BEYOND AI

Beyond the visible: retrieving information from magnetoencephalography in epilepsy thanks to AI techniques and invasive EEG.

1. EXCELLENCE

1.1. Pre-proposal's context, positioning and objective(s)

Objectives and research hypotheses

Epilepsy impacts between 0.5 and 1% of the world population, which makes it one of the major neurological diseases. Around 1/3 of the patients are resistant to pharmacological treatment, which represents more than 200000 people in France only. For these patients the best alternative is brain surgery, which consists in resecting the brain areas responsible for triggering the seizures, the 'epileptogenic zone' (EZ). The success of surgery crucially depends on the correct definition of the EZ. In a first step, non-invasive measures such as EEG and imaging are used. A promising non-invasive tool is magnetoencephalography (MEG), which consists in capturing the brain's magnetic field, with both excellent temporal resolution and very good spatial properties. In a second step, electrodes can be implanted directly within the brain – this is stereotaxic EEG (SEEG) (Bartolomei et al., 2017).

The main biomarker of epilepsy is the onset of seizures, which is clearly visible on SEEG, typically as a discharge involving high frequencies. The rest of the recording time is called 'interictal' (between seizures, which is the most frequent state in which the patient is), where interictal epileptiform discharges can be captured, with complex relationship with seizures [REF]. Thus, there is a need to refine biomarkers from the interictal period, as this is the state commonly recorded with scalp EEG and MEG. Thus, a maximum amount of information needs to be retrieved from the non-invasive phase in order to better plan SEEG (Malinowska et al., 2014).

This is where modern AI techniques can come into play. These techniques are able to find complex patterns that are hidden in the original signals, and thereby largely improve sensitivity compared to human observation. The goal of this project is to learn patterns from invasive (SEEG) data with exquisite sensitivity and signal to noise ratio, and then adapt and transfer these markers in order to boost non-invasive (MEG) analysis. Specifically, signal representations (patterns) will be learned from SEEG and transferred in MEG analysis in order to improve sensitivity and specificity. We will take advantage of a unique database including invasive and non-invasive data, with human labels arising from world-level experts in epilepsy, in order to catch markers of the epileptogenic zone that go beyond visual analysis.

The project is a collaboration between the clinical epilepsy department of Timone hospital (F Bartolomei, F Bonini), experts in SEEG and presurgical evaluation, the Institut de Neurociences des Systèmes (CG Bénar), experts in signal analysis in epilepsy, and the Laboratoire d'Informatique et Systèmes (M Ouladsine), experts in artificial intelligence. The markers resulting from this project will be valorised though a collaboration with the Mag4Health company, which designs next-generation MEG sensors, and is a partner of APHM and INS through the Amidex industrial chair.

Position of the project in relation to the state of the art

The most classical way of doing machine learning in epilepsy is to consider features extracted in the data using prior knowledge on patterns of interest. In this line, Du et al have used a set of features derived from intracerebral EEG (Du et al., 2026) with resulting area under the curve (AUC) of the ROC ranging from 0.767 to 0.798 for predicting the EZ. However, they needed to include ictal parameters in order to reach this performance. In our group, in a PhD thesis funded by Institut Laënnec, we have performed such analysis on non-invasive MEG data, using Independent Component Analysis (ICA) as a way to preprocess the data (Semeux-Bernier et al., 2025). We found very good results for separating artefacts and brain-related components, suggesting that this approach can be an important step in preprocessing data. However, we found only a moderate score with an F1 around 0.5 for detection of epileptic components, suggesting more advanced methods should be used – which is what we propose here.

In order to progress beyond classical feature-based approach, it has been proposed to use deep learning methods. In this framework, large neural nets are setup, which can learn directly from the data the best data representation and features, without requiring *a priori* features derived from human expertise. Thus, Nejedly et al have used a temporal autoencoder for dimensionality reduction and a small number of expert-provided gold-standard labels

(Nejedly et al., 2023). They found an AUC of ROC up to 0.879, and an AUC under precision-recall curve of 0.74. It is important to note that their database was composed of small data segments that were preselected, which is not real-life condition where data is continuous and with high dimensionality. The transfer from several segments (typically balanced) to continuous time (largely unbalanced) is expected to lower drastically performance (Mouches et al., 2023). In MEG, Mouches et al have proposed to use a feature-based artificial neural network (ANN) and a convolutional neural network (CNN), trained on a database of 59 patients (Mouches et al., 2023). The performance are better that state-of-the art model, but remain to be improved (F1 = 0.46). A difficulty of this model is that it operates on the raw multi-channel data. This means that a difficult spatial processing needs to be learnt, whereas location and spatial properties of epileptic sources can vary from a patient to another. We propose an alternative, ICA, which adapts (learns) spatial patterns within each patient and reduces the problem to 1D (Semeux-Bernier et al, submitted).

What we plan here is to focus on the interictal state, as seizures are rare and can be difficult to record with non-invasive tools, because of the typical small recording time of non-invasive measure, but also because movement-related artefacts). We aim at improving feature-based learning by using methods that will reveal features that are not visible Moreover, we plan to use measures of performance that are adapted to the imbalance EW/non EZ and that thus reflect the clinical needs, namely precision (or positive predictive value PPV) and recall (sensitivity). Lastly, we intend to use intracerebral data in a first step – which has high signal to noise ratio and high confidence labelling (ground truth) in order to transfer the model to more difficult non-invasive data (transfer learning).

- ### Methodology to reach the scientific objectives of the project, detailed description of the intended method(s)

This PhD thesis proposes to leverage multimodal artificial intelligence for non-invasive epilepsy diagnosis and prediction of surgical outcome: SEEG→MEG learning transfer relying on, representational learning, modality fusion, and explainable models, as well as exploring the possibility of transfer learning from SEEG to MEG.

1) Databases: We will use two sets of existing retrospective data, collected during presurgical evaluation of epilepsy at the Epilepsy and Cerebral Rythmology department of Timone hospital in Marseille. The first is intracerebral data (SEEG, around 250 patients), collected during phase 2 of presurgical evaluation (invasive phase). The second is Magnetoencephalography (around 300 patients) acquired thanks to a day-hospital in collaboration between APHM and the MEG platform in Marseille, hosted by the hospital. SEEG data typically consists of 150-200 contacts recorded within the brain. The database contains 1 to 3 runs of 30 minutes to one hour per patient, in the interictal state (i.e. between seizures). The labels will consist in channels marked as epileptogenic by clinicians. MEG data consists in 248 channels, recorded over 3 to 5 runs of 10 minutes each. The labels are twofold: epileptic events marked across all channels (time stamps). In a series of 50 patients, we have both MEG and SEEG recorded simultaneously. This will permit to tune parameters on MEG analysis with a ground truth recorded within the brain. For all patients, we will have MRI data in order to build biophysical models.

2) Modelling: Several approaches will be compared. Firstly, a reproducible pipeline will handle signal preprocessing, artefact mitigation, anatomical alignment (ROIs, shared atlas), and traceability of expert labels. In addition, we will exploit multiple signal dynamics representations (statistics at different orders) of SEEG signals—to extract microscopic information useful both for non-invasive epilepsy diagnosis and for predicting surgical success. Secondly, time–frequency representations, which are usual in EEG analyses for epilepsy, will be extracted and used for self-supervised learning (e.g., contrastive learning, masked modeling). Third, deep convolutional networks that have been already benchmarked on EEG data will be used to form high-level representations of the signals (Schirrmeister et al 2027; Li et al 2025). All these representations will then be tested using supervised learning to predict the SEEG-derived labels (presence of interictal discharge, clinician labelling of contacts). Data fusion will be explored to combine different types of biomarkers, in a way to improve the prediction performance, also getting inspiration from previous work on MRI data for neurological disorders (Bomatter et al 2024).

3) SEEG→MEG domain transfer: Domain adaptation strategies will be developed, including fine-tuning, knowledge distillation, and multi-task learning. The goal is to transfer biomarkers learned from SEEG to interictal MEG while preserving their discriminative power.

The epileptogenic zone (EZ) will be modelled as a brain network using dynamic graph neural networks. MEG/EEG/imaging fusion will be implemented through attention mechanisms while explicitly accounting for missing modalities. The model will output region-wise probabilistic maps.

4) Prognostic models and explainability

A model predicting surgical outcome (Engel/ILAE) will be trained from multimodal representations and clinical data. Explainability techniques (ROI-level and frequency-level attribution, variable importance) and uncertainty estimation will be integrated. We will cross-validate the algorithm on a series of test data acquired in a clinical setting and not used for training. We will extend and develop collaborations with two high-level clinical centres recording MEG data, in Lyon (HCL, J Jung) and in Erlangen (S. Rampp).

• Originality and innovative aspects of the planned research

The originality of this project is to use both intracerebral (ground truth) data and non-invasive in order, in the end, to produce non-invasive tools.

The datasets that we will use are unique, in size and in the clinical expertise that has been put in the labelling. The epilepsy centre and research team in Marseille are at the highest level worldwide for epilepsy evaluation an signal processing. Very few centres worldwide have simultaneous recordings of MEG and SEEG, which is a unique ground truth.

On the AI aspect, the project introduces learning explicitly anchored to invasive ground truth (SEEG) and transferred to non-invasive modalities. It combines graph-structured multimodal fusion, self-supervised learning, and explainable models. Beyond descriptive approaches, it aims at a complete decision-support tool. The aim is to compare different representations on the SEEG/MEG time series, in particular their relevance for the clinical prediction considered here.

• Added-value in terms of scientific contribution

In methodological terms, the project will address a difficult issue of the high dimensionality of the data, with potentially very few important segments that are overflown by background activity, and very high inter-patient variability. The specific methodological contributions will be

- A SEEG→MEG transfer framework for neurophysiological signals.
- Robust multimodal fusion under missing data and network structure constraints.
- Calibrated models integrating explainability and uncertainty.

In clinical terms, it will give very useful tools in order to screen large amounts of data and present to the clinicians patterns of interest. The specific applied contributions will be

- New interictal biomarkers exploitable in MEG.
- A pre-operative prognostic model for surgical success.

Knowledge production:

The project will improve our understanding of the relationships between interictal signatures, the epileptic network, and surgical outcomes, and will pave the way for clinically deployable multimodal AI tools.

Potential for valorization:

The DynaMaP team is considering to create a start-up in order to turn the existing open access software AnyWave (> 3600 downloads, used all over the world) into a medical device with certification. The algorithm developed in this project could be used as a starting building block for this future commercial software. We are currently in discussion with the Société d’Accéleration Technologique (Satt SudEst) for all these valorization aspects.

1.2. Interdisciplinary and intersectoral dimension of the project

Complementarity of partners

DynaMaP team (INS): The project will be mainly hosted by the DynaMaP team (lead C. Bénar) of the Institut de recherche des Systèmes. The Dynamap team is located within the clinical department of Timone hospital (lead by F. Bartolomei) and has a long-lasting history of collaboration between clinicians and methodologists. One member of the clinical team (Francesca Bonini), our MEG specialist, has just obtained a 'contrat d'interface' from Inserm and will be able to help the candidate for the clinical interpretation of results. The candidate will be able to attend clinical meetings in order to understand the challenges of presurgical evaluation as well as the clinical applications of his/her work. There is currently a project on the new generation of sensors (ERC OptiMEG, PI C Bénar) , which will directly benefit from the knowledge acquired on classical MEG data, and which team will provide an excellent environment for scientific interactions and knowledge sharing.

LIS team: Mustapha Ouladsine received his PhD in Control Engineering from the University of Henri Poincaré (Nancy, France) in 1993. He is currently a Full Professor at Aix-Marseille University (AMU). He serves as Vice-President of Aix-Marseille University in charge of Digital Affairs for Research and as Scientific and Technical Director of the Laënnec Institute for Digital Sciences and Artificial Intelligence in Healthcare. He founded and directed the Laboratory of Informatics and Systems (LIS – CNRS UMR 7020) from 2018 to 2022. LIS conducts both fundamental and applied research in computer science, control systems, signal processing, and image processing. Since 2016, his research has increasingly focused on artificial intelligence applied to healthcare, particularly competitive learning using neural networks for medical diagnosis.

BraiNets team (INT): M Gilson is a professor in computational neuroscience, with expertise in neurophysiological signals and their processing for clinical applications (https://matthieugilson.eu/). He cosupervises 4 PhD students on different topic including biomarkers for bipolar disorder from MRI data and dynamic model inference from MEG data for cognition. He will provide support in the computational part, as well as the implementation of analysis pipelines on the high-performance computing resources (e.g. https://mesocentre.univ-amu.fr/).

Interdisciplinary methodological approach

The Dynamap team has a long lasting expertise in signal processing in relation with clinicians. This can be used in order to preprocess the data (in particular dimensionality reduction and time-frequency analysis) in order to reduce the size of the AI model, and thus require less data. The team has also expertise in data management and pipeline analysis (acquired during the RHU Epinov project, for which it was responsible for setting up the data transfer and database) that can benefit the project. The LIS and INT teams have expertise in artificial intelligence applied to health and brain data respectively.

Hosting arrangements and describe and time sharing

The candidate will be primarily hosted in the DynaMaP team at the Timone hospital, with one day a week in the partner laboratory (LIS). The candidate will attend team meetings of the two teams. Meeting will be organised every two weeks with the supervising team (CG Bénar, M Ouladsine, M Gilson, F Bonini).

Intersectoral dimension of the proposal

One partner of the project will be the clinical department of Timone hospital. The candidate will benefit from daily interaction with clinicians, which will enable her/him to understand well the challenges of applied research in a medical environment: knowledge on neurology, on the needs of clinicians, on data analysis by experts.

Another partner is the Mag4Health company, which designs magnetoencephalography sensors of the next generation (Optically pumped magnetometers, OPMs). The algorithms developed here will benefit directly analysis of the future data, as OPM signals are of the same nature as classical MEG as available here.

2. IMPACT

2.1. Expected impact of the project on the candidate's career

The skills acquired in the project will be numerous and multidisciplinary: signal processing, machine learning with cutting-edge techniques, epilepsy diagnostic, brain mapping, imaging, electrophysiology. In particular, the candidate will master a brain mapping method, magnetoencephalography, with both excellent temporal resolution and high spatial resolution - which is expected to experience a boom in the near future thanks to the development of next-generation sensors that will democratize the technique. These skills will benefit the candidate for future positions either in the academics (postdoctoral study in methodology or clinical research) or the industry (data analyst, clinical software companies…).

2.2. Expected impact for the thematic axis

The main thematic axis addressed here will be « Artificial Intelligence and Applications » . The project addresses the difficult issue of finding biomarkers in the very large-dimensional data that are acquired for presurgical evaluation of epilepsy, thanks to modern artificial intelligence tools.

In terms of research on AI models, the project will allow to improve models that can handle high dimensional and multimodal data, in a very concrete application and benefiting from interaction between clinicians who are highly trained and recognised experts on the one hand and methodologists on the other hand. Theses models will be of interest for the all community of research on clinical data analysis with electrophysiology.

In terms of impact of AI-derived tools, the findings of this project will contribute to improve presurgical evaluation of epilepsy based on non-invasive measures. This means less risks for the patients as well a drastic reduction in costs – as SEEG is a very length and heavy procedure requiring surgery and an immobilization of 10 days in hospital. In more fundamental terms, the understanding of the relationships between interictal activity (between seizures) and ictal (seizures). This is still an open issue, which has direct consequences for presurgical evaluation, in order to complement ictal biomarkers by interictal ones.

2.3. Dissemination, exploitation and communication activities planned

The use of artificial intelligence, and in particular transfer learning, is a key scientific driver of this project. Knowledge transfer between complementary modalities such as SEEG and MEG will help overcome limitations related to data scarcity and signal heterogeneity. By leveraging models pre-trained on rich SEEG datasets, this approach is expected to significantly improve MEG analysis while reducing the need for modality-specific annotated data.

This strategy will enable robust and generalizable results with strong potential for high-impact scientific publications. We expect to be able to publish the results in renown journals within the field of clinical brain mapping: Brain, Annals of Neurology, Epilepsia. If the transfer between SEEG and MEG is efficient, we are confident we can go to more generalists journals such as Nature Communications or Scientific reports. We have at INS a person dedicated to public outreach (fête de la science, semaine du cerveau, dissemination in schools). The candidate will be encourage to present to these events.

Transfer learning offers clear added value for industrial and clinical translation, as adaptable methods across acquisition systems are highly attractive for stakeholders. Specifically, there will be several complementary strategies. Deposit of inventions through the SATT will support structured valorization and efficient technology transfer toward innovative clinical applications. Moreover, Several companies could be interested by the development: Natus-Micromed, that manufactures most of the epilepsy investigation systems in Europe, or Mag4Health, the company that designs the new sensors and with which we have an industrial chair for collaboration.

3. IMPLEMENTATION

3.1. Work plan

The project will be divided into two work packages. One on SEEG, the other on MEG data. The division of tasks will be the following:

WP 1: Development and application of models on intracerebral EEG (SEEG)

Task 1.0 Bibliography

Task 1.1 Preprocessing of SEEG database. Creation of pipelines for feeding data from existing databases into AI models. Deliverable: a pipeline of analysis in Python. Milestone M1.1 : Preliminary test of a simple processing on a series of 10 patients.

Task 1.2: development of AI models. Milestone M1.2: application of the model on a reduced database with full marking by experts.

Taks 1.3: Application of the model to the whole series of patient. Assessment of performance using cross validation. Deliverable D1.1: report on performance analysis.

Tasks 1.4. Writing of the first article. Deliverable D1.2: submitted article

Between WP 1 and WP 2. A first secondment (S1) will be performed in the group of Karim Jerbi in Montreal, a recognized expert in articial intelligence for electrophysiological signals, notably MEG. Karim Jerbi holds the Canada Research Chair in Computational Neuroscience and Cognitive Neuroimaging and is director of UNIQUE, Quebec's neuro-AI research center.

WP 2: Transfer of model to MEG

Task 2.1 Preprocessing of MEG database. Creation of pipelines for feeding data from existing databases into AI models. Deliverable: a pipeline of analysis in Python. Milestone M2.1: Preliminary test of a simple processing on a series of 10 patients.

Task 2.2: development of two AI models. The first will be using the representations learned on SEEG. The second will be directly learning from MEG. Milestone M2.2: application of the model on a reduced database with full marking by experts.

Task 2.3: Application of the models to the whole series of patient. Assessment of performance using cross validation, comparison of the models. Deliverable D2.1: metrics of performance of the models in a clinical MEG application

Tasks 2.4. Writing of the second article. Deliverable D2.2: submitted article

After WP2, there will a second stay in a foreign lab (secondment 2, S2), namely the clinical unit of Stefan Rampp in Erlangen. Stefan Rampp is a world recognised expert in clinical MEG. He is the chair of the Meg center in Erlangen, and a member of the Magnetoencephalography task force from of the International league against epilepsy (ILAE). He is the author of an authoritative study on the clinical use of MEG in a series of 1000 patients (which is extremely large cohort for the field).

Please see Gantt Chart below.

BEYOND-AI	Y1				Y2				Y3			
	1-3	4-6	7-9	10-12	1-3	4-6	7-9	10-12	1-3	4-6	7-9	10-12
WP1												
T1.0	🟨											
T1.1		M1.1	🟨									
T1.2		🟨	M1.2	🟨								
T1.3				D1.1								
T1.4					D1.2							
S1: Montreal						🟩						
WP1												
T2.1							M2.1					
T2.2							🟧	M2.2				
T2.3								🟧	D2.1			
T2.4									🟧	D2.2		
S2: Erlangen										🟩		
Writing of thesis											🟦	🟦

3.2. Ethical issues

The data used in this project will be retrospective clinical data, that was gathered during presurgical evaluation of patients in the epileptology and cerebral rythmology department of the Timone hospital. The standard procedure for using this data for research is a declaration to the dedicated portal (“Portail d’Accès aux Données de Santé”, PADS). We already obtained the authorization for the MEG data (APHM: “PADS23-231 Apprentissage automatique pour améliorer le diagnostic non-invasif de l’épilepsie”). We will ask for the same authorization for the SEEG data, and no difficulty is expected.

The results of the artificial intelligence algorithm will be help to the diagnosis. It will not be used directly to plan surgery, but instead used – as any other tool – within a complete examination of all available data. IN other words, it will be a help but will not replace the clinician’s expertise.

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