

IN PARTNERSHIP WITH: **CNRS**

Université de Lorraine

Activity Report 2015

Project-Team NEUROSYS

Analysis and modeling of neural systems by a system neuroscience approach

IN COLLABORATION WITH: Laboratoire lorrain de recherche en informatique et ses applications (LORIA)

RESEARCH CENTER **Nancy - Grand Est**

THEME **Computational Neuroscience and Medecine**

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1. Members

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2. Overall Objectives

2.1. General Objectives

The team aims at understanding the dynamics of neural systems on multiple scales and develops methods to invent monitoring devices. The approach is inspired by systems neuroscience, which relates microscopic modifications in neural systems to macroscopic changes in behavior. The team employs this systems neuroscience approach and develops models and data analysis tools in order to bridge the gap between microscopic and mesoscopic, and mesoscopic and macroscopic/behavior activity. These bridges are necessary to better understand neural systems and, in turn, control the neural systems. They also may allow to develop data monitors utilising the derived principles. As a long-term goal, the team shall develop such devices in medicine with application in general anaesthesia.

3. Research Program

3.1. Main Objectives

The main challenge in computational neuroscience is the high complexity of neural systems. The brain is a complex system and exhibits a hierarchy of interacting subunits. On a specific hierarchical level, such subunits evolve on a certain temporal and spatial scale. The interactions of small units on a low hierarchical level build up larger units on a higher hierarchical level evolving on a slower time scale and larger spatial scale. By virtue of the different dynamics on each hierarchical level, until today the corresponding mathematical models and data analysis techniques on each level are still distinct. Only few analysis and modeling frameworks are known which link successfully at least two hierarchical levels.

Once having extracted models for different description levels, typically they are applied to obtain simulated activity which is supposed to reconstruct features in experimental data. Although this approach appears straight-forward, it implies various difficulties. Usually the models involve a large set of unknown parameters which determine the dynamical properties of the models. To optimally reconstruct experimental features, it is necessary to formulate an inverse problem to extract optimally such model parameters from the experimental data. Typically this is a rather difficult problem due to the low signal-to-noise ratio in experimental brain signals. Moreover, the identification of signal features to be reconstructed by the model is not obvious in most applications. Consequently an extended analysis of the experimental data is necessary to identify the interesting data features. It is important to combine such a data analysis step with the parameter extraction procedure to achieve optimal results. Such a procedure depends on the properties of the experimental data and hence has to be developed for each application separately. Machine learning approaches that attempt to mimic the brain and its cognitive processes had a lot of success in classification problems in a last decade. These hierarchical and iterative approaches use non-linear functions, which imitate neural cell responses, to communicate messages between neighboring layers. In our team, we work towards developing polysomnography-specific classifiers that might help in linking the features of particular interest for building systems for sleep signal classification with sleep mechanisms, with the accent on memory consolidation during the Rapid Eye Movement (REM) sleep phase.

3.2. Challenges

Eventually the implementation of the models and analysis techniques achieved promises to be able to construct novel data monitor. This construction involves additional challenges and stipulates the contact to realistic environments. By virtue of the specific applications of the research, the close contact to hospitals and medical enterprises shall be established in a longer term in order to (i) gain deeper insight into the specific application of the devices and (ii) build specific devices in accordance to the actual need. Collaborations with local and national hospitals and the pharmaceutical industry already exist.

3.3. Research Directions

• From the microscopic to the mesoscopic scale:

One research direction focuses on the *relation of single neuron activity* on the microscopic scale *to the activity of neuronal populations*. To this end, the team investigates the stochastic dynamics of single neurons subject to external random inputs and involving random microscopic properties, such as random synaptic strengths and probability distributions of spatial locations of membrane ion channels. Such an approach yields a stochastic model of single neurons and allows the derivation of a stochastic neural population model.

This bridge between the microscopic and mesoscopic scale may be performed via two pathways. The analytical and numerical treatment of the microscopic model may be called a *bottom-up approach*, since it leads to a population activity model based on microscopic activity. This approach allows to compare theoretical neural population activity to experimentally obtained population activity. The *top-down approach* aims at extracting signal features from experimental data gained from neural populations which give insight into the dynamics of neural populations and the underlying microscopic activity. The work on both approaches represents a well-balanced investigation of the neural system based on the systems properties.

• From the mesoscopic to the macroscopic scale:

The other research direction aims to link neural population dynamics to macroscopic activity and behaviour or, more generally, to phenomenological features. This link is more indirect but a very powerful approach to understand the brain, e.g., in the context of medical applications. Since real neural systems, such as in mammals, exhibit an interconnected network of neural populations, the team studies analytically and numerically the network dynamics of neural populations to gain deeper insight into possible phenomena, such as traveling waves or enhancement and diminution of certain neural rhythms. Electroencephalography (EEG) is a wonderful brain imaging technique to study the overall brain activity in real time non-invasively. However it is necessary to develop robust techniques based on stable features by investigating the time and frequency domains of brain signals. Two types of information are typically used in EEG signals: (i) transient events such as evoked potentials, spindles and K-complexes and (ii) the power in specific frequency bands.

4. Application Domains

4.1. General Remarks

The research directions of the team are motivated by general anaesthesia (GA) that has attracted our attention in the last years. The following sections explain in some detail the motivation of our work on the four major phenomena of GA: loss of consciousness, immobility, amnesia and analgesia.

During general anaesthesia, the electroencephalogram (EEG) on the scalp changes characteristically: increasing the anaesthetic drug concentration the amplitudes of oscillations in the alpha band ($\sim 8 - 12$ Hz) and in the delta band (2 − 8Hz) increase amplitudes in frontal electrodes at low drug concentrations whereas the spectral power decreases in the gamma band ($\sim 20 - 60$ Hz). This characteristic change in the power is the basis of today's EEG-monitors that assist the anaesthetist in the control of the anaesthesia depths of patients during surgery. However, the conventional monitors exhibit a large variability between the patients detected anaesthetic depth and their real depth. Moreover, a certain number of patients re-gain consciousness during surgery (about $1 - 2$ out of 1000) and a large percentage of patients suffer from diverse after-effects, such as nausea or long-lasting cognitive impairments such as partial amnesia (from days to weeks). Since surgery under general anaesthesia is part of a hospital's everyday practice, a large number of patients suffer from these events everyday. One reason for the lacking control of such disadvantageous effects is the dramatic lack of knowledge on what is going on in the brain during general anaesthesia and a weak EEG-online monitoring system during anaesthesia. Consequently, to improve the situation of patients during and after surgery and to develop improved anaesthetic procedures or even drugs, research is necessary to learn more about the neural processes in the brain and develop new monitoring machines.

4.2. Level of Consciousness

The EEG originates from coherent neural activity of populations in the cortex. Hence to understand better the characteristic power changes in EEG during anaesthesia, it is necessary to study neural population dynamics subject to the concentration of anaesthetic drugs and their action on receptors on the single neuron level. We study mathematical models which will be constrained by the signal features extracted from experimental data, such as EEG (data provided by Jamie Sleigh, University of Auckland and Christoph Destrieux, University of Tours), Local Field Potentials (data provided by Flavio Frohlich, University of North Carolina - Chapel Hill) and behavior. The combination of model and analysis of experimental data provides the optimal framework to reveal new knowledge on the neural origin of behavioral features, such as the loss of consciousness or the uncontrolled gain of consciousness during surgery. For instance, modelling studies show that the characteristic changes of spectral power (second-order statistics) are not sufficient to deduce all underlying neural mechanisms. Consequently, additional higher-order statistical measures may provide additional insight into underlying neural mechanisms and may provide a novel marker for the loss of consciousness.

Moreover, the constant supervision of anaesthetized patients in intensive care is a demanding task for the medical staff. It is almost not possible to take care of a patient constantly and hence todays' medicine demands monitoring devices that control automatically the level of anaesthetic drugs based on the patients' neural activity (e.g., EEG). Brain-Computer-Interfaces (BCI) have already demonstrated their potential for the detection of consciousness in non-responsive patients. We will apply the data analysis techniques known in BCI to extract new markers for the depth of anaesthesia. More specifically, for deeper anaesthesia, auditoryevoked and Event-Related Desynchronization/Event-Related Synchronization (ERD/ERS) BCI could be used to better identify the state of consciousness in patients under anaesthesia. In this context, we have established a first contact to the University of Wuerzburg. Another research direction will link intracranial EEG and scalp EEG by characterising micro-awake episodes during sleep.

4.3. Immobility

A research direction will be to leverage the relationship between the motor activity and anesthesia. Indeed, even if no movement is visually perceptible, a study by electroencephalographic recordings of brain activity in motor areas, quantifying the characteristics of amplitude and phase synchronization observed in the alpha and beta frequency bands, may reveal an intention movement. This feature is important because it demonstrates that the patient is aware. Thus, we will develop an experimental protocol in collaboration with an anesthesiologist of the regional hospital on stimulating the median nerve at forearm level to track the evolution of the shape of the beta rebound in the motor cortex for various doses of the anesthetic agent.

4.4. Amnesia

Patients sometimes develop post-traumatic disorders associated with the surgery they underwent because they either woke up during the surgery or because the amnesiant effect of the general anaesthesia was only partial, declarative memory being maintained in some unexplained cases. It is still unknown how memory can be maintained under general anaesthesia and it needs to be investigated to improve the recovery from anaesthesia and to avoid as much as possible post-traumatic disorders. To learn more about memory under anaesthesia, we will focus our theoretical studies on the oscillation regimes observed in the hippocampus, mainly in the theta and gamma ranges, respectively $(0.5 - 4)$ Hz) and $(20 - 80)$ Hz), which are correlated with memory formation and retrieval.

4.5. Analgesia

One of the most important aspect in general anaesthesia is the loss of pain. During surgery, it is very difficult to find out whether the anaesthetized patient feels pain and hence will develop cognitive impairment after surgery. Today, the anesthesiologist knows and detects physiological signs of pain, such as sweat, colour of skin or spontaneous involuntary movements. However, more objective criteria based on EEG may assist the pain detection and hence improves the patients' situation. To this end, we analyze large sets of patient EEGdata observed during surgery and aim to extract EEG signal features of pain.

5. Highlights of the Year

5.1. Highlights of the Year

- Laurent Bougrain co-organized an international Brain-Computer Interfaces competition on *Error Potential Detection with Cross-subject Generalization* with Maureen Clerc, Fabien Lotte, Emmanuel Maby, Jérémie Mattout and Théodore Papadopoulo. 311 participants of 260 different teams in the world participated to the competition. Gao Shangkai and Bin He were in the advisory board. IEEE EMBS, Inria, and Institute for Engineering in Medicine at University of Minnesota were sponsors of this event. The prizes have been presented to winners during the IEEE EMBS Neural Engineering conference, April 22-24, 2015. The winner has been invited to publish a manuscript at IEEE Transactions on Biomedical Engineering. <https://www.kaggle.com/c/inria-bci-challenge>
- We stepped up our collaboration with the department of anesthesia of the university hospital in Nancy (Dr. Denis Schmartz and Pr. Claude Meistelmann) leading to a PhD thesis co-funded by the school of medicine of the university of Lorraine, Inria, the Lorraine laboratory for research in computer science (LORIA), the Lorraine Region and the urban community of Nancy. The PhD will start in January 2016 on the study of the dynamics of cerebral motor patterns during general anesthesia with Sébastien Rimbert under the supervision of Axel Hutt and Laurent Bougrain.

6. New Software and Platforms

6.1. AnaesthesiaSimulator

KEYWORDS: General anaesthesia - Spiking neural networks - Health FUNCTIONAL DESCRIPTION

AnaesthesiaSimulator simulates the activity of networks of spiking neurons subject to specific receptor dynamics. The tool is a platform to test effects of anaesthetics on neural activity and is still in its first stage of development. The neural activity can be visualized in a 2D and 3D-plot evolving in time. It is written in Python, open-source and involves heavily the simulation package BRIAN ¹.

- Participants: Axel Hutt and Laure Buhry
- Partner: University of Auckland
- Contact: Axel Hutt
- • URL: <https://gforge.inria.fr/projects/anasim/>

6.2. NeuralFieldSimulator

NeuralFieldSimulator KEYWORDS: Neurosciences - Simulation - Health FUNCTIONAL DESCRIPTION

The NeuralFieldSimulator computes numerically activity in two-dimensional neural fields by solving integraldifferential equations involving transmission delays and visualizes the spatio-temporal activity. The tool includes a GUI that allows the user to choose field parameters. It is written in Python, open-source and is aimed to be promoted to become a major graphical visualization tool in the domain of neural field theory. We aim to establish this simulation software as the first open-source standard simulator for the neural field research community.

- Participants: Axel Hutt and Eric Nichols
- Partner: Kevin Green, University of Ontario, Canada
- Contact: Axel Hutt
- • URL: <https://gforge.inria.fr/projects/nfsimulator/>

6.3. OpenVIBE

KEYWORDS: Neurosciences - Interaction - Virtual reality - Health - Real time - Neurofeedback - Brain-Computer Interface - EEG - 3D interaction

FUNCTIONAL DESCRIPTION

OpenViBE is a software platform for real-time neurosciences (that is, for real-time processing of brain signals). It can be used to acquire, filter, process, classify and visualize brain signals in real time from various signal sources. OpenViBE is free and open source software. It works on Windows and Linux operating systems. This year, Neurosys was in charge of the linux release. the main development efforts concern machine learning: Multi-layer perceptrons have been added as classification methods and evaluation plugins allow to get standalone visualization for Kappa coefficient, Receiving Operative Curve (ROC) curve and general statistics.

- Participants: Yann Renard, Anatole Lécuyer, Fabien Lotte, Bruno Renier, Vincent Delannoy, Laurent Bonnet, Baptiste Payan, Jozef Legény, Jussi Tapio Lindgren, Alison Cellard, Loïc Mahé, Guillaume Serrière, Marsel Mano, Maureen Clerc Gallagher, Théodore Papadopoulo, Laurent Bougrain, Jérémy Frey and Nathanaël Foy
- Partners: INSERM CEA-List GIPSA-Lab
- Contact: Anatole Lécuyer
- • URL: <http://openvibe.inria.fr>

6.4. BRIAN Contributions

KEYWORDS: Spiking neurons models - Neurosciences - BRIAN

¹ <http://briansimulator.org/>

FUNCTIONAL DESCRIPTION

6.4.1. Spiking Neuron Templates

BRIAN-compatible libraries has been developed by the team for various ionic currents to be assembled together to create template neurons. The purpose of these is to speed up simulation set-up time and reduce code duplication across simulation scripts. Template neurons are defined by the ionic currents that flow through their membrane. Implemented templates include:

- Hodgkin-Huxley pyramidal neuron (leak, sodium and potassium)
- Hodgkin-Huxley pyramidal neuron with calcium-activated non-specific (CAN) receptors (leak, sodium, potassium, m-current, calcium, CAN)
- Hodgkin-Huxley fast-spiking inhibitory hippocampal (leak, sodium, potassium, m-current)

Implemented ionic current libraries include:

- Traub and Miles Hodgkin-Huxley (I_{Leak} , I_K , I_{Na}) implementation;
- M-Current (I_M) implementation;
- Calcium current (I_L) implementation;
- Calcium pump mechanisms $\left(\frac{dCa}{dt}\right)$ implementation;
- Calcium-activated non-selective current (I_{CAN}) implementation;
- Wang and Buszáki inhibitory Hodgkin-Huxley (I_{Leak}, I_K, I_{Na}) implementation;

The current library is easily extensible by third-party users due to its hierarchical design. The template neurons and their currents are defined as YAML ² files, which are conveniently parsed by a Python library which acts as an interface to the BRIAN simulator API's.

6.4.2. BRIAN Simulation Parameters

A python library which acts as a wrapper for BRIAN simulations, allowing the user to define simulation parameters in external YAML files, which are then parsed and forwarded to the BRIAN simulator. In addition, simulation parameters can be overridden via the command-line when invoking the python script containing the simulation.

- Participants: Francesco Giovannini
- Contact: Francesco Giovannini
- • URL: <http://www.briansimulator.org>

7. New Results

7.1. From the Microscopic to the Mesoscopic Scale

Participants: Laure Buhry, Axel Hutt, Francesco Giovannini, Jean-Baptiste Schneider In collaboration with LieJune Shiau (University of Houston)

2 <http://www.yaml.org/>

7.1.1. Memory and Anaesthesia

7.1.1.1. Hippocampal Memory Networks

To improve our understanding of the effects of anaesthesia on the neural correlates of memory, we focussed on how anaesthetics disrupt the interaction between the hippocampus and the cerebral cortex. As a first step towards this objective Francesco Giovannini modelled a hippocampal pyramidal neuron using the Hodgkin-Huxley model capable of exhibiting long-lasting persistent firing activity when subject to a strong transient stimulus [\[16\]](#page-21-0). This behaviour is underlay by an intrinsic membrane current activated by the increase of intracellular calcium ions, following the discharge of an action potential by the neuron, in accord with that displayed in neural recordings of hippocampal slice preparations. Connecting these persistent firing neurons in a network comprising strong local excitation yields a wide range of behaviours depending on the interaction between CAN and synaptic currents. Indeed, the network model is capable of displaying rhythmic behaviour in the form of short synchronised bursts with intra-burst frequencies of $20 - 40 Hz$ and inter-burst frequencies of $3 Hz$. Furthermore, coupling CAN-equipped pyramidal neurons with a population of fast-spiking inhibitory interneurons yields emerging synchronous activity whose frequency is modulated by the strength of this coupling. These results hint towards a possible mechanism for the generation of memory-related oscillatory activity in the hippocampus.

7.1.1.2. Anaesthetic Effects on Hippocampal Oscillations

We investigated the effects of propofol-mediated tonic inhibition on the synchronous activity elicited in a network of hippocampal inhibitory interneurons. This work was conducted in collaboration with Jean-Baptiste Schneider, as part of hist 2-month internship. We studied the effect of propofol-induced tonic inhibition on the oscillations elicited in a network of hippocampal Hodgkin-Huxley gamma-aminobutyric acid $(GABA)$ interneurons by studying the action of propofol on extrasynaptic GABAergic receptors. Our results [\[15\]](#page-21-1) show that increasing doses of propofol reduce the overall network activity and slow down its oscillations until a critical value at which the synchronisation increases abruptly at values of twice the synchronisation displayed in the absence of tonic inhibition, and the mean firing rate increases. This emergence of synchronous activity mediated by anaesthetic perfusion point towards a possible mechanism for the emergence of paradoxical excitation under general anaesthesia.

In this context, Laure Buhry works with LieJune Shiau (University of Houston) on a better understanding of the models used by the community of computational neuroscientists. The goal is to show in which extent models are comparable or interchangeable. We focus on the comparison of oscillatory mechanisms of neuronal populations in different spiking models, especially in the Hodgkin-Huxley and the adaptive exponential integrate-and-fire model (AdEx). Especially, we have shown that a same number of synaptic connection per neuron is necessary to elicit synchronization in inhibitory neural networks of adaptive exponential integrate and fire neurons as in networks of Hodgkin-Huxley neurons. We have also conducted an extensive study regarding the effects of the different parameters of the AdEx model on the synchronization mechanisms in inhibitory neural networks, particularly in the context of gamma oscillations. A manuscript will be submitted soon to the Journal of Computational Neuroscience.

7.1.1.3. Noise Effects on Neural Rhythms

We have continued working on the effect of additive noise on neural oscillations and have shown that additive noise modulates the frequency of self-sustained neural rhythms [\[3\]](#page-19-4).

7.2. From the Mesoscopic to the Macroscopic Scale

Participants: Laurent Bougrain, Axel Hutt, Pedro Garcia-Rodriguez, Eric Nichols, Guillaume Serrière, Tamara Tosic, Mariia Fedotenkova, Meysam Hashemi, Benjamin le Golvan, Cecilia Lindig-Leon, Sébastian Rimbert.

7.2.1. Level of Consciousness

7.2.1.1. Spatio-temporal Dynamics in Neural Fields

Neural fields serve as a model for experimental macroscopic activity. We have developed a numerical simulator NeuralFieldSimulator $[21]$. In addition, we have worked out a neural neural field model that exhibits a sequence of metastable activity states as observed in experimental data [\[4\]](#page-19-5).

7.2.1.2. Synchronisation in Local Field Potentials under Anaesthesia

We have applied advanced data analysis techniques based on wavelet analysis to detect instantaneous partial synchronisation in experimental data [\[5\]](#page-20-0).

7.2.1.3. Statistical Frequency-dependent Analysis by Recurrence Plots

Participants : Axel Hutt, Mariia Fedotenkova, Tamara Tosic

In collaboration with Flavio Frohlich, Peter Beim Graben and Kristin K. Sellers

For decades, research in neuroscience has supported the hypothesis that brain dynamics exhibits recurrent metastable states connected by transients, which together encode fundamental neural information processing. To understand the system's dynamics it is important to detect such recurrence domains, but it is challenging to extract them from experimental neuroscience datasets due to the large trial-to-trial variability. We proposed a methodology to extract recurrent metastable states in univariate time series by transforming datasets into their time-frequency representations and computing recurrence plots based on instantaneous spectral power values in various frequency bands [\[6\]](#page-20-1). Additionally, a new statistical inference analysis compares different trial recurrence plots with corresponding surrogates to obtain statistically significant recurrent structures. This combination of methods is validated by applying it to two artificial datasets. In a final study of visuallyevoked Local Field Potentials in partially anesthetized ferrets, the methodology is able to reveal recurrence structures of neural responses with trial-to-trial variability. Focusing on different frequency bands, the deltaband activity is much less recurrent than alpha-band activity. Moreover, alpha-activity is susceptible to prestimuli, while delta-activity is much less sensitive to pre-stimuli. This difference in recurrence structures in different frequency bands indicates diverse underlying information processing steps in the brain.

7.2.2. Motor System

Participants: Laurent Bougrain, Axel Hutt, Benjamin le Golvan, Cecilia Lindig-Leon, Sébastian Rimbert, Guillaume Serrière

7.2.2.1. Motor Patterns during General Anesthesia

Participants: Laurent Bougrain, Axel Hutt, Cecilia Lindig-Leon, Sébastian Rimbert, Guillaume Serrière The dosage of the anesthetic agent is tricky: too low, it does not achieve a sufficient loss of consciousness and may lead to a partial memorization during surgery and a post-operative trauma; too strong, it is dangerous for people with respiratory or heart problems. To better monitor the effect of the current dosage, we propose to study the dynamics of the motor brain activity during anesthesia. The relationship between motor brain activity and anesthesia is not intensively studied. Yet even if no physical movement by the patient is visually detectable, an electroencephalographic analysis of brain activity in motor areas may reveal an intention movement. This information is important because it demonstrates that the patient is conscious. We started to define a clinical protocol in collaboration with anesthesiologists of the hospital in Nancy to investigate is possibility. To reduce the duration of the protocol, we studied the minimum duration of a motor imagery to allow its detection from EEG recordings [\[23\]](#page-21-3). A large number of Brain-Computer Interfaces (BCIs) are based on the detection of motor imagery related features in the electroencephalographic signal. In most BCI experimental paradigms, subjects realize continuous motor imagery, i.e. a prolonged intention of movement, during a time window of a few seconds. Then, the system detects the movement based on the event-related desynchronization (ERD) and the event-related synchronization (ERS) principles. We studied if a discrete motor imagery, corresponding to a single short motor imagery, would allow a better detection of ERD and ERS patterns than a continuous motor imagery. Indeed, the results of experiments involving 11 healthy subjects suggest that a continuous motor imagery generates a later ERS as well as a more variable and less detectable ERD than discrete motor imagery [\[11\]](#page-20-2). This finding suggests an improved experimental paradigm. We deeper investigated the amplitude and latency of EEG Beta activity during real movements, discrete and continuous motor imageries [\[22\]](#page-21-4).

7.2.2.2. Motor Patterns during Combined Movements

Participants: Laurent Bougrain, Cecilia Lindig-Leon

Imaginary motor tasks cause brain oscillations that can be detected through the analysis of electroencephalographic (EEG) recordings. We studied whether or not the characteristics of the brain activity induced by the combined motor imagery (MI) of both hands can be assumed as the superposition of the activity generated during simple hand MIs. After analyzing the sensorimotor rhythms in EEG signals of five healthy subjects, results show that the imagination of both hands movement generates in each brain hemisphere similar activity as the one produced by each simple hand MI in the contralateral side [\[8\]](#page-20-3). Furthermore, during simple hand MIs, brain activity over the ipsilateral hemisphere presents similar characteristics as those observed during the rest condition. Thus, it is shown that the proposed scheme is valid and promising for brain-computer interfaces (BCI) control, allowing to easily detect patterns induced by combined MIs. Based on these results, we proposed a new method to extend the classic Common Spatial Pattern (CSP) algorithm to a multi-class approach which analyses both brain hemispheres separately to solve, together with a stepwise classification strategy, a multi-label BCI problem. After testing the proposed approach over the EEG signals of six healthy subjects performing a four-class multi-label task involving simple and combined hand MIs together with the rest condition, results show that this technique is plausible for BCI control [\[7\]](#page-20-4). In terms of accuracy, it outperforms the classical one-vs-one approach by 20% and has the same performance as the one-vs-all method. Nevertheless, to solve a multi-label classification problem involving k classes, the proposed method requires only $log2(k)$ classifiers, whereas the one-vs-one method uses $k(k-1)/2$ classifiers and the one-vs-all k classifiers, thereby the new approach simplifies the classification task and seems promising for solving multilabel problems involving numerous classes.

7.2.2.3. On-line Detection of the End of Motor Imageries

Participants : Cécilia Lindig-León, Laurent Bougrain and Sébastien Rimbert

Limb movement execution or imagination induce sensorimotor rhythms that can be detected in electroencephalographic (EEG) recordings. We presented the interest of considering not only the beta frequency band but also the alpha band to detect the elicited EEG rebound, i.e. the increasing of oscillatory power synchronization, at the end of motor imageries [\[9\]](#page-20-5), [\[19\]](#page-21-5). This phenomenon can be stronger over the alpha than the beta band and it is experimentally demonstrated [\[9\]](#page-20-5) that the analysis on the alpha band improves the detection of the end of motor imageries. Moreover a variant method to compute the oscillatory power without referring to a baseline period is proposed; such capacity is useful for self-paced BCI control.

7.2.3. Pain under General Anaesthesia

7.2.3.1. Detection of EEG-signal Features for Pain under General Anaesthesia

Participants : Axel Hutt, Mariia Fedotenkova

In collaboration with Peter Beim Graben and James W. Sleigh

Nowadays, surgical operations are impossible to imagine without general anaesthesia, which involves loss of consciousness, immobility, amnesia and analgesia. Understanding mechanisms underlying each of these effects guarantees well-controlled medical treatment. Our work focuses on analgesia effect of general anaesthesia, more specifically, on patients reaction on nociception stimuli. The study was conducted on dataset consisting of 230 EEG signals: pre- and post-incisional recordings for 115 patients, who received desflurane and propofol. Initial analysis was performed by power spectral analysis, which is a widespread approach in signal processing. Power spectral information was described by fitting the background activity and measuring power contained in delta and alpha bands according to power of background activity. The fact that power spectrum of background activity decays as frequency increasing is well known and thoroughly studied. Here, traditional $1/f^{\alpha}$ behaviour of the decay was replaced by a Lorentzian model to describe the power spectrum of background activity. Due to observed non-stationary nature of EEG signals spectral analysis does not suffice to reveal significant changes between two states. A further improvement was done by expanding spectra with time information. To obtain time-frequency representations of the signals conventional spectrograms were used as well as a spectrogram reassignment technique. The latter allows to ameliorate readability of a spectrogram by reassigning energy contained in spectrogram to more precise positions. Subsequently, obtained spectrograms were used in recurrence analysis and its quantification by complexity measure. Recurrence analysis allows to describe and visualise dynamics of a system and discover structural patterns contained in the data. Structure of each recurrence plot is characterised by Lempel–Ziv complexity measure [5], which shows a difference between pre- and post-incision [\[13\]](#page-20-6).

8. Bilateral Contracts and Grants with Industry

8.1. Bilateral Contracts with Industry

8.1.1. CertiViBE

Laurent Bougrain is a member of the steering committee of OpenViBE and CertiViBE.

CertiViBE, a medically certifiable core for OpenViBE, the software for Brain Computer Interfaces and Neuroscience research. It is a iLAB project between the Inria project-team Hybrid and Mensia Technologies SA [\(http://www.mensiatech.com/\)](http://www.mensiatech.com/)

Founded in 2012, Mensia Technologies is a medical-device spin-off of Inria owning an exclusive worldwide license of the OpenViBE software for commercial applications. So far, OpenViBE has raised a lot of interest in the research community, especially on medical applications. However, OpenViBE being a research-software, it does not yet matches the requirements of medical devices in terms of stability, performance, documentation, as well as engineering processes in general, slowing down the transfer of OpenViBE-based medical research to the industry. Within the CertiViBE project, Inria and Mensia Technologies are putting their task forces and respective expertise together to deliver a certifiable core for the OpenViBE software. While the OpenViBE software will continue to be published as an Open Source software, the project will dramatically facilitate the transfer of the research made with OpenViBE as it will be built on ready-to-certify foundations, following the processes and normative regulation of medical devices development including risk analysis, quality assurance and medical device software development and maintenance.

9. Partnerships and Cooperations

9.1. Regional Initiatives

In the *Contrat de Plan État Région (CPER) IT2MP* 2015-2020 on *Technological innovations, modeling and Personalized Medicine*, we are contributing on platform SCIARAT (*cognitive stimulation, Ambient Intelligence, Robotic assistance and Telemedicine*). Contact in Neurosys is Laurent Bougrain.

9.2. National Initiatives

- • Inria Technological development action (ADT): OpenViBE-NT This is a three-year multi-site project (2012–2015) to develop OpenViBE further on several fronts such as usability, new algorithms and scope of applicability. Teams of the ADT are Hybrid(Rennes), Athena (Sophia), Potioc (Bordeaux) and Neurosys. Coordinator is Laurent Bougrain.
- Multidisciplinary Exploratory Project (PEPS 2014) Bio-Maths-Info (BMI): *Characterising the laminar profile of motor cortical oscillatory synchronization during visuomotor behavior with new analysis tools.*

Oscillations are omnipresent in the brain, but their function is still disputed. In motor cortex, beta and gamma oscillations are often observed, but their proposed roles in sensorimotor behavior are largely overlapping. While much is known on the laminar distribution of oscillations in sensory areas, the very sparse data on the laminar profile of motor cortical oscillations largely limits their functional interpretations. The 2-years project studies the layer specificity of monkey motor cortical oscillations and oscillatory interactions between the primary motor cortex (M1) and the dorsal premotor cortex (PMd) during visuomotor behavior. Extending conventional tools, such as coherency analysis, Neurosys develops a new method to quantify short-lasting partial amplitude and phase synchronization in single-trial data, based on wavelets, exploiting the predefined vicinity of contacts on the laminar probes. The application of this new method to the data recorded in Marseille will reveal instantaneous amplitude and phase synchronization between cortical layers and between the brain areas *M*1 and *P*Md, providing novel insights into the functional roles of beta and gamma oscillations in visuomotor behavior. The experimental partner at the *Institut de Neurosciences de la Timone* in Marseille is Bjork Kilavik. The contact in Neurosys is Axel Hutt.

9.3. European Initiatives

9.3.1. FP7 & H2020 Projects

The *ITN*-project *Neural Engineering Transformative Technologies (NETT)* ³ (2012-2016) is a Europe-wide consortium of 18 universities, research institutes and private companies which together hosts 17 PhD students and 3 postdoctoral researchers over the next 4 years. Neural Engineering brings together engineering, physics, neuroscience and mathematics to design and develop brain-computer interface systems, cognitive computers and neural prosthetics. Neurosys organized a NETTworkshop about *Neural Engineering in Medicine and related fields* in Nancy, 2-3 July 2015. Neurosys hosted a PhD-student, Maciej Jedynak, from Pompeu Fabra university (Spain) for one month in fall 2015. Contact is Axel Hutt.

9.3.2. Collaborations in European Programs, except FP7 & H2020

Program: ERC Starting Grant

Project acronym: MATHANA

Project title: Mathematical Modeling of Anaesthesia

Duration: January 2011 – October 2015

Coordinator: Axel Hutt

Abstract: MATHANA aims to study mathematically spatially extended neural systems and reveal their spatio-temporal dynamics during general anaesthesia.

9.3.3. Collaborations with Major European Organizations

Lifestyle Research Association (LIRA): Philips (Netherlands), Fraunhofer (Germany), Inria

Sleep is an essential part of a healthy life, but many people have trouble getting enough uninterrupted sleep. Special sensors installed in a mobile phone or bed can analyze activities, stress patterns and sleep sequences and provide ideas for new strategies and, eventually, products that support a healthier night's sleep. NEUROSYS has a Post-doc project running merging all sensor signals in a single data analysis technique to improve existing sleep monitors.

9.4. International Initiatives

9.4.1. Inria International Partners

9.4.1.1. Informal International Partners

- We collaborate with Jamie Sleigh (University of Auckland, New Zealand), who provides us with experimental EEG-data obtained in humans during anaesthesia (A. Hutt).
- In the collaboration with Flavio Frohlich (University of North Carolina Chapel Hill), we receive experimental data measured intracranially in ferrets and analyse them on spectral properties (A. Hutt).
- In the collaboration with Jérémy Lefebvre (University of Lausanne), we have been working out together a stochastic delayed neural field analysis leading to new insights into the effects of additive noise (A. Hutt).

³ <http://www.neural-engineering.eu/>

- The collaboration with Peter beim Graben (Humboldt University Berlin) on recurrence data analysis has led to analysis techniques to detect meta-stable states in EEG-signals (A. Hutt).
- We have an ongoing collaboration with Pr. Motoharu Yoshida at the Ruhr University Bochum, Germany, aiming to study the role of persistent firing neurons in memory and more specifically in neural network synchronization. M. Yoshida provides us with biological data that we combine with simulations to test hypotheses on memory formation (L. Buhry).
- We also collaborate with Pr. LieJune Shiau (University of Houston, Texas, USA) on more theoretical approaches concerning the role of intrinsic neuronal dynamics in network synchronization and brain oscillations (L. Buhry).

9.5. International Research Visitors

9.5.1. Visits of International Scientists

- We have hosted Peter beim Graben (Humboldt University Berlin) in April and May on recurrence data analysis has led to analysis techniques to detect meta-stable states in EEG-signals.
- Jérémie Lefebvre, 10 days, Scientist at Toronto Western Research Institute, University Health Network, and Assistant Professor at Department of Mathematics, University of Toronto: *Shaping oscillations in the damaged brain*.
- Fatiha Hendel, three weeks, Assistant professor at Université des Sciences et de la Technologie d'Oran :
- *9.5.1.1. Internships*
	- Kanishka Basnayake, first year master student (July 5th 2015-September 6th 2015): EPFL summer Internship. *Modelling of gamma oscillation in networks of adaptive exponential integrate-and-fire neurons*.

10. Dissemination

10.1. Promoting Scientific Activities

10.1.1. Scientific Events Organisation

10.1.1.1. Member of Organizing Committees

- NETT workshop about *Neural Engineering in Medicine and related fields* in Nancy, 2-3 July 2015 (A. Hutt, L. Bougrain)
- • BCI competition, IEEE Neural Engineering Conference, Montpellier, 2015 (L. Bougrain).

10.1.2. Scientific Events Selection

10.1.2.1. Chair of Conference Program Committees

Chair of the international workshop *Neural Engineering in Medicine and Related Fields*, July 2-3, Nancy

10.1.2.2. Member of Conference Program Committees

- • Workshop *Neural Engineering in Medicine and Related Fields*, July 2-3, Nancy (A. Hutt, L. Bougrain)
- French conference on machine learning CAP 2015 (L. Bougrain)
- IEEE International Conference on Systems, Man, and Cybernetics (SMC) special sessions on Brain-Machine Interfaces, Hong Kong, 2015 (L. Bougrain)
- • International Joint Conference on Artificial Intelligence (IJCAI) 2015 (L. Bougrain)

10.1.2.3. Reviewer

- French conference on machine learning CAP 2015 (L. Bougrain)
- IEEE International Conference on Systems, Man, and Cybernetics (SMC) special sessions on Brain-Machine Interfaces, Hong Kong, 2015 (L. Bougrain)
- • International Joint Conference on Artificial Intelligence (IJCAI) 2015 (L. Bougrain)

10.1.3. Journal

10.1.3.1. Reviewer - Reviewing Activities

Nonlinearity, Neurocomputing, Journal of Computational Neuroscience, SIAM Journal of Applied Dynamical Systems, Journal of Mathematical Neuroscience, Frontiers in Neurology, Physical Review E, Physical Review Letters, Journal of Neuroscience (A. Hutt); PLoS Computational Biology, Frontiers in Computational Neuroscience (L. Buhry); Reviewing activities: IEEE Transactions on Signal Processing, ACM Transactions on Sensor Networks, Signal Processing: Image Communication (T. Tosic)

10.1.4. Invited talks

- • Tutorial "Fundamentals in Neural Field and Neural Mass models", Computational Neuroscience Conference, July 17 and 18, Prague (A. Hutt);
- Seminar talk "Noise-induced neural oscillations", Max Planck Institute for Brain Research, May 26, Frankfurt am Main (A. Hutt);
- Seminar talk "Brain Signals Analysis for Brain-Machine Interfaces", UCL-France Workshop *Virtual reality in rehabilitation, accessibility and mobility*, Univ. College London, May 21-22, London (L. Bougrain)
- Seminar talk "EEG-based control of a Jaco robotic arm", International workshop *Neural Engineering in Medicine and Related Fields*, July 2-3, Nancy (L. Bougrain);
- Tutorial "Time-frequency analysis", Ludwig-Maximilians-Universität (LMU), Nov. 2015, Munich (M. Fedotenkova)
- Seminar talk "Distinguishing between pre- and post-incision under general anesthesia by spectral and recurrence analysis of EEG", Ludwig-Maximilians-Universität (LMU), Nov. 2015, Munich (M. Fedotenkova)

10.2. Teaching - Supervision - Juries

10.2.1. Teaching

Engineering School: L. Bougrain, *Artificial Intelligence*, 109h, 3rd year, Telecom Nancy, France Engineering School: L. Bougrain, *Brain-Computer interfaces*, 4.5h, 3rd year, Supelec, France Engineering School: T. Tosic, *Process and knowledge modeling*, 27h, 3rd year, École des Mines Nancy, France

Engineering School: T. Tosic, *Informatique I*, 20h, 2nd year, École des Mines Nancy, France Engineering School: T. Tosic, *Techniques et solutions informatiques*, 24h, 3rd year, École des Mines Nancy, France

Engineering School: T. Tosic, *ARTEM workshop ABCD Web*, 40h, 3rd year, ICN, Ecole d'art et design, École des Mines, France

Engineering School: A. Hutt, *Pépites Algorithmiques*, 9h, niveau M1, École des Mines Nancy, France

Engineering School: F. Giovannini, *Artificial Intelligence*, 32h, 3rd year, Telecom Nancy, France

Engineering School: F. Giovannini, *Techniques and tOols for Programming*, 32h, 1st year, Telecom Nancy, France

Licence: L. Buhry, *Applications en Sciences Cognitives*, 3h, niveau L1 MIASHS, University of Lorraine, France

Licence: L. Buhry, *Programmation Python*, 37h, niveau L1 MIASHS, University of Lorraine, France

Licence: L. Buhry, *IA et Résolution de problèmes*, 25h, niveau L3 MIASHS, University of Lorraine, France

Licence: L. Bougrain, *mobile development*, 35h, Licence of computer science (3st year), University of Lorraine, France

Licence: L. Bougrain, *artificial intelligence*, 35h, Licence of computer science (3st year), University of Lorraine, France

Licence: L. Bougrain, *optimization*, 37.5h, Licence of computer science (3st year), University of Lorraine, France

Master: L. Buhry, *Algoritmique pour l'intelligence artificielle*, 31h, niveau Master 1 SCA (Sciences Cognitives et Applications), University of Lorraine, France

Master: L. Buhry, *IA fondamentale et fouille de données*, 18h, niveau Master 1 SCA (Sciences Cognitives et Applications), University of Lorraine, France

Master: L. Buhry, *Formalismes de Représentation et Raisonnement*, 25h, niveau Master 1 SCA (Sciences Cognitives et Applications), University of Lorraine, France

Master: L. Buhry, *Memory and Machine Learning (in English)*, 38h, niveau Master 1 SCA (Sciences Cognitives et Applications), University of Lorraine, France

Master: L. Buhry, *Neurosciences Computationnelles*, 25h, niveau Master 2 SCMN, University of Lorraine, France

Master: L. Bougrain, *Machine learning*, 18h, Master of computer science, 2st year, University of Lorraine, France

Master: L. Bougrain, *Human factors*, 30h, Master of computer science 1st year, University of Lorraine, France

10.2.2. Supervision

- • PhD in progress: Meysam Hashemi, Analytical and numerical studies of thalamo-cortical neural population models during general anesthesia, May 2012, A. Hutt
- PhD in progress: Mariia Fedotenkova, Detection of EEG-signal features for pain under general anaesthesia, November 2013, A. Hutt
- PhD in progress: Cecilia Lindig-Leon, Multilabel classification for a 3D control of a robotic arm using band-specific EEG markers associated with a motor task, November 2013, L. Bougrain and A. Hutt
- PhD in progress: Francesco Giovannini, Mathematical modelling of the memory system under general anesthesia, October 2014, L. Buhry and A. Hutt
- Winter 2015 Internship: Jean-Baptiste Jordan Schneider (M1 Biology, univ. de Lorraine), *Investigating the Effects of Propofol-Induced Tonic Inhibition on Rhythmic Neural Activity in a Hippocampal Interneuron Network* (F. Giovannini, L. Buhry)
- Master research project (2nd year): Louis Viard (Engineering School Ecole des Mines de Nancy), *Detection of micro-awake episodes in sleep signal using time-frequency descriptors* (T. Tosic)
- Master thesis: Sébastien Rimbert (master of cognitive science, univ. de Lorraine) *Study of the dynamics of brain motor components during anesthesia* (L. Bougrain)
- Master thesis: Benjamin Le Golvan (master of biomedical engineering, univ. de Lorraine) *Longitudinal study of motor activities* (L. Bougrain)

10.2.3. Juries

• Axel Hutt was member of PhD committee of Arnaud Legendre, University of Mulhouse, as reviewer. He has participated in the candidates defence October 28 2015.

10.2.4. Commitees

- • Member of the IES committee (Commission Information et Edition Scientifique) at Inria Nancy–Grand-Est (Laurent Bougrain)
- • Member of Inria committee COST-GTRI to evaluate Inria Associate Teams (Axel Hutt).

10.3. Popularization

- Talks at Science and You: atelier scolaire "Femmes et sciences : une équation facile à résoudre !" June 5th 2015 (L. Buhry)
- Talk during the National Brain week: Brain, Consciousness and Anesthesia, March 24th 2015, central hospital, Nancy (D. Schwartz, A. Hutt, L. Bougrain)
- Exhibit at Loria's open day for master students: controlling a robotic arm using EEG, April 9th, 2015 (L. Bougrain, B. le Golvan)

11. Bibliography

Publications of the year

Doctoral Dissertations and Habilitation Theses

[1] M. HASHEMI. *Analytical and numerical studies of thalamo-cortical neural populationmodels during general anesthesia*, Université de Lorraine, January 2016, <https://hal.inria.fr/tel-01265962>

Articles in International Peer-Reviewed Journals

- [2] M. HASHEMI, A. HUTT, J. SLEIGH. *How the cortico-thalamic feedback affects the EEG power spectrum over frontal and occipital regions during propofol-induced anaesthetic sedation*, in "Journal of computational neuroscience", August 2015, 56 p. [*DOI :* 10.1007/S10827-015-0569-1], [https://hal.archives-ouvertes.fr/](https://hal.archives-ouvertes.fr/hal-01176545) [hal-01176545](https://hal.archives-ouvertes.fr/hal-01176545)
- [3] J. LEFEBVRE, A. HUTT, J.-F. KNEBEL, K. WHITTINGSTALL, M. MURRAY. *Stimulus statistics shape oscillations in non-linear recurrent neural networks*, in "Journal of Neuroscience", February 2015, vol. 35, n o 7, pp. 2895-2903 [*DOI :* 10.1523/JNEUROSCI.3609-14.2015], <https://hal.inria.fr/hal-01091816>
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International Conferences with Proceedings

- [7] C. LINDIG-LEÓN, L. BOUGRAIN. *A multi-label classification method for detection of combined motor imageries*, in "2015 IEEE International Conference on Systems, Man, and Cybernetics - SMC2015", Hong Kong, Hong Kong SAR China, IEEE, October 2015, <https://hal.inria.fr/hal-01180399>
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Scientific Books (or Scientific Book chapters)

[10] F. LOTTE, L. BOUGRAIN, M. CLERC. *Electroencephalography (EEG)-based Brain-Computer Interfaces*, in "Wiley Encyclopedia of Electrical and Electronics Engineering", Wiley, 2015, 44 p. [*DOI :* 10.1002/047134608X.W8278], <https://hal.inria.fr/hal-01167515>

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- [12] S. RIMBERT, N. KEMPF, V. MAPELLI, K. RIVALIN. *Etude oculométrique et comportementale durant la réalisation d'un "Où est Charlie ?" : mise en évidence des différentes stratégies utilisées par les joueurs*, Nancy Université, June 2015, <https://hal.inria.fr/hal-01152036>

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- [13] M. FEDOTENKOVA, A. HUTT, P. BEIM GRABEN, J. W. SLEIGH. *Distinguishing between pre- and post-incision under general anesthesia by spectral and recurrence analysis of EEG data*, September 2015, Bernstein Conference 2015, Poster [*DOI :* 10.12751/NNCN.BC2015.0142], <https://hal.inria.fr/hal-01247128>
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