similar in essence to the adaptive design optimisation (ADO) presented in Chapter 2. However, here we have implemented it<sup>16</sup> within the generic computational framework of active inference [115], which is based on an extension of the free energy principle for the brain [116], [117] to the optimisation of future or expected free energy with respect to actions. Elegantly, free energy provides a common criterion for optimising perception and action, by coupling them within a single probabilistic model of the task to be performed.

<sup>16</sup> As part of Jelena Mladenovic's PhD work [114] (co-supervised with Fabien Lotte)

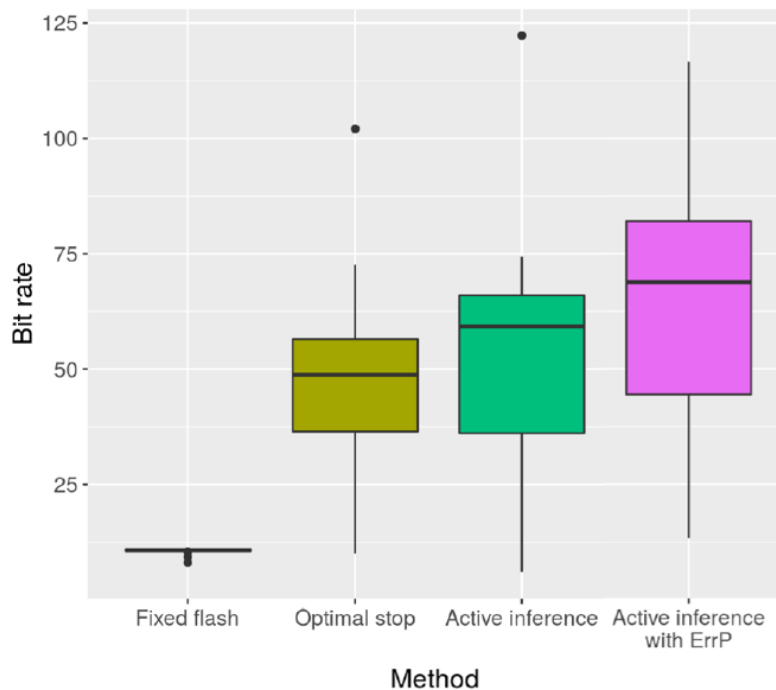
Using already acquired data from 18 subjects having performed a P300 speller BCI task, we assessed this active inference add on through realistic simulations mimicking online data processing.

We compared four conditions:

- The **conventional P300 speller** with a fixed number of pseudo-randomized sequences;
- The conventional P300 speller endowed **with optimal stopping**;
- The Active Inference P300 speller, endowed **with optimal stopping and active sampling**;
- The above Active Inference P300 speller **complemented with automated error correction**.

Figure 18 shows the information transfer rate (Bit rate) obtained over simulations with each of these four methods [118].

**Interestingly, each of these adaptive features contributes to further improvements in performance.** Of course, it would be important to implement this approach for a true online empirical evaluation. Nevertheless, these realistic simulations are particularly interesting because they use the same data for each of the four methods compared.



**Figure 18:** Real data based simulations comparing, in bits/min, the default P300 speller (fixed flash) with three adaptive P300 speller with additive features: optimal stopping, active sampling and automated error correction (adapted from [118]).

This section has described three complementary ways of improving BCI performance (automated error correction, optimal stopping and active sampling). We have illustrated this on the P300 speller, but it could be considered for other BCI applications. The improvements observed are directly inspired by human adaptive behaviour and can in fact be implemented in a framework specifically designed to model human behaviour (active inference). Interestingly, we have empirically observed that when the machine is made adaptive, the human in the loop may perceive this as an incentive to perform even better (a collaboration effect).

In the next section, we look at another way of trying to improve EEG BCI performance: exploring other features for EEG-based decoding, in the case of motor imagery.

## Revisiting sensorimotor rhythms for motor imagery BCI

Motor imagery BCIs using EEG have been extensively studied in the hope of developing effective assistive devices for people with severe motor impairments [119], or offering rehabilitation therapies to restore function, for example after a stroke [109]. However, despite considerable efforts, the effectiveness of these BCIs as clinical tools remains limited. Strikingly, most of these efforts have been devoted to developing new machine learning algorithms or new training strategies. In contrast, the EEG signals used to decode commands based on motor imagery have never been questioned, namely beta event related desynchronization (ERD) [120].

However, while changes in frequency band power provide some insights into movement, they fail to consider important information in the temporal domain. Specifically, time-frequency analyses often overlook temporal variability and waveform shape of signals, thereby missing the occurrence of neural activity as bursts rather than oscillations and the presence of non-sinusoidal waveform shapes in oscillations. Recent findings demonstrate that sensorimotor activity in the beta band primarily occurs as discrete transient bursts rather than continuous oscillations. These bursts have been shown to play a crucial role in predicting response times before movement and indicating behavioural errors after movement, surpassing the significance of changes in beta amplitude [44]. This strongly suggests that we should not overlook the occurrence of beta bursts in neural activity and account for their temporal variability, their waveform shapes as refined neurophysiological markers for BCI research [121].

Recently<sup>17</sup>, we started exploring this lead by developing a beta burst extraction method from peaks in a highly resolved time-frequency decomposition (using superlets [122]), followed by a PCA in order to summarize the variability of burst shapes during real or imaginary movements [123]. By selecting the few components (i.e., shape dimensions) that appear to be most discriminant between, e.g., left- and right-hand imaginary movements, one can compute the dynamics of the rate of bursts with such shapes, for each trial and use those as features for binary classification (see Figure 19).

We evaluated this approach and compared it to classical beta power based decoding, on several open datasets [124], using a cross-validation procedure. **We found that classification features based on patterns of beta burst modulations yield decoding results that are equivalent to or better than typically used beta power, providing insights into the specificity of these biomarkers [125].**

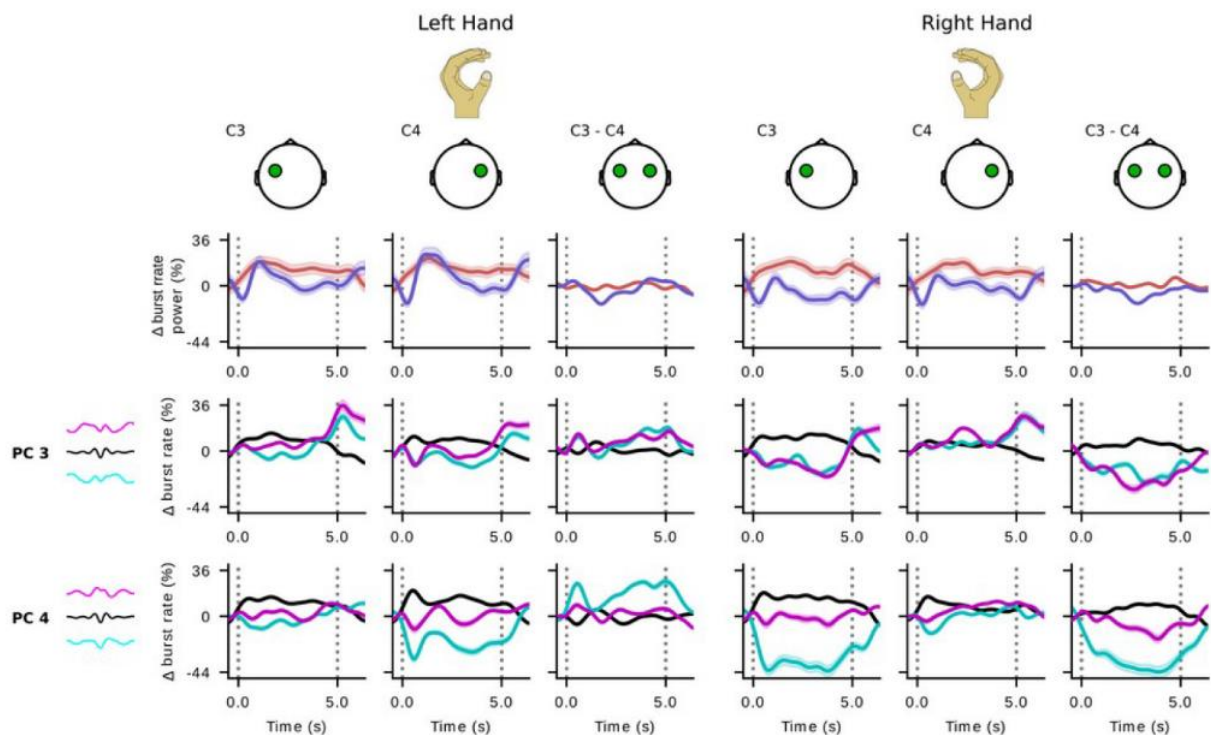
**Our most recent efforts have been devoted to extending this approach, which was limited to the bilateral central, C3 and C4, EEG sensors for computational reasons, to all sensors and making it compatible with online implementation<sup>18</sup>.**

Finally, we are about to launch an original study, using EEG and MEG, to further explore the relationship between the characteristics of beta bursts and parameters of real and imaginary hand movements.

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<sup>17</sup> As part of Sotirios Papadopoulos's PhD work (ongoing, co-supervised with James Bonaiuto)

<sup>18</sup> It will be demonstrated soon this year 2024 at the Cybathlon BCI competition in Zürich, with a young volunteer being in a locked-in state.



**Figure 19:** Trial-averaged, baseline-corrected overall burst rate, beta band power and burst rate modulation of three burst groups along components 3 and 4 for a representative subject. For both conditions and channels, beta band power changes (purple trace) roughly track the overall burst rate modulation (red trace). Burst rate modulation for different burst groups varies per condition, channel and component. The differential modulation of burst rate is particularly pronounced contralaterally, in channel C4 during “left hand” trials and channel C3 during “right hand” trials along the fourth component (adapted from [125]).

## Is EEG BCI suitable for helping patients without means of communication?

Patients who may be partially conscious but lack the means to communicate include people with global paralysis following a brainstem stroke (locked-in state (LIS)), people with advanced amyotrophic lateral sclerosis (ALS) or people diagnosed with a disorder of consciousness<sup>19</sup>. These people are all natural candidates to benefit from an EEG BCI in order to recover some form of communication (at least a ‘yes/no’ code).

However, it turns out that even patients who are known to be conscious and still have control of very few muscles, e.g., to control vertical eye movements, usually show poor performance in controlling a BCI.

We experienced this painfully ourselves in 2010 with a 38-year-old woman in LIS, who despite repeated trials over several weeks using a P300 speller, and an above-chance signal classification showing that she had understood our instructions, achieved very poor communication performance, much poorer than the least motivated and most tired naïve control subjects [128].

<sup>19</sup> They may even be people clinically assessed as being in a coma [126], [127].

Given that P300 spelling relies on vision and requires the ability to maintain overt attention on the target, we felt that this might not be the most appropriate paradigm for patients with global paralysis and decided to develop a binary auditory BCI to produce 'yes/no' responses<sup>20</sup>.

In a nutshell, this BCI relied on two different sound streams delivered simultaneously to the left ('no' sound) and the right ('yes' sound) ear. Subjects had to focus their attention on one ear to select the corresponding answer. To help them anchoring their attention, they were instructed to count the few deviant sounds (of longer duration) within each stream.

We tested 7 people with severe motor disabilities (3 LIS and 4 ALS patients), as well as 18 control participants. The latter did control the BCI quite well, with an average accuracy of 86%. 10 out the 18 healthy subjects had an accuracy above 90%. However, most of the patients could not produce online performance above chance level, except for two people with ALS who obtained 100% accuracy [129]. This disappointing result underlines the challenge of restoring communication using auditory BCI, despite promising results in healthy subjects.

Naturally, in patients, signal quality is often degraded and can affect performance. However, this alone does not explain such a difference in performance. Instead, we believe that these patients, whose mental functions are usually considered to be preserved, have cognitive impairments that prevent them from controlling a BCI. Specifically, we hypothesised that the partial loss of oculomotor control, which on the one hand makes them particularly dependent on a BCI for communication, leads to an alteration in their spatial covert attention capacity, which is essential for controlling an EEG BCI [130].

In order to test this hypothesis and explore the clinical, cognitive and oculomotor characteristics of these patients that might be predictive of their BCI performance, we launched a multicentre study including patients with global paralysis as well as tetraplegics and healthy control subjects. Data acquisition has just been completed. Data analysis is underway.

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<sup>20</sup> As part of Perrine Seguin's PhD work (ongoing, co-supervised with Emmanuel Maby).

# CHAPTER IV

## Conclusion and perspectives<sup>21</sup>

*“I've learnt that the road to progress is neither quick nor easy.”*

*Marie Skłodowska-Curie (Physicist and Chemists, 1867 - 1934)*

Although it has crossed the century mark, EEG remains a resolutely modern technique that has seen remarkable advancements over the past 25 years, as has its younger sister, MEG. The work shortly presented in this report is part of a general trend aimed at pushing the boundaries of EEG, whether in terms of spatial resolution, temporal precision, or fields of application. This quest for innovation has notably paved the way for the use of EEG in BCI, thus illustrating the ever-growing potential of this century-old technique.

Despite more than two decades of international research and development efforts, including significant private investment, the clinical applications of EEG BCI have not yet fully realised their potential in the medical field. Although progress has been made, the transition from the laboratory to widespread clinical use remains a challenge. At present, no EEG BCI device has definitively proven its efficacy and commercial viability to the point of revolutionising patient care or establishing a new medical paradigm.

This gap between promise and practice highlights the complexity of translating cutting-edge neurotechnology into practical, everyday medical solutions. However, it also highlights the immense opportunities available to researchers in this field. As we stand on the brink of potential breakthroughs, the next wave of advances could reshape the landscape of neurological or psychiatric interventions.

From now on, I hope to contribute to this exciting venture, together with my colleagues and collaborators, as well as bright new students and dynamic, supportive organisations such as CORTICO<sup>22</sup>.

Here is a concise overview of the subjects, the scientific, methodological and technical aspects, and the initiatives that I intend to investigate, build on and develop over the coming months and years.

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<sup>21</sup> Suggestion d'écoute pendant la lecture de ce chapitre [Sicilienne, Op. 78 \(youtube.com\)](#)

<sup>22</sup> [CORTICO](#) is the “Collectif pour la Recherche Transdisciplinaire sur les Interfaces Cerveau-Ordinateur » (The French association for BCI)

### ***Clinical applications***

I intend to mostly focus on applications of EEG BCI for the quantitative and objective functional assessment of cognitive dimensions (e.g., attention in ADHD, awareness in patients with disorders of consciousness, atypical perception in autism) and the development and validation of non-pharmacological rehabilitation approaches (e.g., in ADHD or Stroke).

Here I intend to leverage EEG BCI for two primary objectives: (1) to develop quantitative and objective functional assessments of cognitive dimensions, including attention in ADHD, awareness in disorders of consciousness, and atypical perception in autism; and (2) to advance and validate non-pharmacological rehabilitation approaches, particularly for ADHD and stroke recovery. By employing EEG BCI methodologies, this work will seek to enhance our understanding of neurological conditions and contribute to the development of evidence-based, non-invasive diagnostic and therapeutic interventions.

Over the last few years, together with my colleague Emmanuel Maby, in collaboration with clinical departments (and Vania Herbillon, Neuropsychologist), we have worked on P300-based EEG BCI games for the evaluation and possibly the rehabilitation of children with attention deficits [131]. We conducted a preliminary clinical trial<sup>23</sup> (unpublished yet) which confirmed the feasibility of such approaches as well as the relevance of targeting the P300 component to probe attention.

The application of EEG BCI in assessing patients with disorders of consciousness (DoC) presents a promising avenue for research [133]. Current diagnostic tools for DoC patients have limitations that warrant further investigation. Passive protocols, such as those detecting Mismatch Negativity (MMN) or P300 responses [72], lack personalization and suffer from low signal-to-noise ratios. Moreover, their passive nature precludes direct probing of awareness. Conversely, active paradigms, which rely on verbal instructions, may be too demanding for many subjects, potentially leading to false negatives and ambiguous interpretations.

An adaptive EEG BCI approach could potentially bridge this gap by combining the advantages of passive methods with personalization and model-based analysis. This novel approach would target specific, interpretable processes, such as perceptual learning, which may serve as robust predictors of awareness and functional recovery. By leveraging the strengths of both passive and active paradigms, this method could enhance the diagnostic and prognostic capabilities for DoC patients, addressing some of the current limitations in assessment tools.

### ***Theoretical and fundamental projects***

The advancement of EEG BCI for diverse applications is intrinsically linked to ongoing fundamental scientific research. The efficacy and success of these interfaces are contingent upon elucidating the computational mechanisms underlying specific neurophysiological markers, which remain to be precisely identified and validated. Consequently, BCI research must be firmly grounded in basic neuroscientific investigations of brain functions, and their neurophysiological substrates. This approach necessitates a synergistic integration of empirical observations with quantitative computational models of neurocognitive processes, fostering a comprehensive understanding of the neural dynamics involved in BCI operation.

Along this line, our current research projects encompass several interconnected areas of neuroscience and cognitive psychology. We are exploring the potential application of the active inference (Bayesian) framework and of reinforcement learning principles<sup>24</sup> to model BCI and Neurofeedback training [134]. This approach may offer novel insights into the underlying mechanisms of these interventions.

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<sup>23</sup> As part of Mélodie Fouillen's PhD work [132] (co-supervised with Emmanuel Maby)

<sup>24</sup> As part of Côme Annicchiarico's Phd work (ongoing, co-supervised with Fabien Lotte, INRIA Bordeaux)

Concurrently, we are developing and validating a suite of behavioural assessments designed to elucidate executive function processes in children with ADHD and neurotypical controls. These assessments specifically target computational hypotheses related to effort allocation, effort evaluation, and self-confidence, potentially revealing key differences in cognitive processing between these populations<sup>25</sup>.

Besides, our team's expertise in neurophysiological markers of active perception is significantly enhanced by the contributions of Mathilde Bonnefond. Her research program focuses on empirically evaluating her theory regarding the functional role of nested oscillations, particularly in the context of context-dependent perception and attention. This work could provide crucial information on the temporal dynamics of neuronal information processing and on the neurophysiological markers that should be targeted in future BCIs.

Finally, we have recently initiated an ambitious, multi-scale project led by Françoise Lecaigard. It aims to refine our understanding of sensory adaptation and mismatch responses within the theoretical framework of predictive coding. By integrating *in vitro* recordings using multi-electrode arrays (MEAs), *in vivo* laminar MEG experiments, and *in silico* simulations employing biologically plausible neural networks, we seek to bridge the gap between the cellular, systems, and computational levels<sup>26</sup>.

### ***Methodological and technological developments***

For EEG BCI to be accessible to end-users outside the laboratory, for example at the patient's bedside, or in non-clinical applications, acquisition systems must be robust and easy to install and use. In particular, it is therefore important to involve experts in signal processing and machine learning to improve the online analysis of EEG data. We have ongoing joint projects with Marco Congedo at the GIPSA Lab in Grenoble, who is an expert in developing powerful detection and classification algorithms based on Riemannian geometry [135].

On the hardware front, we are engaged in assessing the next generation of portable, ambient-temperature MEG sensors, specifically Optically Pumped Magnetometers (OPMs). These are being developed by Mag4Health, a spin-off from CEA Grenoble, in partnership with the Lyon MEG CERMEP Platform, led by Denis Schwartz.

Finally, with my colleague Emmanuel Maby, we have initiated a prematurity project supported by CNRS Innovation, with the aim of developing our own head mounted EEG BCI device, combining wireless active sensors with a VR headset, in order to promote and make accessible our developments dedicated to the evaluation of children with ADHD.

### ***Innovation and valorisation***

Emmanuel Maby and I have collaborated extensively on projects with multiple industrial partners, focusing on the application of EEG in diverse real-world scenarios. Our research has encompassed the monitoring of various states, including sleep patterns, vigilance levels, cognitive and physical load, and fatigue.

Through these collaborations, we have acquired substantial expertise in utilizing a wide range of EEG systems and implementing EEG in challenging and unconventional environments. The knowledge and experience we have accumulated have proved invaluable to our ongoing valorisation efforts.

We are now leveraging our theoretical work, software developments, and hardware innovations to create a novel EEG BCI assessment tool for children with ADHD. This ongoing project aims to translate our research into practical clinical applications, potentially to improve the management of ADHD.

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<sup>25</sup> As part of Kris Barc's PhD work (ongoing, co-supervised with Jean Daunizeau, ICM Paris)

<sup>26</sup> In collaboration with Matteo Di Vol (CPJ – Computational Neurosciences – Université Lyon 1)

### ***Working environment***

To conduct my research project, I am benefitting from the very stimulating and enjoyable environment of the COPHY (*Computation, Cognition and Neurophysiology*) team of the Lyon Neuroscience Research Center (CRNL), which I am leading together with my colleague Mathilde Bonnefond, since its official creation in January 2021. At that time, the team included 4 permanent researchers, 2 research engineers and 1 clinician. Since then, we have recruited another INSERM researcher (Romain Ligneul) and a young INRIA researcher (Elif Köksal-Ersöz) will be joining us very soon.

Indeed, shortly after the creation of the Lyon INRIA centre, and given our unique positioning in-between empirical neurosciences, health applications, computational modelling, digital and technological developments, we have applied for becoming an INRIA project team. The evaluation process is underway.

Finally, I also very much enjoy being involved in new Master teaching unit in computational Neurosciences, which I contributed to conceive, organize and teach. Together with Matteo Di Volo, we now plan to open a full path for M2 students, starting in September 2025. Our aim is to both familiarize neuroscience students with computational modelling, and attract engineering students to neuroscience.

# Acknowledgments

A number of conflicting feelings naturally arise when, as is the case here, you have to look back and try to sum up a large part of the work you've been involved in over several years. But one thing stands out: the fact that this work has not been solitary and that it owes a great deal to many people I have met along the way and who have been involved in different manners, at different stages. So as not to be too long, I will distinguish three main categories of people.

First come mentors, models or guides, that is people who taught me when I was new to the field or nearly. These people inspired me and also had a profound impact on my path and choices. In particular, I am deeply grateful to Mélanie Pélégrini-Issac, Habib Benali, Karl Friston and Olivier Bertrand.

Naturally, next come the dear colleagues, collaborators, and among them close friends. Many thanks to them: Corine Amat, Nathalie André-Obadia, Christian Berthomier, James Bonaiuto, Mathilde Bonnefond, Romain Bouet, François Cabestaing, Anne Caclin, Maureen Clerc, Marco Congedo, Jean Daunizeau, Matteo Di Volo, Alessandro Farne, Guillaume Flandin, Florent Gobert, Marie Gomot, Julie Grèzes, Rik Henson, Vania Herbillon, Mateus Joffily, Julien Jung, Stefan Kiebel, Anatole Lecuyer, Jacques Luauté, Antoine Lutz, Jean-Marc Lina, Fabien Lotte, Françoise Lecaigard, Emmanuel Maby, Dominique Morlet, Jérémie Pariente, Christoph Phillips, Karen Reilly, Christina Schmitz, Denis Schwartz.

I would like to conclude by mentioning all the students I have been working with. Many master's students and young engineers as well as post-docs have contributed to these projects, notably Alexandre Mollaret, but most of the work has been carried out with a smaller number of doctoral students. Even the best artificial intelligence would struggle to write a good song with the following list, but each of these names will always sound good to my ears. I hope they have forgiven me as much as I have forgiven them. All my best wishes to Margaux Perrin, Gaëtan Sanchez, Françoise Lecaigard, Laurie-Anne Sapey-Triomphe, Mélodie Fouillen, Jelena Mladenovic, Loïc Delobel and Alexandre Bleuzé. And good luck to Perrine Seguin, Côme Annicchiarico, Sotirios Papadopoulos and Kris Barc.

# References

My publications appear in bold

- [1] S. Baillet, J. C. Mosher, et R. M. Leahy, « Electromagnetic brain mapping », *IEEE Signal Processing Magazine*, vol. 18, n° 6, Art. n° 6, nov. 2001, doi: 10.1109/79.962275.
- [2] S. Baillet, « Magnetoencephalography for brain electrophysiology and imaging », *Nat Neurosci*, vol. 20, n° 3, p. 327-339, mars 2017, doi: 10.1038/nn.4504.
- [3] **C. Phillips, J. Mattout, et K. Friston, « Forward models for EEG », in *Statistical Parametric Mapping*, Elsevier, 2007, p. 352-366. doi: 10.1016/B978-012372560-8/50028-0.**
- [4] **F. Lecaigard et J. Mattout, « Forward Models for EEG/MEG », in *Brain Mapping*, Elsevier, 2015, p. 549-555. doi: 10.1016/B978-0-12-397025-1.00330-4.**
- [5] J. C. Mosher, R. M. Leahy, et P. S. Lewis, « EEG and MEG: forward solutions for inverse methods », *IEEE Trans. Biomed. Eng.*, vol. 46, n° 3, p. 245-259, mars 1999, doi: 10.1109/10.748978.
- [6] J. Kybic, M. Clerc, O. Faugeras, R. Keriven, et T. Papadopoulos, « Generalized head models for MEG/EEG: boundary element method beyond nested volumes », *Phys. Med. Biol.*, vol. 51, n° 5, p. 1333-1346, mars 2006, doi: 10.1088/0031-9155/51/5/021.
- [7] P. H. Schimpf, « Application of Quasi-Static Magnetic Reciprocity to Finite Element Models of the MEG Lead-Field », *IEEE Trans. Biomed. Eng.*, vol. 54, n° 11, p. 2082-2088, nov. 2007, doi: 10.1109/TBME.2007.895112.
- [8] H. Hallez, B. Vanrumste, P. Van Hese, Y. D'Asseler, I. Lemahieu, et R. Van de Walle, « A finite difference method with reciprocity used to incorporate anisotropy in electroencephalogram dipole source localization », *Phys Med Biol*, vol. 50, n° 16, p. 3787-3806, août 2005, doi: 10.1088/0031-9155/50/16/009.
- [9] N. Yavich, N. Koshev, M. Malovichko, A. Razorenova, et M. Fedorov, « Conservative Finite Element Modeling of EEG and MEG on Unstructured Grids », *IEEE Trans. Med. Imaging*, vol. 41, n° 3, p. 647-656, mars 2022, doi: 10.1109/TMI.2021.3119851.
- [10] **J. Mattout, M. Pelegrini-Issac, L. Garnero, et H. Benali, « Multivariate source prelocalization (MSP): Use of functionally informed basis functions for better conditioning the MEG inverse problem », *NeuroImage*, vol. 26, n° 2, p. 356-373, juin 2005, doi: 10.1016/j.neuroimage.2005.01.026.**
- [11] **J. Mattout, M. Pélégrini-Issac, A. Bellio, J. Daunizeau, et H. Benali, « Localization Estimation Algorithm (LEA): A Supervised Prior-Based Approach for Solving the EEG/MEG Inverse Problem », in *Information Processing in Medical Imaging*, vol. 2732, C. Taylor et J. A. Noble, Éd., in *Lecture Notes in Computer Science*, vol. 2732, Berlin, Heidelberg: Springer Berlin Heidelberg, 2003, p. 536-547. doi: 10.1007/978-3-540-45087-0\_45.**
- [12] **E. Lapalme, J.-M. Lina, et J. Mattout, « Data-driven parceling and entropic inference in MEG », *NeuroImage*, vol. 30, n° 1, p. 160-171, mars 2006, doi: 10.1016/j.neuroimage.2005.08.067.**
- [13] C. Grova, J. Daunizeau, J.-M. Lina, C. G. Bénar, H. Benali, et J. Gotman, « Evaluation of EEG localization methods using realistic simulations of interictal spikes », *NeuroImage*, vol. 29, n° 3, p. 734-753, févr. 2006, doi: 10.1016/j.neuroimage.2005.08.053.
- [14] R. A. Chowdhury *et al.*, « MEG–EEG Information Fusion and Electromagnetic Source Imaging: From Theory to Clinical Application in Epilepsy », *Brain Topogr*, vol. 28, n° 6, p. 785-812, nov. 2015, doi: 10.1007/s10548-015-0437-3.
- [15] Z. Cai *et al.*, « Evaluation of a personalized functional near INFRARED optical tomography workflow using maximum entropy on the mean », *Human Brain Mapping*, vol. 42, n° 15, p. 4823-4843, oct. 2021, doi: 10.1002/hbm.25566.
- [16] D. Suma, J. Meng, B. J. Edelman, et B. He, « Spatial-temporal aspects of continuous EEG-based neurobotic control », *J. Neural Eng.*, vol. 17, n° 6, p. 066006, déc. 2020, doi: 10.1088/1741-2552/abc0b4.
- [17] O. Hauk, « Keep it simple: a case for using classical minimum norm estimation in the analysis of EEG and MEG data », *NeuroImage*, vol. 21, n° 4, p. 1612-1621, avr. 2004, doi: 10.1016/j.neuroimage.2003.12.018.
- [18] R. D. Pascual-Marqui, M. Esslen, K. Kochi, et D. Lehmann, « Functional imaging with low-resolution brain electromagnetic tomography (LORETA): a review », *Methods Find Exp Clin Pharmacol*, vol. 24 Suppl C, p. 91-95, 2002.
- [19] A. Hillebrand, K. D. Singh, I. E. Holliday, P. L. Furlong, et G. R. Barnes, « A new approach to neuroimaging with magnetoencephalography », *Hum Brain Mapp*, vol. 25, n° 2, p. 199-211, juin 2005, doi: 10.1002/hbm.20102.

- [20] C. Phillips, J. Mattout, M. D. Rugg, P. Maquet, et K. J. Friston, « An empirical Bayesian solution to the source reconstruction problem in EEG », *NeuroImage*, vol. 24, n° 4, p. 997-1011, févr. 2005, doi: 10.1016/j.neuroimage.2004.10.030.
- [21] J. Mattout, C. Phillips, W. D. Penny, M. D. Rugg, et K. J. Friston, « MEG source localization under multiple constraints: an extended Bayesian framework », *NeuroImage*, vol. 30, n° 3, Art. n° 3, avr. 2006, doi: 10.1016/j.neuroimage.2005.10.037.
- [22] J. Mattout, C. Phillips, R. Henson, et K. Friston, « MEG Source Localization under Multiple Constraints: An Extended Bayesian Framework », in *Complex Medical Engineering*, J. L. Wu, K. Ito, S. Tobimatsu, T. Nishida, et H. Fukuyama, Éd., Tokyo: Springer Japan, 2007, p. 383-395. Consulté le: 27 janvier 2016. [En ligne]. Disponible sur: [http://www.springerlink.com/index/10.1007/978-4-431-30962-8\\_33](http://www.springerlink.com/index/10.1007/978-4-431-30962-8_33)
- [23] K. Friston *et al.*, « Multiple sparse priors for the M/EEG inverse problem », *NeuroImage*, vol. 39, n° 3, p. 1104-1120, févr. 2008, doi: 10.1016/j.neuroimage.2007.09.048.
- [24] R. N. Henson, G. Flandin, K. J. Friston, et J. Mattout, « A Parametric Empirical Bayesian framework for fMRI-constrained MEG/EEG source reconstruction », *Human Brain Mapping*, vol. 31, n° 10, Art. n° 10, oct. 2010, doi: 10.1002/hbm.20956.
- [25] J. Daunizeau *et al.*, « Symmetrical event-related EEG/fMRI information fusion in a variational Bayesian framework », *NeuroImage*, vol. 36, n° 1, p. 69-87, mai 2007, doi: 10.1016/j.neuroimage.2007.01.044.
- [26] J. Daunizeau, J. Mattout, D. Clonda, B. Goulard, H. Benali, et J.-M. Lina, « Bayesian Spatio-Temporal Approach for EEG Source Reconstruction: Conciliating ECD and Distributed Models », *IEEE Trans. Biomed. Eng.*, vol. 53, n° 3, p. 503-516, mars 2006, doi: 10.1109/TBME.2005.869791.
- [27] W. D. Penny, K. E. Stephan, A. Mechelli, et K. J. Friston, « Comparing dynamic causal models », *NeuroImage*, vol. 22, n° 3, p. 1157-1172, juill. 2004, doi: 10.1016/j.neuroimage.2004.03.026.
- [28] N. J. Trujillo-Barreto, E. Aubert-Vázquez, et P. A. Valdés-Sosa, « Bayesian model averaging in EEG/MEG imaging », *NeuroImage*, vol. 21, n° 4, p. 1300-1319, avr. 2004, doi: 10.1016/j.neuroimage.2003.11.008.
- [29] G. Flandin et W. D. Penny, « Bayesian fMRI data analysis with sparse spatial basis function priors », *NeuroImage*, vol. 34, n° 3, p. 1108-1125, févr. 2007, doi: 10.1016/j.neuroimage.2006.10.005.
- [30] R. E. Kass et A. E. Raftery, « Bayes Factors », *Journal of the American Statistical Association*, vol. 90, n° 430, p. 773-795, juin 1995, doi: 10.1080/01621459.1995.10476572.
- [31] W. D. Penny *et al.*, « Comparing Families of Dynamic Causal Models », *PLoS Comput Biol*, vol. 6, n° 3, p. e1000709, mars 2010, doi: 10.1371/journal.pcbi.1000709.
- [32] K. E. Stephan, J. Mattout, O. David, et K. J. Friston, « Models of functional neuroimaging data », *Curr Med Imaging Rev*, vol. 2, n° 1, Art. n° 1, févr. 2006.
- [33] R. N. Henson, J. Mattout, K. D. Singh, G. R. Barnes, A. Hillebrand, et K. Friston, « Population-level inferences for distributed MEG source localization under multiple constraints: Application to face-evoked fields », *NeuroImage*, vol. 38, n° 3, p. 422-438, nov. 2007, doi: 10.1016/j.neuroimage.2007.07.026.
- [34] L. Rigoux, K. E. Stephan, K. J. Friston, et J. Daunizeau, « Bayesian model selection for group studies - revisited », *NeuroImage*, vol. 84, p. 971-985, janv. 2014, doi: 10.1016/j.neuroimage.2013.08.065.
- [35] J. Mattout, R. N. Henson, et K. J. Friston, « Canonical Source Reconstruction for MEG », *Computational Intelligence and Neuroscience*, vol. 2007, p. 1-10, 2007, doi: 10.1155/2007/67613.
- [36] J. Ashburner et K. J. Friston, « Nonlinear spatial normalization using basis functions », *Hum Brain Mapp*, vol. 7, n° 4, p. 254-266, 1999, doi: 10.1002/(SICI)1097-0193(1999)7:4<#x0003c;254::AID-HBM4<#x0003e;3.0.CO;2-G.
- [37] R. N. Henson, Y. Goshen-Gottstein, T. Ganel, L. J. Otten, A. Quayle, et M. D. Rugg, « Electrophysiological and haemodynamic correlates of face perception, recognition and priming », *Cereb Cortex*, vol. 13, n° 7, p. 793-805, juill. 2003, doi: 10.1093/cercor/13.7.793.
- [38] R. N. Henson, J. Mattout, C. Phillips, et K. J. Friston, « Selecting forward models for MEG source-reconstruction using model-evidence », *NeuroImage*, vol. 46, n° 1, p. 168-176, mai 2009, doi: 10.1016/j.neuroimage.2009.01.062.
- [39] F. Lecaigard, « Predictive coding in auditory processing: insights from advanced modeling of EEG and MEG mismatch responses », Theses, Université Claude Bernard Lyon 1, 2016. [En ligne]. Disponible sur: <https://hal.science/tel-01403280>
- [40] F. Lecaigard, O. Bertrand, A. Caclin, et J. Mattout, « Empirical evaluation of fused EEG-MEG source reconstruction. Application to auditory mismatch generators », *Neuroscience*, preprint, sept. 2019. doi: 10.1101/765966.

- [41] F. Lecaigard, O. Bertrand, G. Gimenez, J. Mattout, et A. Caclin, « Implicit learning of predictable sound sequences modulates human brain responses at different levels of the auditory hierarchy », *Front. Hum. Neurosci.*, vol. 9, sept. 2015, doi: 10.3389/fnhum.2015.00505.
- [42] V. Litvak *et al.*, « EEG and MEG Data Analysis in SPM8 », *Computational Intelligence and Neuroscience*, vol. 2011, p. 1-32, 2011, doi: 10.1155/2011/852961.
- [43] R. Oostenveld, P. Fries, E. Maris, et J.-M. Schoffelen, « FieldTrip: Open source software for advanced analysis of MEG, EEG, and invasive electrophysiological data », *Comput Intell Neurosci*, vol. 2011, p. 156869, 2011, doi: 10.1155/2011/156869.
- [44] S. Little, J. Bonaiuto, S. S. Meyer, J. Lopez, S. Bestmann, et G. Barnes, « Quantifying the performance of MEG source reconstruction using resting state data », *Neuroimage*, vol. 181, p. 453-460, nov. 2018, doi: 10.1016/j.neuroimage.2018.07.030.
- [45] K. Friston, R. Henson, C. Phillips, et J. Mattout, « Bayesian estimation of evoked and induced responses », *Human Brain Mapping*, vol. 27, n° 9, Art. n° 9, sept. 2006, doi: 10.1002/hbm.20214.
- [46] O. David, S. J. Kiebel, L. M. Harrison, J. Mattout, J. M. Kilner, et K. J. Friston, « Dynamic causal modeling of evoked responses in EEG and MEG », *Neuroimage*, vol. 30, n° 4, Art. n° 4, mai 2006, doi: 10.1016/j.neuroimage.2005.10.045.
- [47] S. S. Meyer *et al.*, « Flexible head-casts for high spatial precision MEG », *Journal of Neuroscience Methods*, vol. 276, p. 38-45, janv. 2017, doi: 10.1016/j.jneumeth.2016.11.009.
- [48] J. J. Bonaiuto *et al.*, « Estimates of cortical column orientation improve MEG source inversion », *Neuroimage*, vol. 216, p. 116862, août 2020, doi: 10.1016/j.neuroimage.2020.116862.
- [49] M. J. Brookes *et al.*, « Magnetoencephalography with optically pumped magnetometers (OPM-MEG): the next generation of functional neuroimaging », *Trends Neurosci*, vol. 45, n° 8, p. 621-634, août 2022, doi: 10.1016/j.tins.2022.05.008.
- [50] R. Spehlmann, « The averaged electrical responses to diffuse and to patterned light in the human », *Electroencephalography and Clinical Neurophysiology*, vol. 19, n° 6, p. 560-569, déc. 1965, doi: 10.1016/0013-4694(65)90241-5.
- [51] S. A. Hillyard, R. F. Hink, V. L. Schwent, et T. W. Picton, « Electrical Signs of Selective Attention in the Human Brain », *Science*, vol. 182, n° 4108, p. 177-180, oct. 1973, doi: 10.1126/science.182.4108.177.
- [52] R. Näätänen et T. Picton, « The N1 wave of the human electric and magnetic response to sound: a review and an analysis of the component structure », *Psychophysiology*, vol. 24, p. 375-425., 1987.
- [53] S. Bentin, T. Allison, A. Puce, E. Perez, et G. McCarthy, « Electrophysiological Studies of Face Perception in Humans », *Journal of Cognitive Neuroscience*, vol. 8, n° 6, p. 551-565, nov. 1996, doi: 10.1162/jocn.1996.8.6.551.
- [54] H. Davis et S. Zerlin, « Acoustic relations of the human vertex potential », *J Acoust Soc Am*, vol. 39, n° 1, p. 109-116, janv. 1966, doi: 10.1121/1.1909858.
- [55] S. Sutton, M. Braren, J. Zubin, et E. R. John, « Evoked-potential correlates of stimulus uncertainty », *Science*, vol. 150, n° 3700, p. 1187-1188, nov. 1965, doi: 10.1126/science.150.3700.1187.
- [56] T. W. Picton, « The P300 wave of the human event-related potential », *J Clin Neurophysiol*, vol. 9, n° 4, p. 456-479, oct. 1992, doi: 10.1097/00004691-199210000-00002.
- [57] M. Kutas et S. A. Hillyard, « Reading senseless sentences: brain potentials reflect semantic incongruity », *Science*, vol. 207, n° 4427, p. 203-205, janv. 1980, doi: 10.1126/science.7350657.
- [58] M. Kutas et K. D. Federmeier, « Thirty years and counting: finding meaning in the N400 component of the event-related brain potential (ERP) », *Annu Rev Psychol*, vol. 62, p. 621-647, 2011, doi: 10.1146/annurev.psych.093008.131123.
- [59] F. Lecaigard et J. Mattout, « Mismatch Negativity: time for deconstruction », 2023, *arXiv*. doi: 10.48550/ARXIV.2310.11247.
- [60] C. Tallon-Baudry et O. Bertrand, « Oscillatory gamma activity in humans and its role in object representation », *Trends in Cognitive Sciences*, vol. 3, n° 4, p. 151-162, avr. 1999, doi: 10.1016/S1364-6613(99)01299-1.
- [61] D. C. Knill et A. Pouget, « The Bayesian brain: the role of uncertainty in neural coding and computation », *Trends Neurosci.*, vol. 27, n° 12, Art. n° 12, déc. 2004, doi: 10.1016/j.tins.2004.10.007.
- [62] K. Doya, Éd., *Bayesian brain: probabilistic approaches to neural coding*. in Computational neuroscience. Cambridge, Mass: MIT Press, 2007.
- [63] D. Marr, *Vision: a computational investigation into the human representation and processing of visual information*. San Francisco: W.H. Freeman, 1982.
- [64] M. O. Ernst et M. S. Banks, « Humans integrate visual and haptic information in a statistically optimal fashion », *Nature*, vol. 415, n° 6870, p. 429-433, janv. 2002, doi: 10.1038/415429a.

- [65] K. P. Körding et D. M. Wolpert, « Bayesian integration in sensorimotor learning », *Nature*, vol. 427, n° 6971, Art. n° 6971, janv. 2004, doi: 10.1038/nature02169.
- [66] R. P. N. Rao, B. A. Olshausen, et M. S. Lewicki, Éd., *Probabilistic Models of the Brain: Perception and Neural Function*. The MIT Press, 2002. doi: 10.7551/mitpress/5583.001.0001.
- [67] R. P. Rao et D. H. Ballard, « Predictive coding in the visual cortex: a functional interpretation of some extra-classical receptive-field effects », *Nat. Neurosci.*, vol. 2, n° 1, Art. n° 1, janv. 1999, doi: 10.1038/4580.
- [68] K. Friston, « A theory of cortical responses », *Philos. Trans. R. Soc. Lond., B, Biol. Sci.*, vol. 360, n° 1456, Art. n° 1456, avr. 2005, doi: 10.1098/rstb.2005.1622.
- [69] D. Rahnev, « The Bayesian brain: What is it and do humans have it? », *Behav Brain Sci*, vol. 42, p. e238, 2019, doi: 10.1017/S0140525X19001377.
- [70] R. Näätänen, « Mismatch negativity (MMN) as an index of central auditory system plasticity », *Int J Audiol*, vol. 47 Suppl 2, p. S16-20, nov. 2008, doi: 10.1080/14992020802340116.
- [71] R. Näätänen, E. S. Sussman, D. Salisbury, et V. L. Shafer, « Mismatch negativity (MMN) as an index of cognitive dysfunction », *Brain Topogr*, vol. 27, n° 4, p. 451-466, juill. 2014, doi: 10.1007/s10548-014-0374-6.
- [72] D. Morlet et C. Fischer, « MMN and Novelty P3 in Coma and Other Altered States of Consciousness: A Review », *Brain Topography*, vol. 27, n° 4, Art. n° 4, juill. 2014, doi: 10.1007/s10548-013-0335-5.
- [73] P. T. Michie, M. S. Malmierca, L. Harms, et J. Todd, « The neurobiology of MMN and implications for schizophrenia », *Biol Psychol*, vol. 116, p. 90-97, avr. 2016, doi: 10.1016/j.biopsycho.2016.01.011.
- [74] S. Schwartz, B. Shinn-Cunningham, et H. Tager-Flusberg, « Meta-analysis and systematic review of the literature characterizing auditory mismatch negativity in individuals with autism », *Neurosci Biobehav Rev*, vol. 87, p. 106-117, avr. 2018, doi: 10.1016/j.neubiorev.2018.01.008.
- [75] **F. Lecaigard, O. Bertrand, A. Caclin, et J. Mattout, « Neurocomputational Underpinnings of Expected Surprise », *J. Neurosci.*, vol. 42, n° 3, p. 474-486, janv. 2022, doi: 10.1523/JNEUROSCI.0601-21.2021.**
- [76] M. J. Rosa, S. Bestmann, L. Harrison, et W. Penny, « Bayesian model selection maps for group studies », *Neuroimage*, vol. 49, n° 1, p. 217-224, janv. 2010, doi: 10.1016/j.neuroimage.2009.08.051.
- [77] H. R. Brown et K. J. Friston, « Dynamic causal modelling of precision and synaptic gain in visual perception - an EEG study », *Neuroimage*, vol. 63, n° 1, p. 223-231, oct. 2012, doi: 10.1016/j.neuroimage.2012.06.044.
- [78] R. Auzztulewicz, N. Barascud, G. Cooray, A. C. Nobre, M. Chait, et K. Friston, « The Cumulative Effects of Predictability on Synaptic Gain in the Auditory Processing Stream », *J Neurosci*, vol. 37, n° 28, p. 6751-6760, juill. 2017, doi: 10.1523/JNEUROSCI.0291-17.2017.
- [79] M. Perrin, « Coadaptation cerveau machine pour une interaction optimale : application au P300-Speller », Theses, Université Claude Bernard - Lyon I, 2012. [En ligne]. Disponible sur: <https://theses.hal.science/tel-01618163>
- [80] W. H. Miltner, C. H. Braun, et M. G. Coles, « Event-related brain potentials following incorrect feedback in a time-estimation task: evidence for a “generic” neural system for error detection », *J Cogn Neurosci*, vol. 9, n° 6, p. 788-798, nov. 1997, doi: 10.1162/jocn.1997.9.6.788.
- [81] M. F. S. Rushworth et T. E. J. Behrens, « Choice, uncertainty and value in prefrontal and cingulate cortex », *Nat Neurosci*, vol. 11, n° 4, p. 389-397, avr. 2008, doi: 10.1038/nn2066.
- [82] L. A. Farwell et E. Donchin, « Talking off the top of your head: toward a mental prosthesis utilizing event-related brain potentials », *Electroencephalogr Clin Neurophysiol*, vol. 70, n° 6, Art. n° 6, déc. 1988.
- [83] **M. Perrin, E. Maby, R. Bouet, O. Bertrand, et J. Mattout, « Detecting and interpreting responses to feedback in BCI », *Proceeding of the 5th International Brain-Computer Interface Conference, Graz 2011*, p. 116-119, 2011.**
- [84] N. Yeung et A. G. Sanfey, « Independent coding of reward magnitude and valence in the human brain », *J Neurosci*, vol. 24, n° 28, p. 6258-6264, juill. 2004, doi: 10.1523/JNEUROSCI.4537-03.2004.
- [85] T. O. Zander, L. R. Krol, N. P. Birbaumer, et K. Gramann, « Neuroadaptive technology enables implicit cursor control based on medial prefrontal cortex activity », *Proc Natl Acad Sci U S A*, vol. 113, n° 52, p. 14898-14903, déc. 2016, doi: 10.1073/pnas.1605155114.
- [86] **J. Mattout, M. Perrin, O. Bertrand, et E. Maby, « Improving BCI performance through co-adaptation: Applications to the P300-speller », *Annals of Physical and Rehabilitation Medicine*, vol. 58, n° 1, Art. n° 1, févr. 2015, doi: 10.1016/j.rehab.2014.10.006.**
- [87] **M. Perrin, E. Maby, S. Daligault, O. Bertrand, et J. Mattout, « Objective and Subjective Evaluation of Online Error Correction during P300-Based Spelling », *Advances in Human-Computer Interaction*, vol. 2012, p. 1-13, 2012, doi: 10.1155/2012/578295.**

- [88] M. G. Philiastides, G. Biele, N. Vavatzanidis, P. Kazzer, et H. R. Heekeren, « Temporal dynamics of prediction error processing during reward-based decision making », *Neuroimage*, vol. 53, n° 1, p. 221-232, oct. 2010, doi: 10.1016/j.neuroimage.2010.05.052.
- [89] **S. Robic et al., « Decision-Making in a Changing World: A Study in Autism Spectrum Disorders », *Journal of Autism and Developmental Disorders*, vol. 45, n° 6, Art. n° 6, juin 2015, doi: 10.1007/s10803-014-2311-7.**
- [90] H. Haker, M. Schneebeli, et K. E. Stephan, « Can Bayesian Theories of Autism Spectrum Disorder Help Improve Clinical Practice? », *Frontiers in Psychiatry*, vol. 7, juin 2016, doi: 10.3389/fpsy.2016.00107.
- [91] **L.-A. Sapey-Triomphe, S. Sonié, M.-A. Hénaff, J. Mattout, et C. Schmitz, « Adults with Autism Tend to Undermine the Hidden Environmental Structure: Evidence from a Visual Associative Learning Task », *J Autism Dev Disord*, vol. 48, n° 9, p. 3061-3074, sept. 2018, doi: 10.1007/s10803-018-3574-1.**
- [92] G. Sanchez, « Real-time electrophysiology in cognitive neuroscience : towards adaptive paradigms to study perceptual learning and decision making in humans », Theses, Université Claude Bernard - Lyon I, 2014. [En ligne]. Disponible sur: <https://theses.hal.science/tel-01058541>
- [93] **G. Sanchez, J. Daunizeau, E. Maby, O. Bertrand, A. Bompas, et J. Mattout, « Toward a New Application of Real-Time Electrophysiology: Online Optimization of Cognitive Neurosciences Hypothesis Testing », *Brain Sciences*, vol. 4, n° 1, Art. n° 1, janv. 2014, doi: 10.3390/brainsci4010049.**
- [94] **G. Sanchez, F. Lecaigard, A. Otman, E. Maby, et J. Mattout, « Active SAMpling Protocol (ASAP) to Optimize Individual Neurocognitive Hypothesis Testing: A BCI-Inspired Dynamic Experimental Design », *Frontiers in Human Neuroscience*, vol. 10, juill. 2016, doi: 10.3389/fnhum.2016.00347.**
- [95] J. Daunizeau, K. Preuschoff, K. Friston, et K. Stephan, « Optimizing Experimental Design for Comparing Models of Brain Function », *PLoS Computational Biology*, vol. 7, n° 11, Art. n° 11, nov. 2011, doi: 10.1371/journal.pcbi.1002280.
- [96] A. Wald, *Sequential analysis*. Mineola, NY: Dover Phoenix Editions, 1947.
- [97] D. R. Cavagnaro, M. A. Pitt, et J. I. Myung, « Model discrimination through adaptive experimentation », *Psychon Bull Rev*, vol. 18, n° 1, p. 204-210, févr. 2011, doi: 10.3758/s13423-010-0030-4.
- [98] T. R. Mullen et al., « Real-Time Neuroimaging and Cognitive Monitoring Using Wearable Dry EEG », *IEEE Trans Biomed Eng*, vol. 62, n° 11, p. 2553-2567, nov. 2015, doi: 10.1109/TBME.2015.2481482.
- [99] I. Daly, R. Scherer, M. Billinger, et G. Müller-Putz, « FORCe: Fully Online and Automated Artifact Removal for Brain-Computer Interfacing », *IEEE Trans Neural Syst Rehabil Eng*, vol. 23, n° 5, p. 725-736, sept. 2015, doi: 10.1109/TNSRE.2014.2346621.
- [100] C. M. Sweeney-Reed, S. J. Nasuto, M. F. Vieira, et A. O. Andrade, « Empirical Mode Decomposition and its Extensions Applied to EEG Analysis: A Review », *Adv. Data Sci. Adapt. Data Anal.*, vol. 10, n° 02, p. 1840001, avr. 2018, doi: 10.1142/S2424922X18400016.
- [101] **A. M. De Freitas, G. Sanchez, F. Lecaigard, E. Maby, A. B. Soares, et J. Mattout, « EEG artifact correction strategies for online trial-by-trial analysis », *J. Neural Eng.*, vol. 17, n° 1, p. 016035, janv. 2020, doi: 10.1088/1741-2552/ab581d.**
- [102] F. Melinscak et D. R. Bach, « Computational optimization of associative learning experiments », *PLoS Comput Biol*, vol. 16, n° 1, p. e1007593, janv. 2020, doi: 10.1371/journal.pcbi.1007593.
- [103] M. Kwon, S. H. Lee, et W.-Y. Ahn, « Adaptive Design Optimization as a Promising Tool for Reliable and Efficient Computational Fingerprinting », *Biol Psychiatry Cogn Neurosci Neuroimaging*, vol. 8, n° 8, p. 798-804, août 2023, doi: 10.1016/j.bpsc.2022.12.003.
- [104] **A. Poublan-Couzardot et al., « Time-resolved dynamic computational modeling of human EEG recordings reveals gradients of generative mechanisms for the MMN response », *PLoS Comput Biol*, vol. 19, n° 12, p. e1010557, déc. 2023, doi: 10.1371/journal.pcbi.1010557.**
- [105] J. del R. Millán et J. M. Carmena, « Invasive or noninvasive: understanding brain-machine interface technology », *IEEE Eng Med Biol Mag*, vol. 29, n° 1, p. 16-22, 2010, doi: 10.1109/memb.2009.935475.
- [106] J. R. Wolpaw, N. Birbaumer, D. J. McFarland, G. Pfurtscheller, et T. M. Vaughan, « Brain-computer interfaces for communication and control », *Clinical Neurophysiology*, vol. 113, n° 6, Art. n° 6, juin 2002, doi: 10.1016/S1388-2457(02)00057-3.
- [107] S. N. Flesher et al., « A brain-computer interface that evokes tactile sensations improves robotic arm control », *Science*, vol. 372, n° 6544, p. 831-836, mai 2021, doi: 10.1126/science.abd0380.
- [108] F. R. Willett, D. T. Avansino, L. R. Hochberg, J. M. Henderson, et K. V. Shenoy, « High-performance brain-to-text communication via handwriting », *Nature*, vol. 593, n° 7858, p. 249-254, mai 2021, doi: 10.1038/s41586-021-03506-2.
- [109] A. Biasiucci et al., « Brain-actuated functional electrical stimulation elicits lasting arm motor recovery after stroke », *Nat Commun*, vol. 9, n° 1, p. 2421, juin 2018, doi: 10.1038/s41467-018-04673-z.

- [110] J.-M. Batail *et al.*, « EEG neurofeedback research: A fertile ground for psychiatry? », *L'Encéphale*, vol. 45, n° 3, p. 245-255, juin 2019, doi: 10.1016/j.encep.2019.02.001.
- [111] R. C. Conant et W. Ross Ashby, « Every good regulator of a system must be a model of that system † », *International Journal of Systems Science*, vol. 1, n° 2, Art. n° 2, oct. 1970, doi: 10.1080/00207727008920220.
- [112] J. Mattout, « Brain-Computer Interfaces: A Neuroscience Paradigm of Social Interaction? A Matter of Perspective », *Frontiers in Human Neuroscience*, vol. 6, 2012, doi: 10.3389/fnhum.2012.00114.
- [113] M. Perrin, E. Maby, O. Bertrand, et J. Mattout, « A virtuous BCI loop: adaptive decision making improves P300-spelling in two ways », *Proceeding of the 6th International Brain-Computer Interface Conference, Graz 2014*, 2014, doi: 10.3217/978-3-85125-378-8-79.
- [114] J. Mladenovic, « Computational Modeling of User States and Skills for Optimizing BCI Training Tasks », Theses, Université de Bordeaux, 2019. [En ligne]. Disponible sur: <https://theses.hal.science/tel-02891919>
- [115] R. Smith, K. J. Friston, et C. J. Whyte, « A step-by-step tutorial on active inference and its application to empirical data », *Journal of Mathematical Psychology*, vol. 107, p. 102632, avr. 2022, doi: 10.1016/j.jmp.2021.102632.
- [116] K. Friston, J. Kilner, et L. Harrison, « A free energy principle for the brain », *Journal of Physiology-Paris*, vol. 100, n° 1-3, Art. n° 1-3, juill. 2006, doi: 10.1016/j.jphysparis.2006.10.001.
- [117] R. Bogacz, « A tutorial on the free-energy framework for modelling perception and learning », *Journal of Mathematical Psychology*, vol. 76, p. 198-211, févr. 2017, doi: 10.1016/j.jmp.2015.11.003.
- [118] J. Mladenovic, J. Frey, M. Joffily, E. Maby, F. Lotte, et J. Mattout, « Active inference as a unifying, generic and adaptive framework for a P300-based BCI », *J. Neural Eng.*, vol. 17, n° 1, p. 016054, févr. 2020, doi: 10.1088/1741-2552/ab5d5c.
- [119] J. R. Wolpaw et D. J. McFarland, « Control of a two-dimensional movement signal by a noninvasive brain-computer interface in humans », *Proceedings of the National Academy of Sciences*, vol. 101, n° 51, Art. n° 51, déc. 2004, doi: 10.1073/pnas.0403504101.
- [120] G. Pfurtscheller et F. H. Lopes da Silva, « Event-related EEG/MEG synchronization and desynchronization: basic principles », *Clinical Neurophysiology*, vol. 110, n° 11, Art. n° 11, nov. 1999, doi: 10.1016/S1388-2457(99)00141-8.
- [121] S. Papadopoulos, J. Bonaiuto, et J. Mattout, « An Impending Paradigm Shift in Motor Imagery Based Brain-Computer Interfaces », *Front. Neurosci.*, vol. 15, p. 824759, janv. 2022, doi: 10.3389/fnins.2021.824759.
- [122] V. V. Moca, H. Bârzan, A. Nagy-Dăbâcan, et R. C. Mureşan, « Time-frequency super-resolution with superlets », *Nat Commun*, vol. 12, n° 1, p. 337, janv. 2021, doi: 10.1038/s41467-020-20539-9.
- [123] M. J. Szul *et al.*, « Diverse beta burst waveform motifs characterize movement-related cortical dynamics », *Prog Neurobiol*, vol. 228, p. 102490, sept. 2023, doi: 10.1016/j.pneurobio.2023.102490.
- [124] V. Jayaram et A. Barachant, « MOABB: trustworthy algorithm benchmarking for BCIs », *J. Neural Eng.*, vol. 15, n° 6, p. 066011, déc. 2018, doi: 10.1088/1741-2552/aadea0.
- [125] S. Papadopoulos, M. J. Szul, M. Congedo, J. J. Bonaiuto, et J. Mattout, « Beta bursts question the ruling power for brain-computer interfaces », *J Neural Eng*, vol. 21, n° 1, janv. 2024, doi: 10.1088/1741-2552/ad19ea.
- [126] J. Claassen *et al.*, « Detection of Brain Activation in Unresponsive Patients with Acute Brain Injury », *N Engl J Med*, vol. 380, n° 26, p. 2497-2505, juin 2019, doi: 10.1056/NEJMoa1812757.
- [127] D. Morlet *et al.*, « Intraclinical detection of voluntary attention in coma and post-coma patients using electrophysiology », *Clinical Neurophysiology*, vol. 145, p. 151-161, janv. 2023, doi: 10.1016/j.clinph.2022.09.019.
- [128] Maby, E *et al.*, « Evaluation in a locked-in patient of the OpenViBE P300-speller », *Proceeding of the 5th International Brain-Computer Interface Conference, Graz 2011*, 2011.
- [129] P. Séguin *et al.*, « The challenge of controlling an auditory BCI in the case of severe motor disability », *J Neuroeng Rehabil*, vol. 21, n° 1, p. 9, janv. 2024, doi: 10.1186/s12984-023-01289-3.
- [130] P. Seguin, E. Maby, F. Perrin, A. Farnè, et J. Mattout, « Is controlling a brain-computer interface just a matter of presence of mind? The limits of cognitive-motor dissociation », 30 septembre 2023, *arXiv: arXiv:2310.00266*. Consulté le: 22 juillet 2024. [En ligne]. Disponible sur: <http://arxiv.org/abs/2310.00266>
- [131] M. Fouillen, E. Maby, L. Le Carrer, V. Herbillon, et J. Mattout, « ERP-based BCI training for children with ADHD: motivations and trial design », *Proceeding of the 7th International Brain-Computer Interface Conference, Graz 2017*, 2017.

- [132] M. Fouillen, « Interface Cerveau-Machine de type P300 pour l'entraînement de l'attention chez les enfants avec TDA-H », Theses, Université de Lyon, 2019. [En ligne]. Disponible sur: <https://theses.hal.science/tel-03285423>
- [133] J. Luauté, D. Morlet, et J. Mattout, « BCI in patients with disorders of consciousness: Clinical perspectives », *Annals of Physical and Rehabilitation Medicine*, vol. 58, n° 1, Art. n° 1, févr. 2015, doi: 10.1016/j.rehab.2014.09.015.
- [134] Annicchiarico, Côme, Lotte, Fabien, et Mattout, Jérémie, « BAYESIAN MODEL OF INDIVIDUAL LEARNING TO CONTROL A MOTOR IMAGERY BCI », doi: 10.3217/978-3-99161-014-4-083.
- [135] A. Bleuzé, J. Mattout, et M. Congedo, « Tangent space alignment: Transfer learning for Brain-Computer Interface », *Front Hum Neurosci*, vol. 16, p. 1049985, 2022, doi: 10.3389/fnhum.2022.1049985.