IN PARTNERSHIP WITH:
CNRS
Université de Lorraine

Activity Report 2016

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

Table of contents

Project-Team NEUROSYS

Creation of the Team: 2013 January 01, updated into Project-Team: 2015 July 01

Keywords:

Computer Science and Digital Science:

3.3. - Data and knowledge analysis
3.4. - Machine learning and statistics
5.1.4. - Brain-computer interfaces, physiological computing
5.9.2. - Estimation, modeling
5.11.1. - Human activity analysis and recognition
6.1.1. - Continuous Modeling (PDE, ODE)
6.1.2. - Stochastic Modeling (SPDE, SDE)
6.1.4. - Multiscale modeling
6.3.4. - Model reduction
8.2. - Machine learning
8.3. - Signal analysis

Other Research Topics and Application Domains:

1.3. - Neuroscience and cognitive science
1.3.1. - Understanding and simulation of the brain and the nervous system
1.3.2. - Cognitive science
1.4. - Pathologies
2.2.2. - Nervous system and endocrinology
2.5.1. - Sensorimotor disabilities

1. Members

Research Scientist

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Laure Buhry [Univ. Lorraine, Associate Professor]
Tamara Tošić [Univ. Lorraine, Temporary Associate Professor]

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Cecilia Lindig-Leòn [Inria]
Sébastien Rimbert [Inria]
Meysam Hashemi [Inria, until Jan. 2016]

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Isabelle Herlich [Inria, from Aug. 2016]
Laurence Félicité [Univ. Lorraine]
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Others

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Jimmy Nex [Inria, Intern, until Jul. 2016]
Louis Viard [Inria, Intern, until Sep. 2016]

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 straightforward, it presents 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 during the 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 monitors. 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 theoretical neural population activity to be compared 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 paragraphs 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 α-band ($\sim 8-12$Hz) and in the $\delta-$band ($2-8$Hz) 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 detected anaesthetic depth and the real depth of patients. 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 every day. 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 Fröhlich, 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 anesthetized patients in intensive care is a demanding task for the personnel in hospital practice. It is almost not possible to take care of a patient constantly and hence the 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, auditory-evoked 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 Würzburg. 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 take benefit of 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 of 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, 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 anesthetized 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 EEG-data 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 has co-supervised and co-written a two-volume book for anyone who uses Brain-Computer Interfaces, in English [17], [18] and for the first time in French [19], [20]. The multidisciplinary work has involved around fifty authors from various backgrounds, who write about their particular area of expertise in a way that makes it accessible to a wider audience. That includes healthcare professionals, video game developers, researchers and students, as well as a much wider audience, curious to explore the philosophical and ethical aspects of this subject. The book also has a practical side, with tutorials illustrating the use of BCI and the OpenViBE software platform (see 6.6 and http://openvibe.inria.fr). Laurent Bougrain contributed to several chapters about the state of the art, medical applications and OpenViBE [15], [10], [12], [13] (French version: [16], [9], [11], [14]).
- We stepped up our collaboration with the *department of neurology of the university hospital in Nancy* (Louise Tyvaert, Louis Maillard, Laurent Koessler) leading to i) a **project PEPS JCJC** on modeling and simulation of the oscillatory activity of the memory system during sleep and under general anesthesia (see section 9.2) a **PhD thesis** started in October 2016 (Amélie Aussel), funded by UL and co-supervised by Laure Buhry (Loria-Neurosys) and Radu Ranta (CRAN). This thesis will make use of SEEG recordings made in epileptic patients and will use preliminary results on hippocampal modelling obtained thanks to the project PEPS JCJC.

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 is planned to 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.

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

6.2. BrianModel

Library of Brian Neuron Models
KEYWORDS: Spiking neural networks - Neurosciences - Numerical simulations
FUNCTIONAL DESCRIPTION

BrianModel is a library of neuron models and ionic currents for the BRIAN simulator. The purpose of BrianModel is to speed up simulation set-up 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, Hodgkin-Huxley pyramidal neuron with CAN receptors, Hodgkin-Huxley fast-spiking inhibitory hippocampal. 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 files, which are conveniently parsed by a Python library which acts as an interface to the BRIAN simulator API's.

- Contact: Francesco Giovannini
- URL: https://github.com/JoErNanO/brianmodel

6.3. MATCWT

continuous wavelet transform
KEYWORDS: Matlab - Visualization - Signal processing
FUNCTIONAL DESCRIPTION

This MATLAB script builds continuous wavelet transform (CWT) allowing to choose scales/frequencies and how to compute cone of influence (COI). It uses built-in MATLAB functions to calculate the transform (cwt.m and cwtft.m). This function returns scalogram, percentage energy for each coefficient of CWT. It also plots CWT (if such option is specified), all the values on the plot are linear ones. Plot function displays COI as hatched regions, to do so an additional function is required. Hatchfill function was used for that. I modifies this function slightly in order to control color of hatch lines and added to the repo for convenience. Otherwise, instead of using hatched regions, COI can be indicated by using MATLAB patch function with alpha set to a value less than 1.

- Contact: Mariia Fedotenkova
- URL: https://github.com/mfedoten/wavelets

6.4. MATSPECTRO

Spectrogram reassignment
KEYWORDS: Matlab - Visualization - Signal processing
FUNCTIONAL DESCRIPTION

This matlab function computes reassigned version of the conventional and multitaper spectrograms. The algorithm is based on Auger and Flandrin method, some parts are adopted from Fulop and Fitz. The idea is to first compute conventional spectrogram, then find optimal (in a sense of energy) time and frequency positions and reassigns values in the spectrogram to this new positions. The difference between conventional and multitaper spectrograms is that multitaper method computes additional spectrogram with each taper. Taper is a generic term for a window function but in this method tapers refer to Slepian sequences. As a result, generally multitaper spectrogram reveals less variance than conventional one.

- Contact: Mariia Fedotenkova
- URL: https://github.com/mfedoten/reasspectro

6.5. NFSimulator

NeuralFieldSimulator
KEYWORDS: Neurosciences - Simulation - Health
FUNCTIONAL DESCRIPTION

The NeuralFieldSimulator computes numerically activity in two-dimensional neural fields by solving integral-differential 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.

- Contact: Axel Hutt
- URL: https://gforge.inria.fr/projects/nfsimulator/

6.6. 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.

- 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 Serriere, Marsel Mano, Maureen Clerc Gallagher, Théodore Papadopoulo, Laurent Bougrain, Jérémy Frey and Nathanaël Foy
- Partners: CEA-List - GIPSA-Lab - INSERM
- Contact: Anatole Lécuyer, Hybrid/Inria Rennes-Bretagne Atlantique
- URL: http://openvibe.inria.fr

6.7. Platforms

6.7.1. EEG experimental room

A room at Inria Nancy - Grand Est is now dedicated to electroencephalographic recordings. An umbrella agreement and several additional experiment descriptions have been approved by the Inria Operational Legal and Ethical Risk Assessment Committee (COERLE).

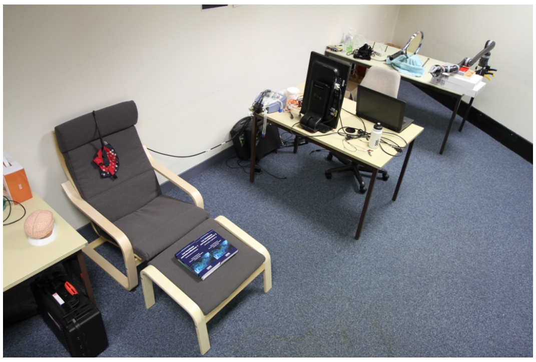

Figure 1. Electroencephalographic Experimental room at Inria Nancy-Grand Est

7. New Results

7.1. From the microscopic to the mesoscopic scale

Participants: Laure Buhry, Francesco Giovannini
In collaboration with Beate Knauer and Motoharu Yoshida (Ruhr University) and LieJune Shiau (University of Houston)

7.1.1. Memory and Anaesthesia

7.1.1.1. The CAN-In model of hippocampal theta oscillations

During working memory tasks, the hippocampus exhibits synchronous theta-band activity, which is thought to be correlated with the short-term memory maintenance of salient stimuli. Recent studies indicate that the hippocampus contains the necessary circuitry allowing it to generate and sustain theta oscillations without the need of extrinsic drive. However, the cellular and network mechanisms supporting synchronous rhythmic activity are far from being fully understood. Based on electrophysiological recordings from hippocampal pyramidal CA1 cells, we have presented a possible mechanism for the maintenance of such rhythmic theta-band activity in the isolated hippocampus [3]. Our model network, based on the Hodgkin-Huxley formalism, comprising pyramidal neurons equipped with calcium-activated non-specific cationic (CAN) ion channels, is able to generate and maintain synchronized theta oscillations ($4 - 12\,Hz$), following a transient stimulation. The synchronous network activity is maintained by an intrinsic CAN current (I_{CAN}), in the absence of constant external input. The analysis of the dynamics of model networks of pyramidal-CAN and interneurons (CAN-In) reveals that feedback inhibition improves the robustness of fast theta oscillations, by tightening the synchronisation of the pyramidal CAN neurons. The frequency and power of the theta oscillations are both modulated by the intensity of the I_{CAN}, which allows for a wide range of oscillation rates within the theta band.

This biologically plausible mechanism for the maintenance of synchronous theta oscillations in the hippocampus aims at extending the traditional models of septum-driven hippocampal rhythmic activity.

7.1.1.2. Generation of gamma oscillations in a network of adaptive exponential integrate and fire neurons

Fast neuronal oscillations in the Gamma rhythm (20-80 Hz) are observed in the neocortex and hippocampus during behavioral arousal. Through a conductance-based, four-dimensional Hodgkin-Huxley type neuronal model, Wang and Buzsáki have numerically demonstrated that such rhythmic activity can emerge from a random network of GABAergic interneurons when their intrinsic neuronal characters and network structure act as the main drive of the rhythm. We investigate Gamma oscillations through a randomly connected network model comprising low complexity, two-dimensional adaptive exponential integrate-and-fire (AdEx) neurons that have subthreshold and spike-triggered adaptation mechanisms. Despite the simplicity of our network model, it shares two important results with the previous biophysical model: the minimal number of necessary synaptic inputs to generate coherent Gamma-band rhythms remains the same, and this number is weakly-dependant on the network size. Using AdEx model, we also investigate the necessary neuronal, synaptic and connectivity properties that lead to random network synchrony with Gamma rhythms. These findings suggest a computationally more tractable framework for studying sparse and random networks inducing cortical rhythms in the Gamma band (Laure Buhry submitted an article to Journal of Computational Neuroscience, currently under major revision).

7.2. From the Mesoscopic to the Macroscopic Scale

Participants: Laurent Bougrain, Axel Hutt, Tamara Tošić, Mariia Fedotenkova, Meysam Hashemi, Cecilia Lindig-Leon, Jimmy, Nex, Sébastien Rimbert.

In collaboration with Stéphanie Fleck (Univ. Lorraine), Nathalie Gayraud (Inria Sophia Antipolis) and Maureen Clerc (Inria Sophia Antipolis)

7.2.1. Level of Consciousness

Participants: Axel Hutt, Meysam Hashemi

Meysam Hashemi defended his thesis about analytical and numerical studies of thalamo-cortical neural population models during general anesthesia. The findings of this thesis provide new insights into the mechanisms responsible for the specific changes in EEG patterns that are observed during propofol-induced sedation. Our results indicate that depending on the mean potential values of the system resting states, an increase or decrease in the thalamo-cortical gain functions results in an increase or decrease in the alpha power, respectively. In contrast, the evolution of the delta power is rather independent of the system resting states; the enhancement of spectral power in delta band results from the increased synaptic or extra-synaptic GABAergic inhibition. Furthermore, we aim to identify the parameters of a thalamo-cortical model by fitting the model power spectrum to the EEG recordings. To this end, we address the task of parameter estimation in the models that are described by a set of stochastic ordinary or delay differential equations [2].

7.2.2. Motor system

Participants: Laurent Bougrain, Cecilia Lindig-Leon, Jimmy, Nex, Sébastien Rimbert.

In collaboration with Stéphanie Fleck (Univ. Lorraine), Nathalie Gayraud (Inria Sophia Antipolis) and Maureen Clerc (Inria Sophia Antipolis)

7.2.2.1. Incremental motor imagery learning for rehabilitation after stroke

After a stroke, Brain-Computer Interfaces (BCI) allows improving rehabilitation of the motor cortex to recover the autonomy of the patient. The design of BCIs has to be done with an in-depth analysis concerning user's conditions during the learning of BCI. Since strokes affect mainly senior citizens, it is very important to guide the design of BCIs to make it usable. We propose to improve the experimental conditions through a new BCI protocol including an incremental motor imagery learning [21].

7.2.2.2. Motor neuroprostheses

We wrote a review that aims to position current neuroprosthetics research between reality and fiction, expectations of persons under a disability, fantasies of the augmented Man and scientific difficulties. Beyond the buzz effect to get the attention of the public and funders, and enthusiasm by journalists for novelty what are the expectations of potential users, the disappointments and the satisfactions of patients, how many persons are equipped, what are the price and the opportunities to use such devices outside of laboratories [5].

7.2.2.3. Classification of Motor patterns

In order to build systems that are able to detect several motor patterns, multiclass schemes need to be applied. We compared a series of multiclass approaches to assert the benefits of hierarchical classification. The compared methods are based on two effective techniques for MI-discrimination, namely, Common Spatial Patterns (CSP) and Riemannian geometry, for which the hierarchical and non-hierarchical approaches have been considered. We include the CSP by Joint Diagonalization method, which corresponds with a non-hierarchical approach; and its hierarchical counterpart, namely, Binary CSP. In addition, the non-hierarchical Minimum Distance to Riemannian Mean method (MDRM) is also evaluated, together with its analogous hierarchical approach; a contribution of the present work called Hierarchical MDRM algorithm (HMDRM). All these methods have been applied on dataset 2a of the BCI competition IV to facilitate their comparison. The highest accuracies were reached by the BCSP and HMDRM methods, confirming the effectiveness of hierarchical algorithms [7].

7.2.2.4. Discrete Motor Imageries for a Faster Detection

We are investigating differences between continuous MIs and discrete MIs corresponding to a 2s MI. Results show that both discrete and continuous MIs modulate ERD and ERS components. Both ERSs are different but ERDs are close in term of power of (de)synchronization. These results show that discrete motor imageries may be preferable for BCI systems design in order to faster detect MIs and reduce user fatigue. [8]

7.2.3. Pain under General Anaesthesia

Participants : Mariia Fedotenkova, Axel Hutt, Tamara Tošić

In collaboration with Peter beim Graben and James W. Sleigh.

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

Mariia Fedotenkova defended her thesis about extraction of multivariate components in brain signals obtained during general anesthesia. We studied analgesia effect of general anesthesia, more specifically, on patients reaction to nociceptive stimuli. We also study differences in the reaction between different anesthetic drugs. The study was conducted on a dataset consisting of 230 EEG signals: pre- and post-incision recordings obtained from 115 patients, who received desflurane and propofol. Combining features obtained with power spectral analysis and recurrence symbolic analysis [22], [6], [23], classification was carried out on a two-class problem, distinguishing between pre-/post-incision EEG signals, as well as between two different anesthetic drugs, desflurane and propofol [1].

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 is a medically certifiable core for OpenViBE, the software for Brain Computer Interfaces and Neuroscience research. It is an Inria innovation lab to boost technology transfers from the Inria project-team Hybrid to Mensia Technologies SA (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 match 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 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 Projet 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

PEPS JCJC INS2I 2016 Modeling and simulation of the oscillatory activity of the memory system during sleep and under general anesthesia (L. Buhry, L. Bougrain).

In order to better understand the mechanisms of amnesia under anesthesia, we propose, on the one hand, to carry out a comparative study, to model and simulate the hippocampal oscillatory activity under general anesthesia and during sleep (tasks 1 and 2). Deep SEEG recordings in epileptic patients during seizures will serve as a reference for modeling and simulation. On the other hand, on the basis of data recorded during sleep, we wish (tasks 3 and 4) to analyze and model the interactions between two structures involved in memory, the hippocampus and the prefrontal cortex, and (tasks 5) propose an automated method to reveal markers of the hippocampal activity characteristics of the sleep stages making use of sole surface recordings. *As it is widely acknowledged that the consolidation of memory occurs mostly during the deep sleep stages, this should make it possible to distinguish the parts of the signal corresponding to periods of consolidation and to propose, through mathematical modeling and simulation, mechanisms explaining the effects of amnesia, or even the absence of memory formation under general anesthesia.

9.3. European Initiatives

9.3.1. FP7 & H2020 Projects

The *ITN*-project *Neural Engineering Transformative Technologies (NETT)* [1] (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 past 4 years. Neural Engineering brings together engineering, physics, neuroscience and mathematics to design and develop brain-computer interface systems, cognitive computers and neural prosthetics. Contact is L. Bougrain.

[1] http://www.neural-engineering.eu/

9.4. International Initiatives

9.4.1. Inria International Partners

9.4.1.1. Informal International Partners

+ We have an ongoing collaboration with Prof. 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 Prof. 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

Prof. LieJune Shiau, University of Houston, June 2016. (collab. with L. Buhry)

10. Dissemination

10.1. Promoting Scientific Activities

10.1.1. Scientific Events Organization

10.1.1.1. Member of the Organizing Committees

- Member of the organization committee of the second OpenViBE workshop as a satellite event of the Brain-Computer Interfaces meeting, May 30th 2016, Asilomar, CA/USA (L. Bougrain) http://openvibe.inria.fr/the-2nd-international-openvibe-workshop-2016-contents/
- Member of the organization committee of the iPAC séminar (Image, Perception, Action et Cognition) (L. Buhry)

10.1.2. Scientific Events Selection

10.1.2.1. Member of the Conference Program Committees

- French conference on machine learning CAP 2016 (L. Bougrain)
- IEEE International Conference on Systems, Man, and Cybernetics (SMC) special sessions on Brain-Machine Interfaces, Budapest, 2016 (L. Bougrain)

10.1.2.2. Reviewer

- Brain-Computer Interfaces meeting 2016 (L. Bougrain)
- IEEE International Conference on Systems, Man, and Cybernetics (SMC) special sessions on Brain-Machine Interfaces, Budapest, 2016 (L. Bougrain)
- French conference on machine learning CAP 2016 (L. Bougrain)
- IEEE International Conference on Acoustic, Speech and Signal Processing - ICASSP, 2016 (T. Tošić)
- IEEE International Conference on Image Processing - ICIP, 2016. (T. Tošić)
- International Conference on Artificial Neural Networks (M. Fedotenkova)

10.1.3. Journal

10.1.3.1. Reviewer - Reviewing Activities

- L. Buhry is a reviewer for Journal of Computational Neuroscience, Frontiers in Computational Neuroscience, Journal of Neural Engineering, IEEE TNN (Transactions on Neural Networks), Neurocomputing, CCSP (Circuits, Sys. & Signal Proc.), IEEE international NEWCAS, Hippocampus
- T. Tošić is a reviewer for IEEE Transactions on Signal Processing (TSP), ACM Transactions on Sensor Networks (TOSN), Signal Processing : Image Communication

10.1.4. Invited Talks

- Active brain-computer interfaces and motor handicap compensation, IFRATH (Institut Fédératif de Recherche sur les Aides Techniques pour personnes Handicapées) and ITMO “Neurosciences, Sciences Cognitives, Neurologie, Psychiatrie”, feb. 4th 2017, INJS Paris (L. Bougrain)
- An introduction to OpenViBE, OpenViBE workshop, satellite event of the Brain-Computer Interfaces meeting, May 30th 2016, Asilomar, CA/USA (L. Bougrain) http://openvibe.inria.fr/the-2nd-international-openvibe-workshop-2016-contents/

10.2. Teaching - Supervision - Juries

10.2.1. Teaching

Engineering school: L. Bougrain, *Interfaces cerveau-ordinateur*, 4.5h, 3rd year, Supelec, France

Engineering school: T. Tošić, *Atelier Artem (Art-Technologie-Management) : ABCDWeb*, 30h, 2nd year, ICN, Ecole d’art et design, École des Mines Nancy, France

Engineering school: T. Tošić, *Parcours de recherche et Initiation à la recherche*, 11h, 2nd and 3rd year, Telecom Nancy and École des Mines Nancy, France

Engineering school: T. Tošić, *Apprentissage automatique - Modélisation avancée des connaissaines*, 58h, 3rd year, École des Mines Nancy, France

Engineering school: T. Tošić, *Tronc Commun d’Informatique - Python*, 140h, 1st year, École des Mines Nancy, France

Engineering school: T. Tošić, *Techniques et Solutions Informatiques*, 47h, 2nd year, École des Mines Nancy, France

Engineering school: T. Tošić, *Pépites Algorithmiques*, 18h, 1st year, École des Mines, France

Engineering school: T. Tošić, *Passerelle au Numérique*, 28h, 1st year, École des Mines, France

Engineering school: T. Tošić, *Model Driven Architecture and UML*, 21h, 2nd year, École des Mines, France

Engineering School: F. Giovannini, *Intelligence artificielle* (3rd year), 34h, Telecom Nancy, France

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

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

Licence: L. Buhry *Probabilités-Statistiques*, 30h, level L1 MIASHS, University of Lorraine, France

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

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

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

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

Master : L. Buhry, *Algorithmique 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*, 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, *Apprentissage automatique*, 18h, Master of computer science, 2st year, University of Lorraine, France

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

10.2.2. Supervision

PhD : Meysam Hashemi, Analytical and numerical studies of thalamo-cortical neural population models during general anesthesia, Univ. Lorraine, Jan. 14, 2016, A. Hutt [2]

PhD : Mariia Fedotenkova, Extraction of multivariate components in brain signals obtained during general anesthesia, Univ. Lorraine, Dec. 2, 2016, A. Hutt [1]

PhD in progress : Cecilia Lindig-Leon, Multilabel classification of EEG-based combined motor imageries implemented for the 3D control of a robotic arm, November 2013, A. Hutt and L. Bougrain

PhD in progress : Francesco Giovannini, Mathematical modelling of the memory system under general anesthesia, Oct. 2014, L. Buhry and A. Hutt

PhD in progress : Sébastien Rimbert Study of the dynamics of brain motor components during anesthesia, January 2016, A. Hutt and L. Bougrain

PhD in progress : Amélie Aussel, Extraction of electrophysiological markers and mathematical modeling of epileptic hippocampus, Oct. 2016, L. Buhry, Patrick Hénaff and R. Ranta

10.2.3. Juries

Laure Buhry was member of the PhD committee of Meysam Hashemi, University of Lorraine.

Laure Buhry was member of the PhD committee of Guillaume Viejo, Université Pierre et Marie Curie, Paris

10.3. Popularization

Interview and demo "Science on live" for the Science Festival 2016 at Cité des sciences et de l'industrie, Forum Explora about "Brain-Computer Interfaces for stroke rehabilitation" Oct. 8, 2016 (L. Bougrain, S. Rimbert). https://www.youtube.com/watch?v=cRCtGuvRW5A

Interview Huffington Post, Oct. 26, 2016 (L. Buhry) (http://www.huffingtonpost.fr/2016/10/26/la-fille-du-train-creativite-imagination/)

Interview for Inria to introduce Neurosys' research on Brain-Computer Interfaces, Oct. 2016 (L. Bougrain) https://www.youtube.com/watch?v=DBajwAI9VEw at 5:38:10

Interview for the Regional TV news (JT 19/20 France 3 Lorraine): Brain-Computer Interfaces, Sept. 29, 2016 (L. Bougrain, S. Rimbert)

Talk during the National Brain Awareness Week: Brain, consciousness and waves, Mar. 18, 2016, Bibliothèque Multimédia Intercommunale, Epinal (L. Buhry, L. Koessler)

Interview for Radio CaraibNancy: Neuroscience in Lorraine, Mar. 16, 2016 (L. Bougrain, S. Caharel and L. Koessler)

Exhibit at Loria's open day for master students and engineers: controlling a robotic arm using EEG, Apr. 9, 2015 (L. Bougrain, J. Nex)

L. Bougrain & B. le Golvan, Neuroprosthetics, Evolution Psychiatrique, Elsevier [5] published on line on Mar. 8, 2016.

11. Bibliography

Publications of the year

Doctoral Dissertations and Habilitation Theses

[1] M. FEDOTENKOVA. *Extraction of multivariate components in brain signals obtained during general anesthesia*, Université de Lorraine, December 2016, https://hal.archives-ouvertes.fr/tel-01415998

[2] 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

[3] F. GIOVANNINI, B. KNAUER, M. YOSHIDA, L. BUHRY. *The CAN-In network: a biologically-inspired model for self-sustained theta oscillations and memory maintenance in the hippocampus* , in "Hippocampus", January 2017 [*DOI :* 10.1002/HIPO.22704], https://hal.archives-ouvertes.fr/hal-01426362

[4] T. TOŠIĆ, K. K. SELLERS, F. FRÖHLICH, M. FEDOTENKOVA, P. BEIM GRABEN, A. HUTT. *Statistical Frequency-Dependent Analysis of Trial-to-Trial Variability in Single Time Series by Recurrence Plots*, in "Frontiers in Systems Neuroscience", January 2016, vol. 9, n^{o} 184 [*DOI :* 10.3389/FNSYS.2015.00184], https://hal.inria.fr/hal-01159664

Articles in National Peer-Reviewed Journals

[5] L. BOUGRAIN, B. LE GOLVAN. *Les neuroprothèses*, in "L'Évolution Psychiatrique", March 2016, https://hal.inria.fr/hal-01287646

Conferences without Proceedings

[6] M. FEDOTENKOVA, P. BEIM GRABEN, J. SLEIGH, A. HUTT. *Time-Frequency Representations as Phase Space Reconstruction in Recurrence Symbolic Analysis*, in "International work-conference on Time Series (ITISE)", Granada, Spain, June 2016, https://hal.archives-ouvertes.fr/hal-01343629

[7] C. LINDIG-LEÓN, N. GAYRAUD, L. BOUGRAIN, M. CLERC. *Comparison of Hierarchical and Non-Hierarchical Classification for Motor Imagery Based BCI Systems*, in "The Sixth International Brain-Computer Interfaces Meeting", Pacific Groove, United States, May 2016, https://hal.inria.fr/hal-01287636

[8] S. RIMBERT, L. BOUGRAIN. *Comparison Between Discrete and Continuous Motor Imageries: toward a Faster Detection*, in "International Brain Computer Interface Meeting 2016", California, United States, May 2016, https://hal.inria.fr/hal-01389948

Scientific Books (or Scientific Book chapters)

[9] L. BOUGRAIN. *Applications médicales: neuroprothèses et neuroadaptation*, in "Brain-Computer Interfaces", M. CLERC, L. BOUGRAIN (editors), Technologie et Applications, ISTE, July 2016, vol. 2, https://hal.inria.fr/hal-01429026

[10] L. BOUGRAIN. *Medical Applications: Neuroprostheses and Neurorehabilitation*, in "Brain-Computer Interfaces", M. CLERC, L. BOUGRAIN, F. LOTTE (editors), Technology and Applications, Wiley-ISTE, July 2016, vol. 2, https://hal.inria.fr/hal-01429029

[11] L. BOUGRAIN, G. SERRIÈRE. *Classification de signaux cérébraux avec OpenViBE*, in "Interfaces cerveau-ordinateur", M. CLERC (editor), Technologie et Applications, ISTE, July 2016, vol. 2, https://hal.inria.fr/hal-01429035

[12] L. BOUGRAIN, G. SERRIÈRE. *Classification of Brain Signals with OpenViBE* , in "Brain-Computer Interfaces", M. CLERC, L. BOUGRAIN, F. LOTTE (editors), Technology and Applications, Wiley-ISTE, July 2016, vol. 2, https://hal.inria.fr/hal-01429033

[13] M. CLERC, L. BOUGRAIN, F. LOTTE. *Conclusion and Perspectives*, in "Brain-Computer Interfaces 2", Wiley-ISTE, July 2016, https://hal.inria.fr/hal-01409032

[14] M. CLERC, L. BOUGRAIN, F. LOTTE. *Conclusion et perspectives*, in "Les interfaces cerveau-ordinateur 2", ISTE, July 2016, https://hal.inria.fr/hal-01408972

[15] M. CLERC, L. BOUGRAIN, F. LOTTE. *Introduction*, in "Brain-Computer Interfaces 1", M. CLERC, L. BOUGRAIN, F. LOTTE (editors), Wiley-ISTE, July 2016, https://hal.inria.fr/hal-01409001

[16] M. CLERC, L. BOUGRAIN, F. LOTTE. *Introduction*, in "Les interfaces cerveau-ordinateur 1", M. CLERC, L. BOUGRAIN, F. LOTTE (editors), Fondements et méthodes, ISTE, July 2016, https://hal.inria.fr/hal-01402594

Books or Proceedings Editing

[17] M. CLERC, L. BOUGRAIN, F. LOTTE (editors). *Brain-Computer Interfaces 1: Foundations and Methods*, Wiley-ISTE, July 2016, https://hal.inria.fr/hal-01408991

[18] M. CLERC, L. BOUGRAIN, F. LOTTE (editors). *Brain-Computer Interfaces 2: Technology and Applications*, Wiley-ISTE, July 2016, https://hal.inria.fr/hal-01408998

[19] M. CLERC, L. BOUGRAIN, F. LOTTE (editors). *Les interfaces Cerveau-Ordinateur 1 : Fondements et méthodes*, ISTE, July 2016, https://hal.inria.fr/hal-01402539

[20] M. CLERC, L. BOUGRAIN, F. LOTTE (editors). *Les interfaces cerveau-ordinateur 2 : Technologie et applications*, ISTE, July 2016, https://hal.inria.fr/hal-01402544

Scientific Popularization

[21] S. RIMBERT, S. FLECK, J. NEX, L. BOUGRAIN. *Nécessité d'un protocole d'apprentissage progressif pour la maîtrise d'une imagination motrice après un AVC*, in "28ième conférence francophone sur l'Interaction

Homme-Machine", Fribourg, Switzerland, Atelier sur les Nouvelles technologies pour les Ainées, défis et perspectives, October 2016, pp. 10-12, https://hal.archives-ouvertes.fr/hal-01386665

Other Publications

[22] M. FEDOTENKOVA, P. BEIM GRABEN, J. SLEIGH, A. HUTT. *Time-Frequency Representations as Phase Space Reconstruction in Symbolic Recurrence Structure Analysis*, December 2016, To appear as a book chapter in the Springer series "Contributions to Statistics", https://hal.archives-ouvertes.fr/hal-01415997

[23] M. FEDOTENKOVA, P. BEIM GRABEN, T. TOŠIĆ, J. SLEIGH, A. HUTT. *Recurrence complexity analysis of oscillatory signals with application to general anesthesia EEG signals*, May 2016, Submitted to Physics Letters A, https://hal.archives-ouvertes.fr/hal-01343631

[24] F. GIOVANNINI, B. KNAUER, M. YOSHIDA, L. BUHRY. *Spiking regimes in model networks of hippocampal persistent firing neurons*, November 2016, Neuroscience 2016, Poster, https://hal.inria.fr/hal-01402515