Activity Report 2016

Team CAMIN

Control of Artificial Movement & Intuitive Neuroprosthesis

Inria teams are typically groups of researchers working on the definition of a common project, and objectives, with the goal to arrive at the creation of a project-team. Such project-teams may include other partners (universities or research institutions).

RESEARCH CENTER
Sophia Antipolis - Méditerranée

THEME
Computational Neuroscience and Medecine

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Team CAMIN

Creation of the Team: 2016 January 01

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Computer Science and Digital Science:

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Other Research Topics and Application Domains:

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2.2.6. - Neurodegenerative diseases
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2. Overall Objectives

2.1. Overall Objectives

CAMIN team research is dedicated to the **design and development of realistic neuroprosthetic solutions for sensorimotor deficiencies** in collaboration with clinical partners. Our efforts are focused on clinical impact: improving the functional evaluation and/or quality of life of patients. Movement is at the center of our investigative activity, and the **exploration and understanding of the origins and control of movement** are one of our two main research priorities. Indeed, optimizing the neuroprosthetic solutions depends on a deeper understanding of the roles of the central and peripheral nervous systems in motion control. The second research priority is **movement assistance and/or restoration**. Based on the results from our first research focus, neuroprosthetic approaches are deployed (fig.1).

Electrical stimulation (ES) is used to activate muscle contractions by recruiting muscle fibers, just as the action potentials initiated in motoneurons would normally do. When a nerve is stimulated, both afferent (sensitive) and efferent (motor) pathways are excited. ES can be applied externally using surface electrodes positioned on the skin over the nerves/muscles intended to be activated or by implantation with electrodes positioned at the contact with the nerves/muscles or neural structures (brain and spinal cord). ES is the only way to restore movement in many situations.

Yet although this technique has been known for decades, substantial challenges remain, including: (i) detecting and reducing the increased early fatigue induced by artificial recruitment, (ii) finding solutions to nonselective stimulation, which may elicit undesired effects, and (iii) allowing for complex amplitude and time modulations of ES in order to produce complex system responses (synergies, coordinated movements, meaningful sensory feedback, high-level autonomic function control).

We investigate functional restoration, as either a **neurological rehabilitation solution** (incomplete SCI, hemiplegia) or for **permanent assistance** (complete SCI). Each of these contexts imposed its own set of constraints on the development of solutions.

Functional ES (FES) rehabilitation mainly involves external FES, with the objective being to increase neurological recuperation by activating muscle contractions and stimulating both efferent and afferent pathways. Our work in this area naturally led us to take an increasing interest in brain organization and plasticity, as well as central nervous system (brain, spinal cord) responses to ES. When the objective of FES is a permanent assistive aid, invasive solutions can be deployed. We pilot several animal studies to investigate neurophysiological responses to ES and validate models. We also apply some of our technological developments in the context of human per-operative surgery, including motor and sensory ES.

CAMIN research will be focused on **exploring and understanding human movement** in order to propose neuroprosthetic solutions in sensorimotor deficiency situations to **assist or restore movement**. Exploration and understanding of human movement will allow us to propose assessment approaches and tools for diagnosis and evaluation purposes, as well as to improve FES-based solutions for functional assistance.

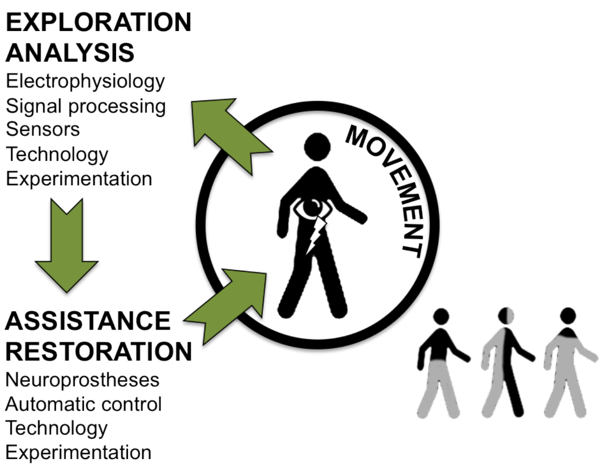


Figure 1. Overview of CAMIN*'s general scientific approach.*

The expertise and skills of our individual team members will be combined to design and develop solutions to restore movement functions.

We have chosen not to restrict our investigation spectrum to specific applications but rather to deploy our general approach to a variety of clinical applications in collaboration with our medical partners. **Our motivation and ambition is to have an effective clinical impact**.

3. Research Program

3.1. Exploration and understanding of the origins and control of movement

One of CAMIN's areas of expertise is **motion measurement, observation and modeling** in the context of **sensorimotor deficiencies**. The team has the capacity to design advanced protocols to explore motor control mechanisms in more or less invasive conditions in both animal and human.

Human movement can be assessed by several noninvasive means, from motion observation (MOCAP, IMU) to electrophysiological measurements (afferent ENG, EMG, see below). Our general approach is to develop solutions that are realistic in terms of clinical or home use by clinical staff and/or patients for diagnosis and assessment purposes. In doing so, we try to gain a better understanding of motor control mechanisms, including deficient ones, which in turn will give us greater insight into the basics of human motor control. Our ultimate goal is to optimally match a neuroprosthesis to the targeted sensorimotor deficiency.

The team is involved in research projects including:

- Peripheral nervous system (PNS) exploration, modeling and electrophysiology techniques
  Electroneurography (ENG) and electromyography (EMG) signals inform about neural and muscular activities. The team investigates both natural and evoked ENG/EMG through advanced and dedicated signal processing methods. Evoked responses to ES are very precious information for understanding neurophysiological mechanisms, as both the input (ES) and the output (evoked EMG/ENG) are controlled. CAMIN has the expertise to perform animal experiments (rabbits, rats, earthworms and big animals with partners), design hardware and software setups to stimulate and record in harsh conditions, process signals, analyze results and develop models of the observed mechanisms. Experimental surgery is mandatory in our research prior to invasive interventions in humans. It allows us to validate our protocols from theoretical, practical and technical aspects.
- Central nervous system (CNS) exploration
  Stimulating the CNS directly instead of nerves allows activation of the neural networks responsible for generating functions. Once again, if selectivity is achieved the number of implanted electrodes and cables would be reduced, as would the energy demand. We have investigated **spinal electrical stimulation** in animals (pigs) for urinary track and lower limb function management. This work is very important in terms of both future applications and the increase in knowledge about spinal circuitry. The challenges are technical, experimental and theoretical, and the preliminary results have enabled us to test some selectivity modalities through matrix electrode stimulation. This research area will be further intensified in the future as one of ways to improve neuroprosthetic solutions.
  We intend to gain a better understanding of the electrophysiological effects of DES through electroencephalographic (EEG) and electrocorticographic (ECoG) recordings in order to optimize anatomo-functional brain mapping, better understand brain dynamics and plasticity, and improve surgical planning, rehabilitation, and the quality of life of patients.
- Muscle models and fatigue exploration
  Muscle fatigue is one of the major limitations in all FES studies. Simply, the muscle torque varies over time even when the same stimulation pattern is applied. As there is also muscle recovery when there is a rest between stimulations, modeling the fatigue is almost an impossible task. Therefore, it is essential to monitor the muscle state and assess the expected muscle response by FES to improve the current FES system in the direction of greater adaptive force/torque control in the presence of muscle fatigue.
- Movement interpretation
  We intend to develop ambulatory solutions to allow ecological observation. We have extensively investigated the possibility of using inertial measurement units (IMUs) within body area networks to observe movement and assess posture and gait variables. We have also proposed extracting gait parameters like stride length and foot-ground clearance for evaluation and diagnosis purposes.

3.2. Movement assistance and/or restoration

The challenges in movement restoration are: (i) improving nerve/muscle stimulation modalities and efficiency and (ii) global management of the function that is being restored in interaction with the rest of the body under voluntary control. For this, both local (muscle) and global (function) controls have to be considered.
Online modulation of ES parameters in the context of lower limb functional assistance requires the availability of information about the ongoing movement. Different levels of complexity can be considered, going from simple open-loop to complex control laws (figure 2).

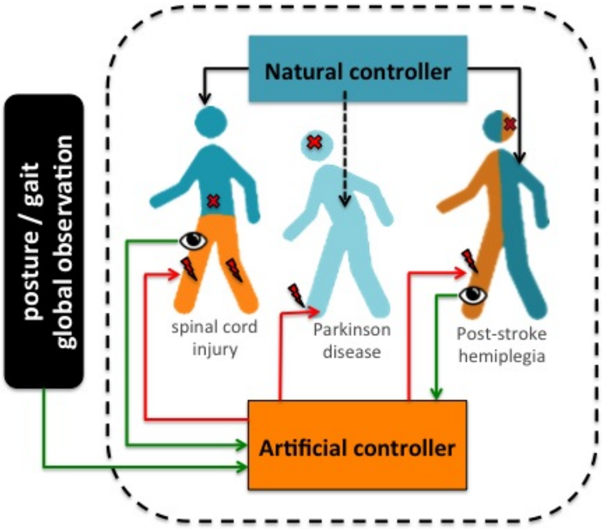


Figure 2. FES assistance should take into account the coexistence of artificial and natural controllers. Artificial controllers should integrate both global (posture/gait) and local (limb/joint) observations.

Real-time adaptation of the stimulation patterns is an important challenge in most of the clinical applications we consider. The modulation of ES parameters in the presence of fatigue or to adapt to context needs for adaptive controllers processing information on movement execution and environmental changes. A minimum number of sensors with minimal impact on patient motion is necessary.

4. Application Domains

4.1. Non invasive stimulation (external FES)

Both triggered open-loop and closed-loop FES controllers that we are developing for movement involve several sensors and stimulators whose activities must be precisely coordinated by the controller. For instance, the stimulation controller is fed back by various sensors, such as limb joint angles, IMUs providing accelerations, and electrophysiological signals like EMG. These signals are then used by feedback controllers to accurately control the artificially actuated limbs by means of stimulators. This distributed architecture is often deployed on a wireless network since it distinctively complies with mobility constraints, leading to good acceptance from human users. The quality of service (QoS) of this network influences the controlled system properties and the quality of control (QoC). The control performance and robustness of this system can be very far from expectations if implementation-induced disturbances are not taken into account. Thus, the overall performance of a real-time control system must be assessed not only with respect to deadlines (as in classical scheduling analysis) but also by considering other criteria such as time-varying delays and jitter. Hence, research on the joint design of control, computation and communication has to be carried out and applied [49] to the particular case of FES control loops distributed over imperfect links and low power nodes. In addition to the elaboration or adaptation of algorithms, specific tools must be further developed to assess the effectiveness of the new control algorithms and to support their implementation. In particular, realistic simulations remain a precious tool ahead of real experiments to ensure that the implementation meets the functional and safety requirements without danger. This is, for example, the case of the hybrid simulation framework of our distributed FES system currently under development [6]. Understanding and modeling the influence of an implementation (support system) on QoC is a challenging objective in a distributed control design process, but it is mandatory to guarantee the system's safety and effectiveness.

4.2. Invasive stimulation (implanted FES)

Invasive FES means that the selectivity issue has to be dealt with, both from theoretical and technological points of view. To take advantage of spatial and topological nerve organization, invasive stimulation must be able to focus the current in specific nerve areas to elicit subgroups of muscles, while avoiding undesired functional effects (i.e., undesired fiber recruitment). Although multipolar electrodes are available, it is still challenging to find the optimal electrode configuration to reach the given 3D current spreading (i.e., selective stimulus). Indeed, this is not intuitive and modeling is mandatory. On the other hand, implantable stimulators must provide for both dynamical electrode configuration and a complex stimulation profile.

Selectively activating part of the nerve requires an active contact configuration (anode, cathode, high impedance), distribution of the current over the selected contacts, and accurate control of the overall total injected current, both from amplitude and time dimensions. To meet these needs, the neurostimulator has been designed based on a 2-stage device [50]. The first stage is the output stage based on a dedicated analog ASIC (application-specific integrated circuit) that is able to drive 12 channels of stimulation in absolute synchronization, with a programmable and controlled current distribution over selected contacts. The latest ASIC version we designed is CORAIL (circuit fabrication by November 2016): this analog/digital integrated circuit ensures current distribution but also such features as the storage of multiple electrode configurations and the possibility to internally combine poles. The second stage consists of a digital architecture embedded in an FPGA containing a dedicated processor for programming complex stimulation profiles, a monitoring module ensuring the respect of safety constraints stemming from both target tissue protection and electrode integrity preservation (in terms of quantity of injected charge limits), and a protocol stack for remote programming and online control of stimulation parameters. This complex digital system was formally developed using HILECOP §6.1.1.

5. Highlights of the Year

5.1. Highlights of the Year

International Functional Electrical Stimulation Society Conference organization

In 2016, CAMIN organized the 20th International Functional Electrical Stimulation Society Conference. 135 participants attended the event. Papers are referenced in Pubmed and published in European Journal of Translationnal Myology. A special issue with a selection of best articles will be published in 2017 in Artificial Organs Journal. http://ifess2016.inria.fr/

Participation into Cybathlon competition

We have participated in the first international competition Cybathlon held in Kloten, Switzerland in October 2016. After more than one year of physical and technical preparation, our team, Freewheels, was present with one complete paraplegic pilot in the FES cycling discipline. http://freewheels.inria.fr/

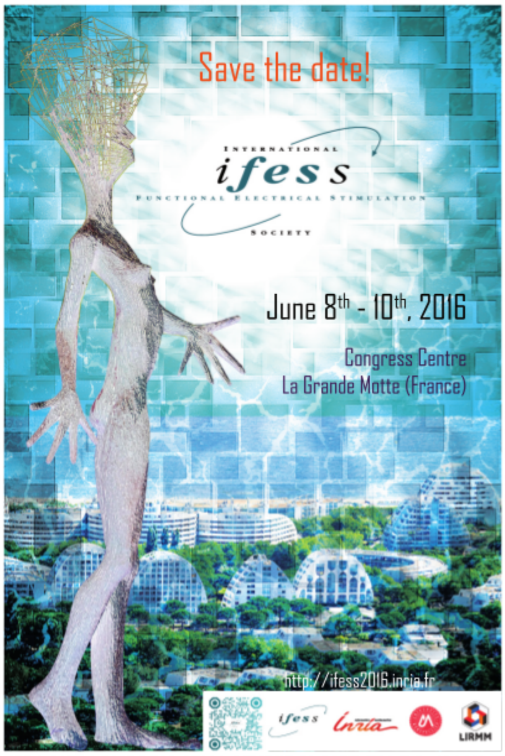


Figure 3. Flyer of IFESS 2016 conference

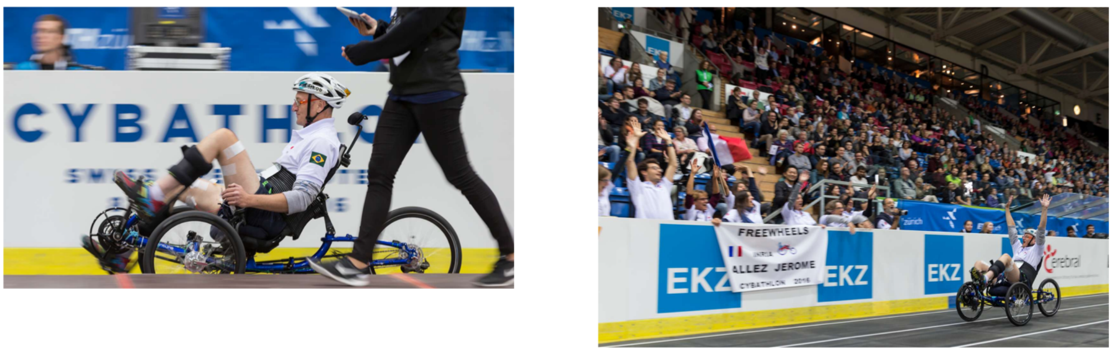


Figure 4. Freewheels team at Cybathlon 2016

6. New Software and Platforms

6.1. Software and platforms

6.1.1. HILECOP

Participants: Baptiste Colombani, David Andreu, Thierry Gil [LIRMM], Robin Passama [LIRMM].

High Level hardware Component Programming
FUNCTIONAL DESCRIPTION: Our SENIS (Stimulation Electrique Neurale dIStribuee) based FES architecture relies on distributed stimulation units (DSU) which are interconnected by means of a 2-wire based network. A DSU is a complex digital system since its embeds among others a dedicated processor (micro-machine with a specific reduced instruction set), a monitoring module and a 3-layer protocol stack. To face the complexity of the units digital part and to ease its prototyping on programmable digital devices (e.g. FPGA), we developed an approach for high level hardware component programming (HILECOP). To support the modularity and the reusability of sub-parts of complex hardware systems, the HILECOP methodology is based on components. An HILECOP component has: a Petri Net (PN) based behavior (fig.5), a set of functions whose execution is controlled by the PN, and a set of variables and signals. Its interface contains places and transitions from which its PN model can be inter-connected as well as signals it exports or imports. The interconnection of those components, from a behavioral point out view, consists in the interconnection of places and/or transitions according to well-defined mechanisms: interconnection by means of oriented arcs or by means of the "merging" operator (existing for both places and transitions).

The Eclipse-based version of HILECOP (registered at the french Agence de Protection des Programmes (APP)) has been refactored: for instance, the application ECore model, a new Eclipse E4 architecture and a set of new features (new link types and new views to connect components) have been developed.

Undergoing work concerns the integration, in the HILECOP tool, of the formalism evolutions that allow behavior agregation as well as exception handling, both for analysis and implementation sides.

Specification of GALS systems (Globally Asynchronous Locally Synchronous) is also an ongoing work, the aim being to take into account deployment properties like connecting different clocks to HILECOP components within a same FPGA, or on a set of interconnected FPGAs (and thus interconnecting them by means of asynchronous signals).

6.1.2. PersoBalance: A Personalized Balance Assessment in Home Rehabilitation

Participants: Maxime Tournier, Alejandro Gonzalez, Philippe Fraisse, Mitsuhiro Hayashibe.

In 2014-2015, the team demonstrated the feasibility of a personalized balance assessment system using low-end sensors for home rehabilitation. The corresponding software (PersoBalance) performs an identification of inertial parameters for a subject using a depth camera and a connected balance board (in this case, a Nintendo Wii BalanceBoard) through a dedicated Kalman filter as the subject assumes various body postures. When the inertial parameters are estimated, the software is then able to compute a stability index for the subject based on criteria found in robotics and biomechanics literature. This year, in order to exploit the newer, more accurate and more robust sensors such as the Microsoft Kinect v2, a new version of the PersoBalance software was engineered. While the core method remainsthe same, several improvement have been made regarding efficiency, user interface and extensibility. The new system is faster, more accurate and robust. It automatically registers the balance board during identification, and features improved graphical feedback during both identification and stability estimation phases. New stability measures were added, and support for online inverse dynamics is on the way. Most of the new version uses a scripting language (Python) except for time-critical algorithm, making the software easily extensible without recompilation. It is supported by Inria ADT PersoBalance2. Currently the software is being adapted to embedded computers in order to provide monitoring data in the City4Age project.

PersoBalance is registered with the Agency for the Protection of Programs (APP) and deposited at the BNF (Bibliotheque Nationale de France). Its registration number is Antepedia Deposit 20150710154654.

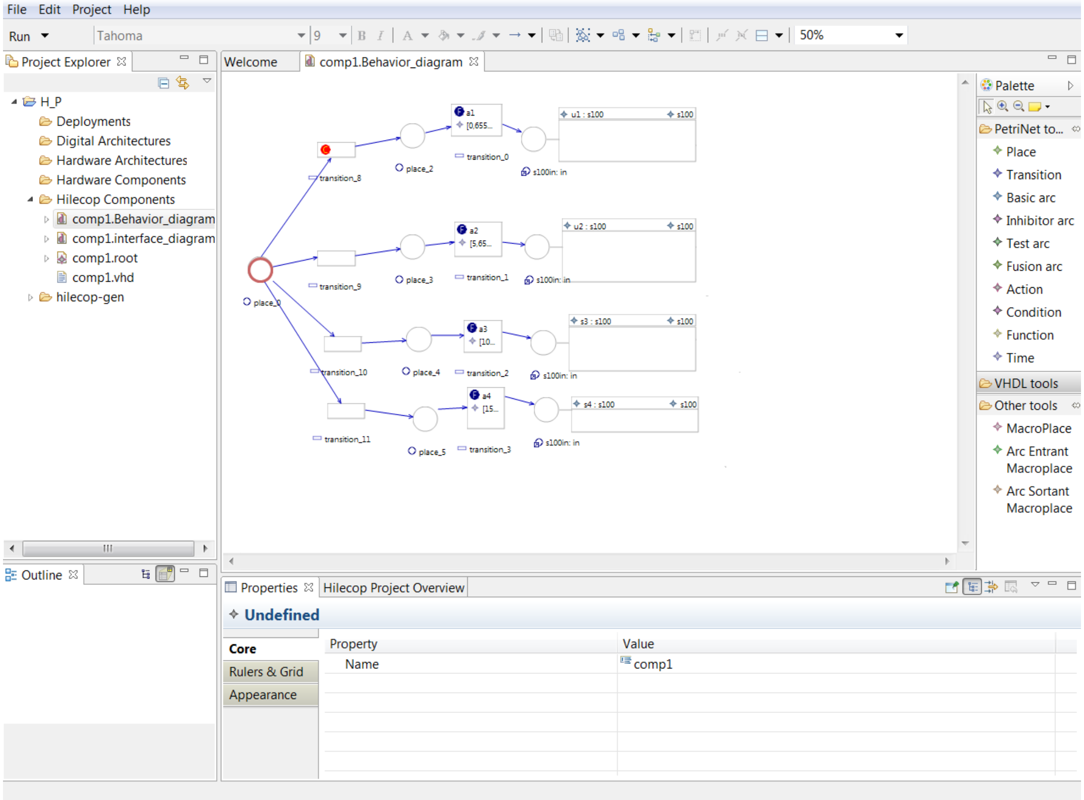


Figure 5. HILECOP screenshot

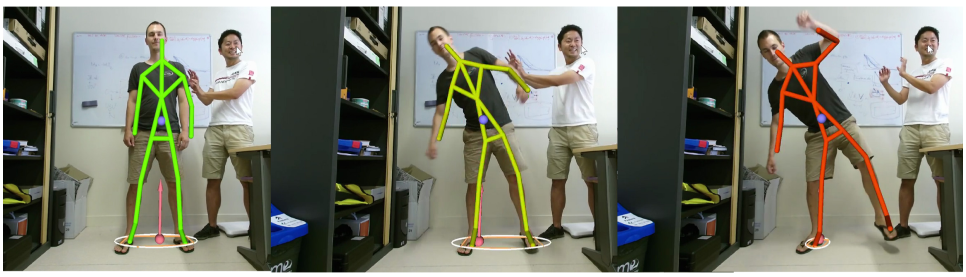


Figure 6. PersoBalance: Online stability estimation, from left to right: as a subject undergoes an unexpected external push, the system automatically estimates the ground reaction forces (pink arrow) and computes a stability index from the position of the ZRAM point relative to the support polygon (white/orange). The skeleton colour changes from green to red as the stability index decreases.

6.1.3. Sensbiotk

Participants: Christine Azevedo Coste, Roger Pissard-Gibollet, Benoît Sijobert.

Sensbiotk is a toolbox in Python for the calibration, the acquisition, the analysis and visualization of motion capture Inertial Measurement Units (IMU). Motion and Gait parameter reconstruction algorithms are also available.

http://sensbio.github.io/sensbiotk/

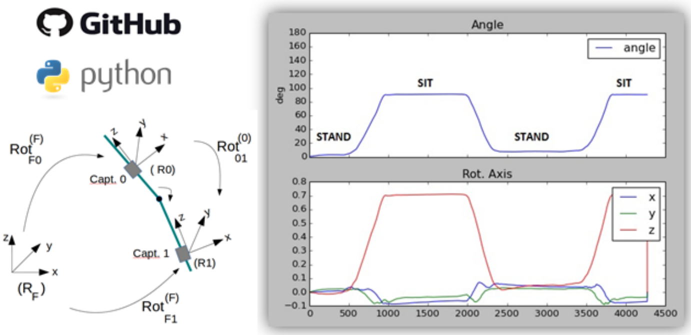


Figure 7. Sensbiotk toolbox for the calibration, the acquisition, the analysis and visualization of motion capture Inertial Measurement Units (IMU)

6.1.4. MOS2SENS

Participants: Mélissa Dali, Olivier Rossel, David Guiraud.

From Model Optimization and Simulation To Selective Electrical Neural Stimulation: it allows to manipulate 3D modeling of nerve and cuff electrodes taking into account anisotropy and the most advanced HH models of the myelinated axons. Based on optimized computing scheme, it allows to predict the acivation areas induced by a complex 3D spreading of the current over a multicontact electrodes. Moreover, the tool allows for performing optimization of the needed current to target a specific cross section of the nerve. Version 1.0 (IDDN.FR.001.490036.000.S.P.2014.000.31230) has been relaesed on december 2014 and v2.0 will be realeased January 2017. The last version includes full interface with OpenMEEG and COMSOL, and many other enhancements concerning both the model itself and the computation scheme.

6.1.5. STIMEP: An advanced real-time stimulation system based on a distributed architecture

Participants: Arthur Hiairrassary, David Andreu, David Guiraud, Olivier Rossel, Thomas Guiho.

The STIMEP has been developed within the EPIONE project (see section 9.3.1) which aims at assessing the use of invasive stimulation to relieve phantom pain. This innovative wearable stimulator allows to safely manipulate sensory afferent signals of an amputee through 4 TIME-4H intra fascicular electrodes, for a total of 56 channels.

The STIMEP is also designed to be controlled in real-time by a hand-prosthesis to generate feedback sensations; it permits as well a complex impedance follow-up.

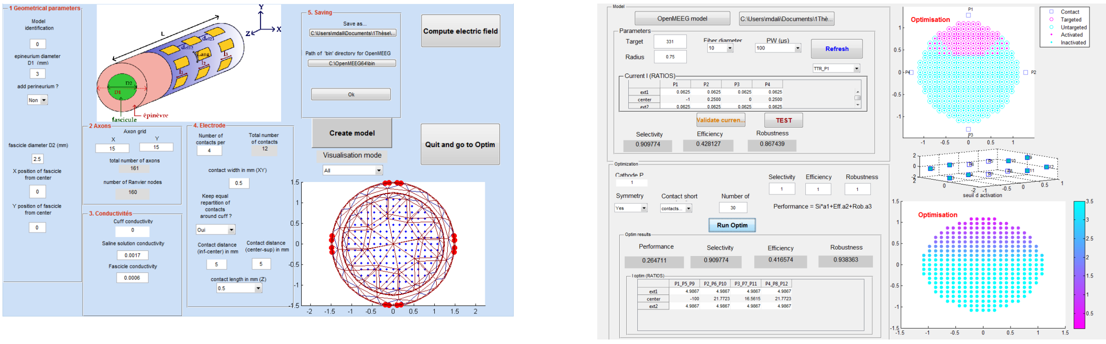


Figure 8. Graphical interface of software MOS2SENS, left: modeling multicontact CUFF electrode, right: optimization for spatial selectivity

The STIMEP is based on a distributed architecture and embeds:

- 1 x controller implemented on μC/OS-II RTOS exchanging data with a PC (USB) or an external device (SPI),
- 4 x neural stimulators with efficient modulation mechanisms to drive up to 4 multicontact electrodes simultaneously and independently,
- 6 x fully configurable procedures (formally modeled by Petri nets):
  - Contacts check, thresholds search, sensations characterization, therapy,
  - Real-time modulation of frequency, intensity and pulse-width,
  - Complex impedance measurement.
- 2 x smart and independent synchronization outputs,
- User and technical logs of relevant information.

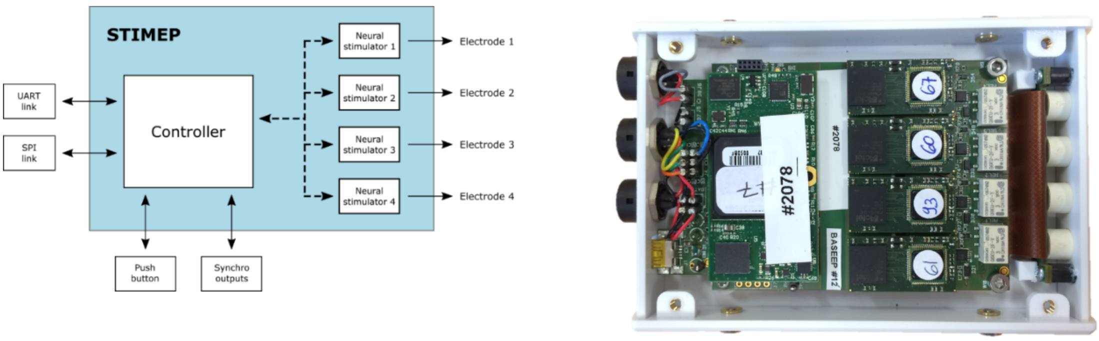


Figure 9. The STIMEP (STIMulator EPione)

The STIMEP is currently used in human trials and drives simultaneously 4 multicontact intrafascicular electrodes with real time control of the intensity, pulse-width and frequency of the stimulation to remove phantom pain and elicit very accurate sensation feedback.

7. New Results

7.1. Movement analysis and interpretation

7.1.1. Inertial Sensor based Analysis of Gait for Children with Cerebral Palsy

Participants: Christine Azevedo Coste, Benoît Sijobert, Jessica Rose [Stanford University].

Analysis of walking abnormalities is important for clinical diagnosis, to guide treatments, and to assess treatment outcomes for gait disorders particularly in children with cerebral palsy (CP). Motion capture, the current gold standard, enables practitioners to perform gait analyses with high accuracy in the laboratory. However, the motion capture technology used is constrained to a small space, the clinical environment may not be relevant to community mobility. This research collaboration investigated the development of a mobile systems using light-weight inertial measurement units (IMU). These sensor-based systems have potential to provide a more efficient, mobile alternative for movement analysis and can offer real-time feedback to patients for more effective rehabilitation. This interdisciplinary collaboration with Professor Jessica Rose, from the Department of Orthopedic Surgery at Stanford University aims to quantitatively assess walking problems associated with CP and related neurological conditions. Despite their small size, ease-of-use, robust design and low-cost, there are numerous recognized technical issues that make the use of IMUs relatively complex moreover in children. Through a series of experiments we leveraged our complementary skills to propose an IMU sensor system and software to extract meaningful gait parameters for rehabilitation of children with CP. A feasibility study was achieved at the Lucile Packard Children's Hospital Motion & Gait Lab in order to solve technical issues and refine calculations validated based on walking patterns recorded by Laboratory-based 3D motion capture data.

7.1.2. Automatic Human Movement Assessment with Switching Linear Dynamic System: Motion Segmentation and Motor Performance

Participants: Baptista Roberto [Universidade de Brasilia, Brasil], Bo Antonio P.l. [Universidade de Brasilia, Brasil], Mitsuhiro Hayashibe.

Performance assessment of human movement is critical in diagnosis and motor-control rehabilitation. Recent developments in portable sensor technology enable clinicians to measure spatiotemporal aspects to aid in the neurological assessment. However, the extraction of quantitative information from such measurements is usually done manually through visual inspection.

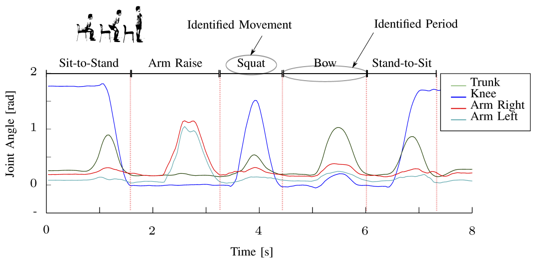
This work presents a novel framework for automatic human movement assessment that executes segmentation and motor performance parameter extraction in time-series of measurements from a sequence of human movements. We use the elements of a Switching Linear Dynamic System model as building blocks to translate formal definitions and procedures from human movement analysis. Our approach provides a method for users with no expertise in signal processing to create models for movements using labeled dataset and latter use it for automatic assessment.

Preliminary tests were carried out involving six healthy adult subjects that executed common movements in functional tests and rehabilitation exercise sessions, such as sit-to-stand and lateral elevation of the arms. Also five elderly subjects, two of which with limited mobility, that executed the sit-to-stand movement. The proposed method worked on random motion sequences for the dual purpose of movement segmentation (accuracy of 72-100%) and motor performance assessment (mean error of 0-12%).

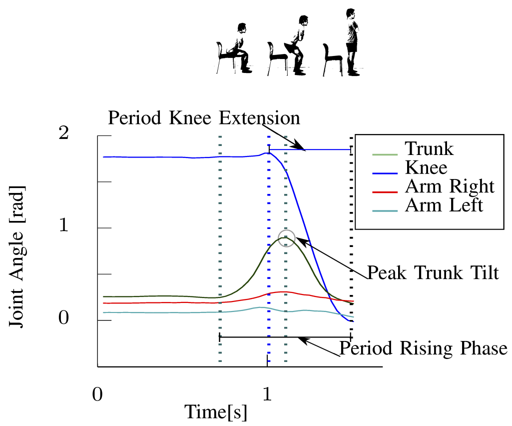
The results of this work have been accepted for publication in the journal IEEE Transactions in Neural Systems and Rehabilitation Engineering.

7.1.3. Inertial Sensor based Analysis of Gait for Post-stroke individuals

Participants: Christine Azevedo Coste, Benoît Sijobert, Jérôme Froger [CHU Nîmes], François Feuvrier [CHU Nîmes].



Movement sequence segmentation and movement type recognition



Motor performance parameters extraction

Figure 10. Dual purpose of the proposed approach: movement segmentation and movement assessment.

Walking impairment after stroke can be addressed through the use of drop foot stimulators (DFS). In these systems, electrical stimulation is applied to activate the common peroneal nerve and elicit ankle dorsiflexion during the swing phase of gait. DFS are generally piloted by a heel switch positioned in the shoe of the affected side with stimulation being triggered ON by heel rise of the affected foot and triggered OFF by heel strike.

Using inertial sensors for modulating FES intensity could provide a more optimized delivery of stimulation and could also enable to regulate dorsiflexion in the presence of disturbances, such as fatigue or stairs. It could also increase the number of potential users of the technology, allowing subjects walking without heel strikes to be stimulated at a correct timing. Meanwhile, pathological post-stroke gait requires the investigation of complex inertial sensors based algorithms for being able to compute different useful gait parameters for later triggering stimulation.

Numerous constraints related to these clinical context, pathology and usability have to be taken into account for providing a reliable patient oriented solution. In this work, we aim to compare accuracy and feasibility of using a minimum amount of inertial sensors instead of the gold standard camera based motion capture, for assessing joint angles and other gait events such as stride length or dorsiflexion speed at heel on. A maximum of 30 subjects will be included in this experimental protocol. Equipped with motion capture targets on which an inertial sensor is set (Figure 11), subjects have to perform an experimental path on a gait carpet. EMG recordings are also performed to monitor and evaluate fatigue. In further works, algorithms from inertial data developed through these study will enable us to evolve toward close loop control, putting together inertial sensors and programmable stimulator in real time ([39]).

7.2. Modeling and identification of the sensory-motor system

7.2.1. Neuroplasticity and recovery in remote (sub)cortical structures following wide-awake surgery of infiltrative low-grade gliomas: investigation of fMRI and EEG signals by standard and nonlinear methods

Participants: Anthony Boyer, Jérémy Deverdun [CHU Montpellier], Hugues Duffau [CHU Montpellier], Emmanuelle Le Bars [CHU Montpellier], Sofiane Ramdani [LIRMM], David Guiraud, Nicolas Menjot de Champfleur [CHU Montpellier], François Bonnetblanc.

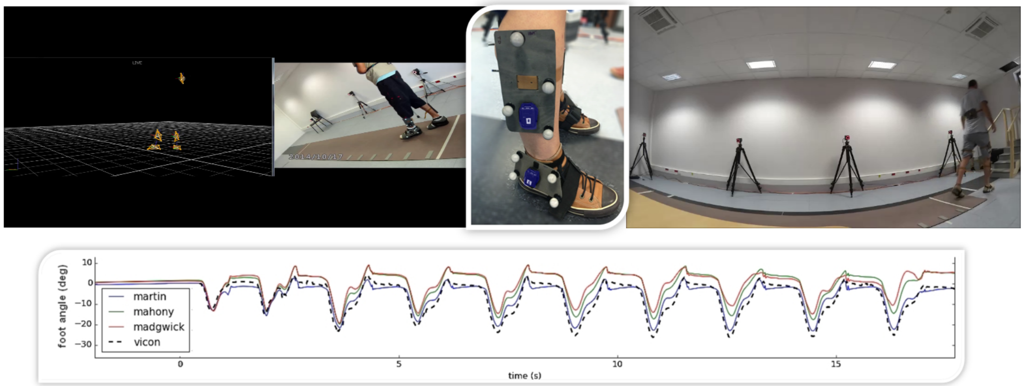


Figure 11. Gait analysis after stroke

Wide-awake surgery of brain tumour is used to optimize the resection of tumoral tissue. Postoperatively, patients show mild and temporary neurological deficits despite massive cerebral resections. Reasons for these impairments along with the compensation mechanisms operating within the cortex and subcortical structures are barely understood. The objective of this project is to reveal the remote effects of the tumour and its resection, to determine their nature measuring changes induced in functional Magnetic Resonance Imagery (fMRI) and electroencephalographic signals using standard and nonlinear methods.

In a first attempt to better understand the direct consequences of wide-awake surgery we focused on the thalamus insofar as, topologically, it is the largest input source and output target of the cortex. It plays a major role in corticosubcortical and corticocortical interactions and is expected to be heavily impacted by the tumour removal while being essential to the recovery process. Studying the thalamus, based on its very particular anatomical properties, could provide essential indications regarding the behaviour of cortical and subcortical centers.

We carried out Amplitude of Low-Frequency fluctuations and Regional Homogeneity analyses on resting state fMRI data before and after the tumour removal, including an original 24h postoperative acquisition. We intended to assess possible changes in spontaneous neuronal activity over time, characterizing different facets of slow-wave hemodynamic fluctuations. We particularly sought evidences of disrupted and atypical neuronal activity emerging within deafferented thalamic subterritories.

This work revealed significant alterations of neuronal activity within distinct thalamic territories, in accordance with its neuro-anatomo-functional organization. We showed a transient decrease of neuronal activity intensity and homogeneity within the ipsilesional thalamus directly related with the anatomical dee- and deafferentation induced by the neurosurgery and a concomitant increase of neuronal activity and temporal synchrony in homologous regions of the contralesional thalamus, leading to a significant interhemispheric imbalance during the immediate postoperative period. Evidences of diaschisis-like phenomenon primarily affecting higher order thalamic nuclei of the ipsilesional thalamus and the extensive involvement of the contralesional thalamus in the postoperative period promote the thesis of transient diaschisis-induced contralesional compensation for patients who underwent wide-awake surgery (Figure 12).

7.2.2. *Understanding the effects of direct electrical stimulation of the brain during wide awake surgery*

Participants: Marion Vincent, François Bonnetblanc, David Guiraud, Hugues Duffau, Mitsuhiro Hayashibe, Olivier Rossel.

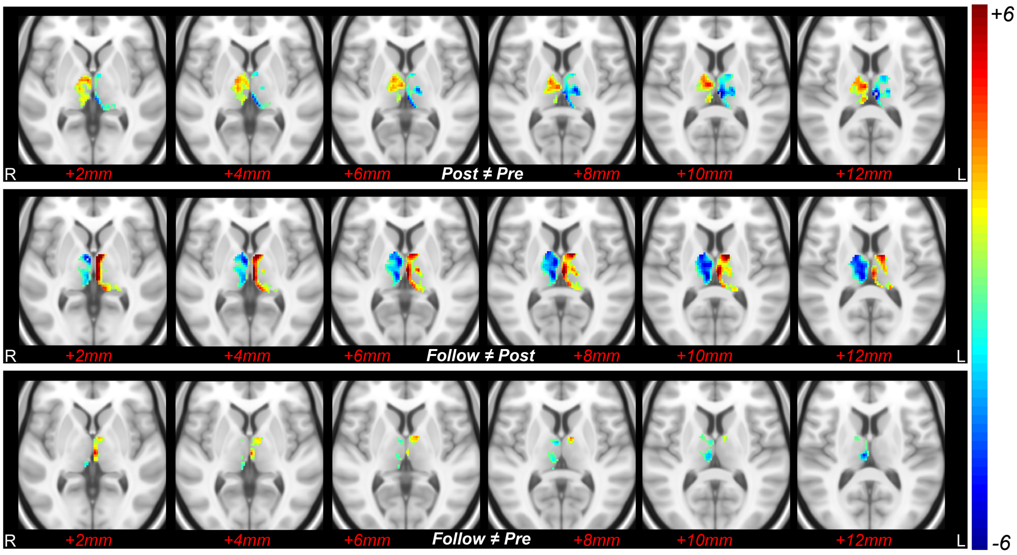


Figure 12. Voxelwise differences in ALFF score over time: ALFF maps were grouped depending on the acquisition date 1_Pre (-48h), 2_Post (+24h), 3_Follow (+3 months) and between-groups contrasts were generated as voxel-wise two-sample t-tests in order to highlight significant differences in scores over time (Post $\neq$ Pre, Follow $\neq$ Post and Follow $\neq$ Pre). Neuroradiological convention.

Real-time functional mapping of the brain combined with direct electrical stimulation (DES) has been widely recommended for the awake neurosurgery of slow-growing and infiltrative brain tumors, to guide the resection [53]. Intra-operative DES is generally applied at 60 Hz in Europe (50 Hz in some other countries) (biphasic stimuli, single pulse duration 1 ms, intensity from 2 to 6 mA under local anesthesia, and during 1 to 5 s). By generating transient perturbations, it allows the real-time identification of both cortical areas and sub-cortical white matter pathways that are essential for the function. Its use lowers the probability of resecting essential functional areas near or within the tumor. However, the electrophysiological effects of DES remain poorly understood, locally and at a more remote distance [36], [9].

The investigation of this topic requires the recording of evoked potential. DES can be used to probe the spatio-temporal connectivity and dynamics of short- or long-range networks in vivo and in real time when combined with electrophysiological recordings (e.g. electroencephalography (EEG) or electroencephalography (ECoG)). This approach has been used for pre-surgical planning of drug-resistant epileptic patients by using an ECoG grid implanted at the surface of the grey matter. Matsumoto et al. [55] sought to measure in vivo connectivity with DES (rather than studying its propagation) but observed that a low-frequency cortical application of DES (1 Hz, constant current, and alternating rectangular wave pulses of 0.3 ms, with an intensity around 10-12 mA) induces 'cortico-cortical' evoked potentials (CCEPs) around 10-50 ms after stimulation. These properties are incompatible with the detection of EPs during awake brain surgery, when DES is classically applied at 60 Hz due to stimulation artefacts. Conversely, 100 ms (i.e. a frequency of 10 Hz) seems to be a sufficient time-window that facilitates real-time averaging to detect these CCEPs for further on-line analysis of brain connectivity during the surgery.

In addition, in the studies mentioned above, ECoG signals were recorded in a classical common mode (CM) configuration, i.e. the signal was measured between each channel of interest and a reference electrode. Also, in all this literature, CCEPs were measured by averaging a large set of trials together. This off-line averaging actually prevents the use of ECoG recording to monitor the evoked potentials on-line. Recently, by lowering the DES frequency to 10 Hz and by using a differential recording mode (DM) for ECoG signals, in which the signal is measured between two adjacent electrodes, we were able to record for the first time on-line CCEPs easily with a standard current amplitude of stimulation (2 ms) and without averaging the data [41] (Figure 13.

Recording ECoG in a DM enabled increasing the focality and the signal to noise ratio of the raw data. Ongoing experiments on new patients corroborate the reproducibility of this protocol. This unusual way of recording ECoG could improve the spatial resolution of the recordings in the three dimensions (in surface and in depth). Moreover, this method was used under general anesthesia but could also be performed on-line during the awake surgery. It would enable the investigation of the connectivity and to probe directly rapid plastic changes of cortical excitability.

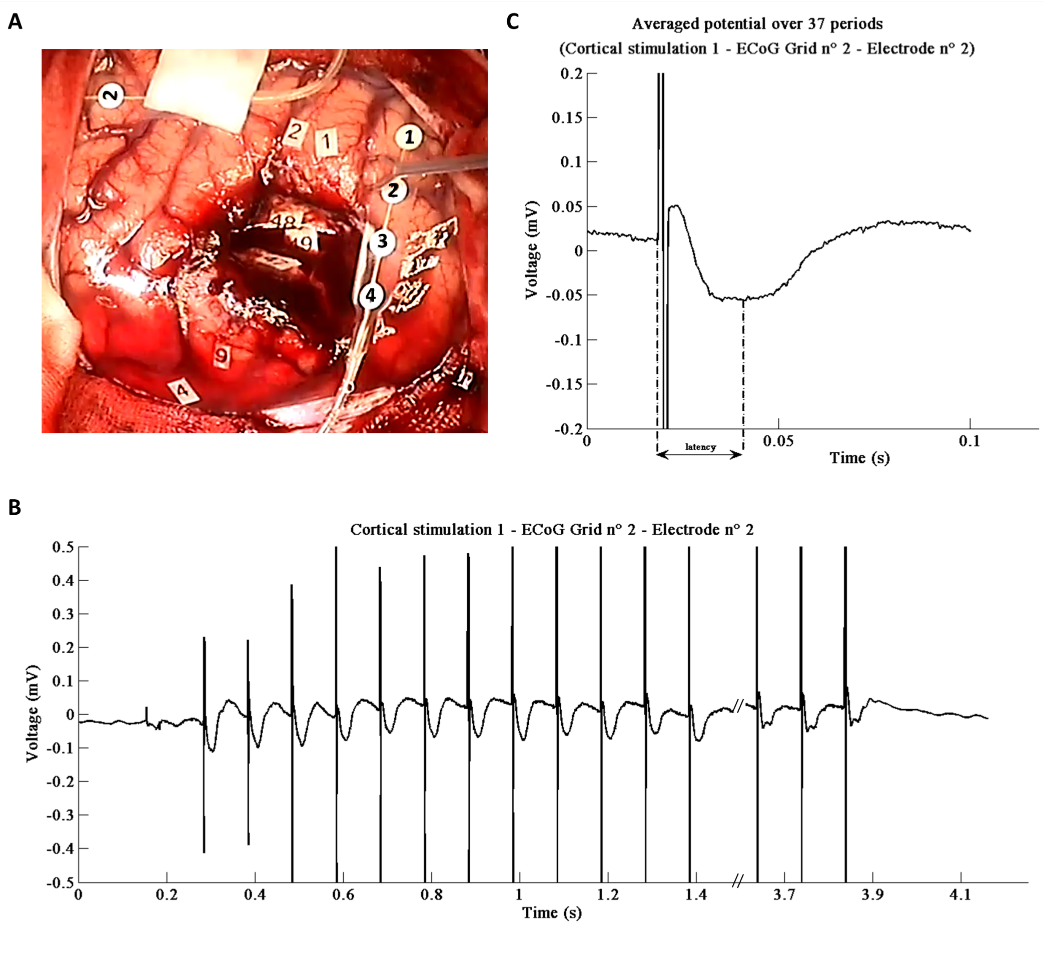


Figure 13. A: DES is applied cortically near the second electrode of the ECoG strip 2 during 3.7 s. B: Magnified view of the ECoG signal corresponding to the stimulation (with the 104 gain). CCEPs can be observed after each stimulation artefact. The last CCEPs are distorted due to the amplifier response. When the amplified signal exceeds the [-5 ; +5] volts range, an oscillation appears. C: Mean CCEP over 37 stimuli, with a latency of 23.7 ± 0.78 ms

7.2.3. A study on the effect of electrical stimulation as a user stimuli for motor imagery classification in Brain-Machine Interface

Participants: Saugat Bhattacharyya, Maureen Clerc, Mitsuhiro Hayashibe.

Functional Electrical Stimulation (FES) provides a neuroprosthetic interface to non-recovered muscle groups by stimulating the affected region of the human body. FES in combination with Brain-machine interfacing (BMI) has a wide scope in rehabilitation because this system directly links the cerebral motor intention of the users with its corresponding peripheral muscle activations. In this paper, we report the preliminary results of the effect of electrical stimulation during a motor imagery training task on healthy subjects and its comparison with visual stimuli.

The experiment designed for this work is divided into three sessions: only visual, only FES and both visual-FES stimuli. The sessions consist of instructing the subjects through a sequence of repetitive stimuli to execute the corresponding motor imagery task, which in our case, is left and right hand movement. The FES session is similar to the visual one except in place of the arrows, stimulation is directly induced in the fore-arm of the hand of interest, without providing any visual information. In the Visual-FES session, both the combined stimulations are time-synchronized to each other. After acquisition, the incoming raw EEG signal is band-pass filtered at 8-30 Hz. Then, common spatial filters (CSP) is applied to extract features relevant to left- and right-motor hand movement EEG signals. CSP is a spatial filter widely used in BMI because the spatial patterns contain highly discriminative features between two classes. In this study, we prepare the feature vectors using 6 spatial filters which is then transferred as inputs to a linear discriminant analysis (LDA) classifier. Finally, the classifier detects the corresponding motor intention of the subject, i.e., left and right motor movement. A block diagram of our experimental setup during Visual-FES session is illustrated in Fig. 14.

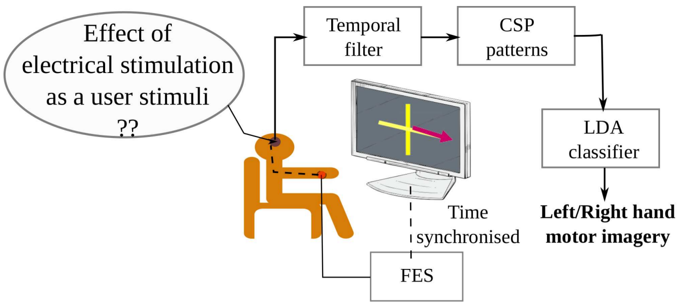


Figure 14. Block diagram of our experimental setup during motor imagery sessions where user stimuli is with conventional visual stimuli, electrical stimulation stimuli or the combined, respectively.

Classification results shows a significant rise in accuracy for 2 (of 3) subjects which suggest a positive influence of FES during motor imagery training of the subjects. It was noted that both the subjects had no previous experience on BMI, then they were not familiar with generating motor imagery with visual stimuli. Visual stimuli are the widely accepted form of motor training but the subject requires constant training to reach an optimal result. Based on the results of this study, we can infer that electrical stimulation can also be used for motor training and it can potentially provide better performance as it can make natural proprioceptive feedback related to motor performance than visual stimuli which requires user's recognition regarding the visual cue.

7.2.4. A Study on the Effect of Electrical Stimulation During Motor Imagery Learning in Brain-Computer Interfacing

Participants: Saugat Bhattacharyya, Maureen Clerc, Mitsuhiro Hayashibe.

Functional Electrical Stimulation (FES) stimulates the affected region of the human body thus providing a neuroprosthetic interface to non-recovered muscle groups. FES in combination with Brain-computer interfacing (BCI) has a wide scope in rehabilitation because this system can directly link the cerebral motor intention of the users with its corresponding peripheral mucle activations. Such a rehabilitative system would contribute to improve the cortical and peripheral learning and thus, improve the recovery time of the patients.

To date, in BCI experiments feedback is commonly provided to the subject by means of a visual medium. On observing the feedback, the subject would attempt to perform his task. It is an interesting notion if one includes electrical stimulation to help in augmenting the performance of the motor task at hand. Thus, in this paper, we report the preliminary results of the effect of electrical stimulation on the learning of the subject during a motor imagery training task on healthy subjects. Through this study, we aim at employing FES as a proprioceptive feedback to the subject to improve the learning of the subject both in terms of accuracy and time.

In this experiment the participants performed four motor tasks: left hand movement, right hand movement, left foot movement and right foot movement across 6 separate sessions. A session provides instructions to the participant through a sequence of visual cues to execute one of the four motor tasks and each visual cue is termed as '*trial*'. Further, for data analysis, each trial are separated into time windows, termed as *epochs*. Each session consists of a feedback session provided visually to the participant at each trial, quantified by the hyperplane distance of the decoder. Before the start of the experiment, the participants undergo a training session for decoder training and to acclimatize to the tasks. Common Spatial Patterns is employed as features which is given as inputs to the Linear Discriminant decoder. The decoder designed in this work is a 2-level hierarchy. The first level classifies between left and right motor imagery and the second level discriminates between hand and foot motor imagery. In 3 of the 6 sessions, surface electrical stimulation (ES) is transmitted to the subject during the feedback period to aid the participant in performing the task. Thus, in this paper, we named the ES induced sessions as FES sessions and the sessions with only visual feedback as VIS sessions.

We report the learning during FES and VIS session feedback for each trial. For this purpose, we measure the distance of the feature vector from the hyperlane for each epoch updated at every 0.125 seconds. We took this parameter to study the feedback effect because the larger the distance from the hyperplane, the higher is the confidence of the classifier to detect the right output. The average feedback curve for all the correctly classified trials of both FES (in blue) and VIS (in red) are shown in Fig. 15. From the curves we assume that greater the slope of the curve, faster is the learning demonstrated by the subject. Subject 1 demonstrates an increasing learning effect (greater slope) for FES feedback for all the limbs, except Right foot as compared to the VIS feedback. The figures for Subject 2 illustrates a more prominent learning effect during FES feedback and it is clearly differentiable for VIS feedback even though Subject 1 showcased a higher increase in accuracy across trials than Subject 2. It is also noted from the figures of both the subjects that VIS feedback has a frequent increasing and decreasing trend of the curve. Subject 3 had a decrease in accuracy during FES feedback as compared to the VIS feedback which can be validated from the figure that the discriminability between the FES and VIS feedback are not as prominent in comparison to the other subjects. We can infer from these results that the electrical stimulation had a positive influence during motor task learning and with an increase in sessions one can assume ES to provide a faster learning. The steady increase of learning during FES sessions can be attributed to the fact that the subjects reported to be more motivated to perform the tasks when an ES was provided and they felt the inclusion of ES helped in their imagination. On the other hand, during VIS sessions the subjects reported to lose motivation in-between the tasks.

7.2.5. NIRS-EEG joint imaging during transcranial direct current stimulation

Participants: Mehak Sood [IIT Hyderabad, India], Pierre Besson [Euromov, UM], Makii Muthalib [Euromov, UM], Utkarsh Jindal [IIT Hyderabad, India], Stéphane Perrey [Euromov, UM], Anirban Dutta, Mitsuhiro Hayashibe.

Transcranial direct current stimulation (tDCS) has been shown to perturb both cortical neural activity and hemodynamics during (online) and after the stimulation, however mechanisms of these tDCS-induced online and after-effects are not known. Here, online resting-state spontaneous brain activation may be relevant to monitor tDCS neuromodulatory effects that can be measured using electroencephalography (EEG) in conjunction with near-infrared spectroscopy (NIRS). We present a Kalman Filter based online parameter estimation of an autoregressive (ARX) model to track the transient coupling relation between the changes

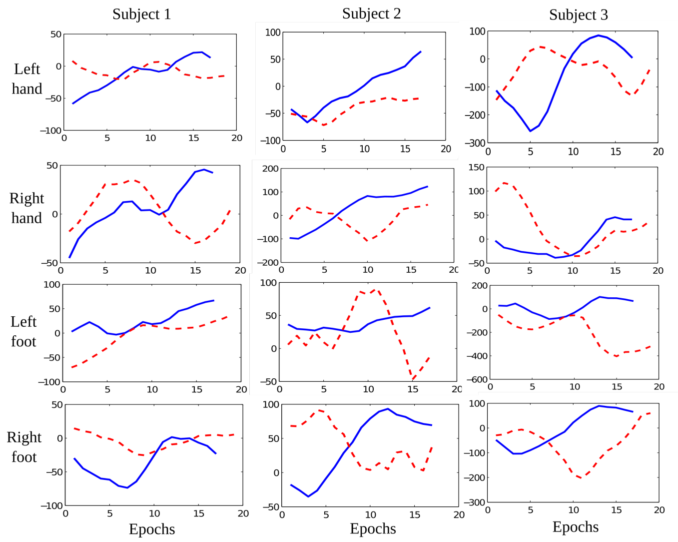


Figure 15. The learning curve of the 3 subjects for the motor imagery correctly classified tasks during FES sessions (in blue –) and VIS sessions (in red –) based on the average hyperplane distance.

in EEG power spectrum and NIRS signals during anodal tDCS (2 mA, 10 min) using a 4x1 ring high-definition montage. Our online ARX parameter estimation technique using the cross-correlation between EEG band-power (0.5-11.25 Hz) and NIRS oxy-hemoglobin signal in the low frequency range was shown in 5 healthy subjects to be sensitive to detect transient EEG-NIRS coupling changes in resting-state spontaneous brain activation during anodal tDCS. Conventional sliding window cross-correlation calculations suffer a fundamental problem in computing the phase relationship as the signal in the window is considered time-invariant and the choice of the window length and step size are subjective. Here, Kalman Filter based method allowed online ARX parameter estimation using time-varying signals that could capture transients in the coupling relationship between EEG and NIRS signals. Our new online ARX model based tracking method allows continuous assessment of the transient coupling between the electrophysiological (EEG) and the hemodynamic (NIRS) signals representing resting-state spontaneous brain activation during anodal tDCS. It is supported by Franco-Indian Inria-DST project funding and by the LabEx NUMEV (ANR-10-LABX-20).

7.2.6. Is EMG a good signal to assess fatigure under FES in different stimulation modes?.

Participants: Willy Fagart, Robin Candau [EUROMOV], Anthony Gelys [Propara Center], Mitsuhiro Hayashibe, David Guiraud.

The study that we have undertaken aims to analyse the neuromuscular fatigue in 3 paralysed subjects with spinal cord injury and to find if there is a link between the torque and the EMG signal. 6 series of 8 trains of stimulation (30 Hz, 400μs, 3 on / 2 off, in maximal intensity) were used to lead a muscular fatigue on the soleus muscle. At the beginning and the end of every series of stimulation, we measured the intermediate state of fatigue by evoking muscular twitch (1Hz, 400 μs and of maximal intensity) on the 2 legs. The temporal component and frequency of electromyographic activity were analyzed. These values were correlated with the torque. At the end of the protocol of stimulation, the torque decreased on 5 legs on 6 (ranging from -39 % to -20 %, p<0,05). A polynomial of degres 2 relation was found between the torque and the peak to peak value of the EMG signal. Nevertheless this relation does not remain reliable in a clinical context with regard to the variability of the data. This variability represents the processes of potentiation of the electric and mechanical answer as well as the expression of the mechanisms which contribute to the muscular fatigue.

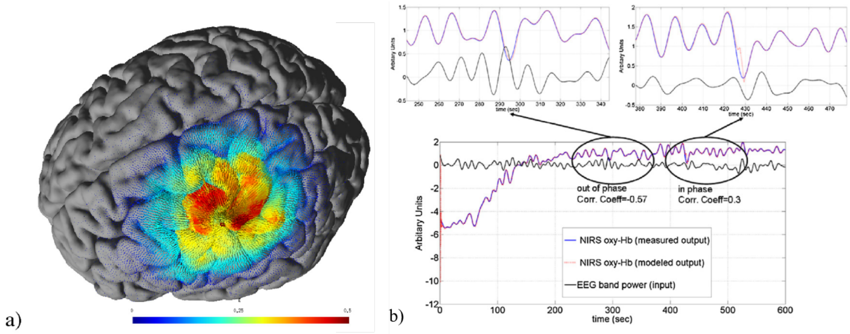


Figure 16. a) Electric field (V/m) estimated at the gray matter surface due to 2 mA anodal HD-tDCS. b) An illustrative example showing the NIRS oxy-Hb signal that was measured (in blue) as well as the predicted NIRS oxy-Hb signal using the ARX online tracking method (in dotted red).

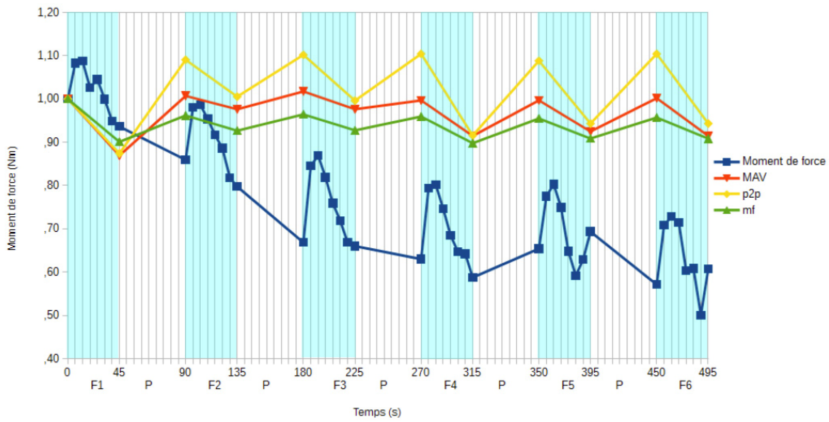


Figure 17. Correlation of different EMG features and torque during (Fn phases) and between (P phases) train of stimulations. Fatigue can be oberved and followed by EMG parameters.

7.2.7. EleVANT project: a diagnostic evaluation of acute stroke by near infrared spectroscopy and transcranial direct current stimulation coupling.

Participants: Victor Vagné, Vincent Costalat, David Guiraud, Emmanuelle Le Bars, Stéphane Perrey [EUROMOV], Olivier Rossel, Mitsuhiro Hayashibe.

Cerebral infarctions can now be treated with new techniques using intravenous thrombolysis and mechanical clearance. Their proven efficacy is directly correlated to the time lapse between the start of symptoms and initiation of treatment. Currently, a definitive diagnosis can only be made once the patient has realized a radiological imaging (CT scan or MRI) on a medical centre equipped with these expensive devices, thus enabling the medical team to initiate the appropriate treatment. Transit times during the pre-hospitalisation phase before diagnosis are therefore often longer and have the greatest negative impact on the patient's prognosis. The association of NIRS and tDCS enables recording modifications in cortical tissue oxygenation induced by electrostimulation. A case-control study demonstrated the capacity of near infra-red spectroscopy (NIRS), combined with transcranial direct current stimulation (tDCS) to diagnose established cerebral ischaemia. According to this study, the affected hemisphere with impaired circulation showed significantly less change in cerebral hemoglobin oxygenation than the healthy side in response to anodal tDCS. This preliminary study showed the feasibility of identifying the lesioned hemisphere in subacute stroke patient. In collaboration with Gui de Chauliac Hospital, I2FH and Euromov, the EleVANT project is aiming to prospectively evaluate the NIRS-tDCS technique in the diagnosis of acute cerebral ischaemia. This low cost technology could be used in a mobile way for the very early diagnosis of cerebral infarction and thus reduce treatment delays, opening the way to a new generation of diagnostic tools. A first NIRS-tDCS helmet prototype was developed to gather our Oxymon NIRS and Starstim tDCS devices, allowing good optodes-scalp and electrodes-scalp contact, while reducing both movement artifact and set-up time. This helmet was improved steps by steps as tests were done to attempt several parameters (among others electrodes location, amplitude and time of stimulation). A 4 NIRS optodes and 2 electrodes montage was retained to test and validate the proof of principle. Preliminary results are encouraging and need further investigation to be strongly validated.

Otherwise, as effects of anodal tDCS on hemodynamic response remain discussed, we'll proceed in parallel with the establishment of MRI protocols to attempt a validation of these effects.

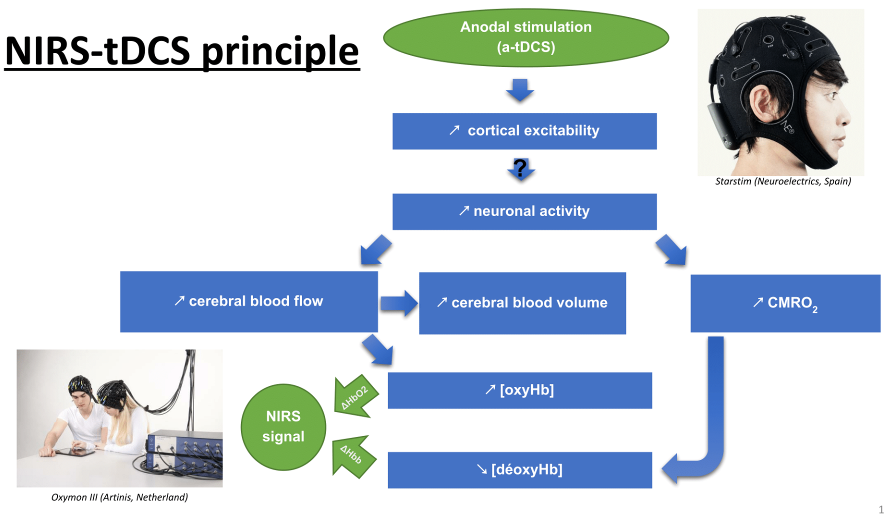


Figure 18.

7.3. Synthesis and Control of Human Functions

7.3.1. FES-assisted cycling in SCI individuals

Participants: Christine Azevedo Coste, Benoît Sijobert, Charles Fattal, Anne Daubigney [COS Divio, Dijon], Jérôme Parent, Antonio Padilha Bo [University Brasilia], Emerson Facin Martins [University Brasilia], Lucas Fonseca [University Brasilia], Juliana Guimaraes [University Brasilia].

During more than one year we have prepared one complete paraplegic patient to participate into FES-cycling discipline at Cybathlon 2016. A research protocol was associated to this physical preparation and several variables have been monitored during the training in order to evaluate performances, physical and psychological state. We have also developped a FES tricycle dedicated to the competition. We have modified a commercial trike and a commercial electrostimulator in order to have a mid cost system, adapted to complete paraplegia, easy to transport and compatible with safe transfers between wheelchair and trike seat. Our pilot reached the objectives: participating into the race, being qualified and cycle 750m in less than 8mn. He has been able during his training to cycle 1km200 in 13mn (fig.19).
In parallel, within CACAO associate team context, our Brazilian partner has trained several pilots using a similar training protocol [24], [22].

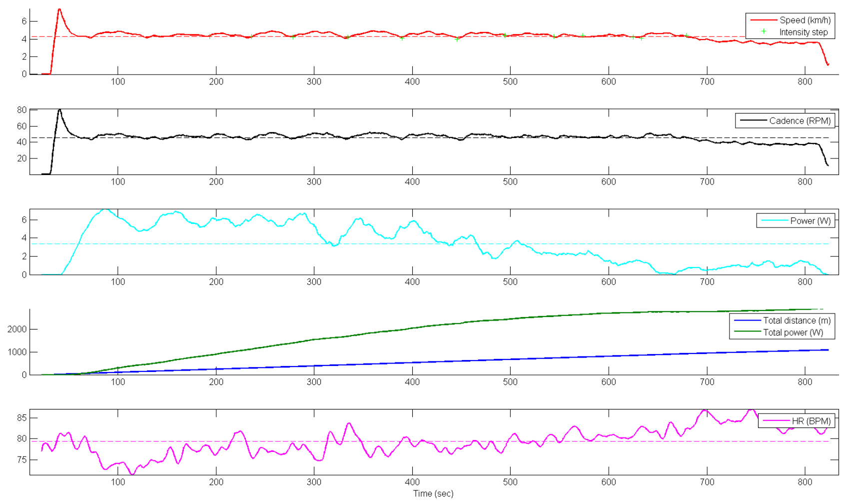


Figure 19. Best cycling performance. From top to bottom: speed (km/h), cadence (RPM), power (W), total distance (m) vs power (W), heart rate (BPM).

7.3.2. FES-assisted transfer in SCI individuals

Participants: Christine Azevedo Coste, Charles Fattal, Emerson Facin Martins [University Brasilia], Lucas Fonseca [University Brasilia], Ana Claudia Lopes [University Brasilia], Roberto Baptista [University Brasilia], Claudia Ochoa [University Brasilia].

One of the research axes investigated in CACAO associate team with Brasilia University is the assistance of seat to seat transfers in spinal cord injured (SCI) individuals. We have initated a research protocol to evaluate the feasibility to reduce arm efforts during pivot transfers by using feet support provided by lower limb muscles stimulation. 2 complete paraplegic patients were included for pilot experiments. Transfer is a key ability and allows greater interaction with the environment and social participation. Conversely, paraplegics have great risk of pain and injury in the upper limbs due to joint overloads during activities of daily living, like transfer. Preliminary results were promissing [30]. Further inclusions will be achieved to confirm these preliminary observations.

7.3.3. *New cueing modality for Parkinson Disease*

Participants: Christine Azevedo Coste, Benoît Sijobert, Christian Geny [CHU Montpellier].

Parkinson's Disease (PD) is the second most common neurodegenerative disorder in the world. It is often related to gait impairments and to a high risk of falls. Among different consequences of this disease, the Freezing of Gait (FOG) is defined as an episodic inability to generate an effective stepping. Subjects report the feeling of having their feet "glued to the ground". Numerous studies used auditory or visual stimulus to prevent FOG to happen.

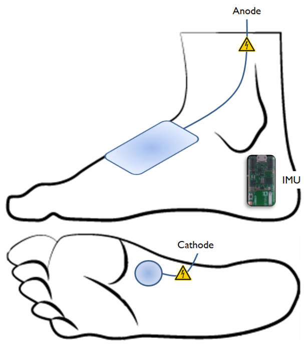


Figure 20. New cueing modality for Parkinson Disease. Electrodes and inertial sensor localization.

In our study, we aimed to investigate the effect of a sensitive cueing on gait disorders in subjects suffering from PD for improving gait and for reducing FOG occurrence. 13 participants with PD were equipped with an electrical stimulator and an inertial measurement unit (IMU) located under the lateral malleolus on the sagittal plane. Electrodes were positioned under the arch of the foot (Fig. 20) and electrical stimulation (ES) parameters adjusted to deliver a sensitive signal. Based on previous studies we achieved using IMU in Parkinson's Disease [52], [51], [56], in this protocol online IMU signal was processed in order to trigger ES at heel off detection (Fig. 21). Starting from a quiet standing posture, subjects were asked to walk at their preferred speed on a path including 5m straight line, u-turn and walk around tasks. 3 situations were considered: no stimulation baseline pre-condition, ES condition, no stimulation baseline post-condition. In ES condition the time to execute the different tasks was globally decreased in all the subjects. In "freezer" subjects, the time to complete the entire path was reduced by 19%. Freezing of Gait (FOG) episodes occurrence was decreased by 12% compared to baseline conditions. This preliminary work showed a positive global effect on gait and FOG in PD of a somatosensory cueing based on sensitive electrical stimulation [32].

7.3.4. *Selective neural electrical stimulation of the upper limb nerves*

Participants: Christine Azevedo Coste, David Guiraud, Wafa Tigra, Jacques Teissier [Clinique Beausoleil], Bertrand Coulet [CHU Montpellier], Charles Fattal, Anthony Gelis [Clinique PROPARA].

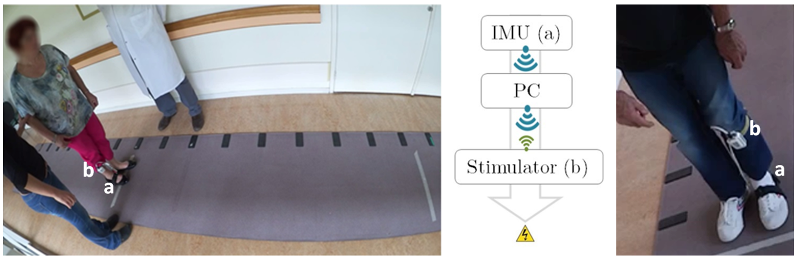


Figure 21. New cueing modality for Parkinson Disease. Experimental setup description.

We have experimented a new approach of selective neural electrical stimulation of the upper limb nerves of two tetraplegic patients. Median and radial nerves are stimulated via a multipolar cuff electrode to elicit movements of wrist and hand in acute conditions during a surgical intervention. Various configurations corresponding to various combinations of a 12- poles cuff electrode contacts are tested. Video recording and electromyographic (EMG) signals recorded via sterile surface electrodes are used to evaluate the selectivity of each stimulation configuration in terms of activated muscles. We succeed to elicit graduated extension of wrist and fingers and graduated wrist flexion. We have also experimented a new human-machine interface to, at term trigger this electrical stimulation by individuals with tetraplegia. We investigated the feasibility of piloting an assistive device by processing supra-lesional muscle responses online. The ability to voluntarily contract a set of selected muscles was assessed in five spinal cord-injured subjects through electromyographic (EMG) analysis. Two subjects were also asked to use the EMG interface to control palmar and lateral grasping of a robot hand (Fig. 22). The use of different muscles and control modalities was also assessed. All patients are able to contract some of the evaluated muscles, preferential mode of pilot is patient dependent (Fig. 23).

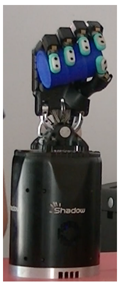


Figure 22. Closure posture of the Shadow robotic hand in the palmar grasp situation.

7.3.5. Spinal cord stimulation investigation

Participants: Christine Azevedo Coste, David Guiraud, Thomas Guiho, Charles Fattal, Luc Bauchet [CHU Montpellier].

Spinal cord injury results in the loss of movement and sensory sensations but also in the disruption of some organ functions. Nearly all spinal cord injured subjects lose bladder control and are prone to kidney failure if they do not apply intermittent (self-) catheterization. Electrical stimulation of the sacral spinal roots with an implantable neuroprosthesis is one option besides self-catheterization to become continent and control micturition. However, many persons do not ask for this neuroprosthetic device (Brindley-Finetech implant)

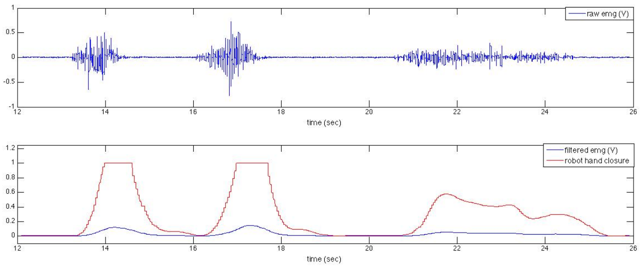


Figure 23. Robot hand trajectories generated from EMG recording for proportional mode. Top: raw EMG, bottom filtered EMG (blue) and hand trajectory (red). 0: hand is open, 1: hand is closed.

since deafferentation and loss of sensory functions and reflexes are serious side effects and since alternative treatments are available to patients (drugs, botulinus toxin. . . .). This PhD work aimed at investigating various techniques for spinal cord electrical stimulation in order to address dysfunctions in spinal cord injured individuals on lesion levels that have an impact on lower limb movements and bladder, bowel and sexual functions. Orderly recruitment of fibers at the spinal cord level should eventually lead to orderly recruitment of the detrusor muscle without activation of the bladder sphincter. Thereby, low pressure voiding, for example, should be obtained but is currently impossible with existing active implantable medical devices. A new large animal model – the domestic pig – was investigated to overcome size effects of rodent models and be able to translate results and technology more easily to human. [23].

7.4. Neuroprostheses and technology

7.4.1. Fast simulation and optimization tool to explore selective neural stimulation

Participants: Mélissa Dali, Olivier Rossel, David Guiraud.

In functional electrical stimulation, selective stimulation of axons is desirable to activate a specific target, in particular muscular function. This implies to simulate a fascicule without activating neighboring ones i.e. to be spatially selective. Spatial selectivity is achieved by the use of multicontact cuff electrodes over which the stimulation current is distributed. Because of the large number of parameters involved, numerical simulations provide a way to find and optimize electrode configuration. The present work offers a computation effective scheme and associated tool chain capable of simulating electrode-nerve interface and finds the best spread of current to achieve spatial selectivity. The software is protected to « Agence de Protection des Programmes « (APP), with the name MOS2SENS and identification IDDN.FR.001.490036.000.S.P.2014.000.31230 [21]

7.4.2. Numerical simulation of multipolar configuration

Participants: Mélissa Dali, Olivier Rossel, David Guiraud.

In the context of functional electrical stimulation of peripheral nerves, the control of a specific motor or sensory functions may need selective stimulation to target the desired effect without others. In implanted stimulation, spatial selectivity is obtained using multipolar CUFF electrodes with specific spread of the current over each contact. Furthermore, electrical stimulation recruits large fibers before small ones, whereas the targeted function could be elicited by a specific fiber type i.e. fiber diameter. In our work, numerical simulations were used to investigate the combination of multipolar configuration and prepulses, in order to obtain spatially reverse recruitment order. Multipolar stimulation provides efficient spatial selectivity, whereas subthreshold prepulses were used to reverse recruitment order with a reasonable increase of the injected charges. We compared several selective configurations combined with prepulses to show that some are able to guarantee both the spatial selectivity while one fiber's diameter can be preferentially activated [42].

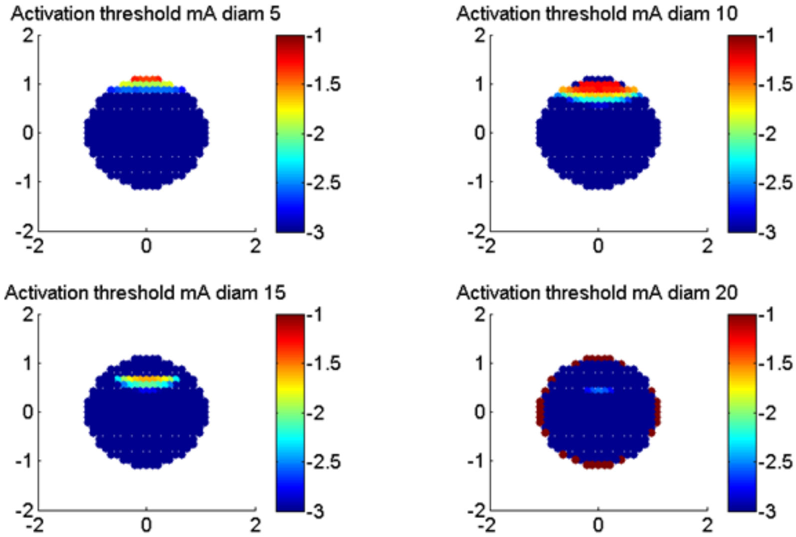


Figure 24. Spatially reverse recruitment order for fiber from 5µm to 20µm diameter obtained by multipolar configuration and prepulse technique

7.4.3. Formal validation for critical embedded systems

Participants: Ibrahim Merzoug, Karen Godary-Dejean, David Andreu.

The works addressed here fall under the domain of formal modelling, semantics and verification methods (model checking). We focus on the analysis part of the HILECOP methodology, integrating the specific execution constraints (non-functional properties) into the validation process to guarantee the validation results. Indeed, the state space that is analyzed is that of the model of the system. It is clear that, if we want to obtain confident validation results, this analyzed state space must include all the possible behaviors of the real system, i.e., when it is executed.

One solution has been studied in the PhD thesis of H. Leroux [54], which lays the foundations of translation rules from the designed model to the analyzed model integrating both implementation and execution constraints. These transformations rules allow analyzing the resulting model with classical Petri nets analysis tools (as the Tina toolbox, and to guarantee the inclusion of the real states and traces into the analyzed state space.

A well-known drawback of such approach is that model checking is a technique that achieves properties verification through an exhaustive analysis of the state graph of the system model. The main limitation of this technique is the state space explosion problem because of its intrinsic exhaustivity. In a first part of the thesis (2015-2016), we proposed a compact state graph, called the Reduced Graph (see figure 25), which preserves all sequences of transitions firing as well as minimal and maximal duration of each sequence. To do so, we extend the partial order semantics to define temporal parallelism relations. According to covering steps approach, we compute our reduced graph reducing transitions interleaving, while keeping potential parallelism information.

But using classical analysis tools forces to analyze an over-set of the real behaviors, which limits the analytical capacities. In particular, the classical semantics of Petri nets considers an asynchronous execution, while in our context they are synchronously executed on FPGA with real parallelism and clock synchronization. Thus, we propose a new states graph which takes into account all the implementation and execution constraints related

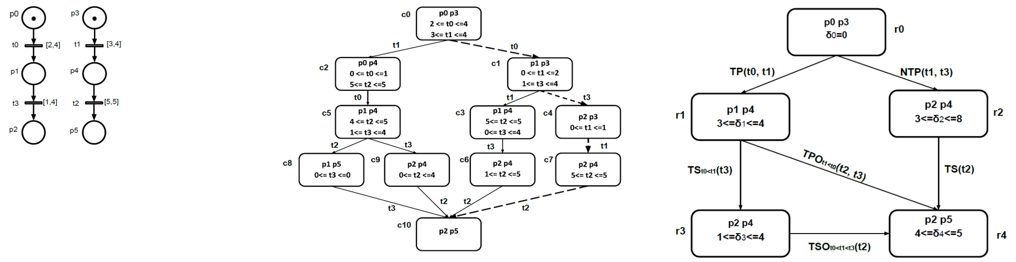


Figure 25. a Time Petri net, its classical State Class Graph and our Reduced Graph

to the target hardware (non-functional properties): the Synchronous Behaviour Graph (SBG). We formally defined the graph and its semantics, illustrating this method on a simple example (see Figure 26). Then, we apply our method on a real industrial model, which is the execution engine embedded in our neurostimulator.

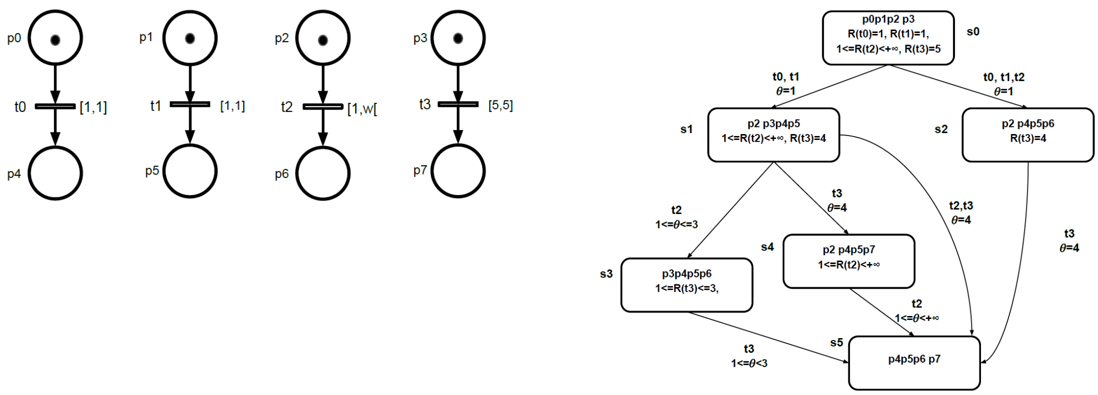


Figure 26. a Time Petri net and its Synchronous Behaviour Graph.

7.4.4. Control and scheduling co-design for stimulation systems

Participants: Daniel Simon, Zineddine Djellouli, David Andreu.

Functional Electrical Stimulation (FES) is used in therapy for rehabilitation or substitution for disabled people. They are control systems using electrodes to interface a digital control system with livings. Hence the whole system gathers continuous-time (muscles and nerves) and discrete-time (controllers and communication links) components. During the design process, realistic simulation remains a precious tool ahead of real experiments to check without danger that the implementation matches the functional and safety requirements [14]. To this aim a real-time open hybrid simulation software has been developed. It is dedicated to the analysis of FES systems deployed over distributed execution resources and wireless links. The simulation tool is especially devoted to the joint design and analysis of control loops and real-time features [6].

Such simulator can be used for the design, testing and preliminary validation of new technologies and implementation. For example, it has been used to evaluate extensions of the STIMAP wireless communication protocol to optimize the network bandwidth when using multiple stimulation sites and control loops. Thanks

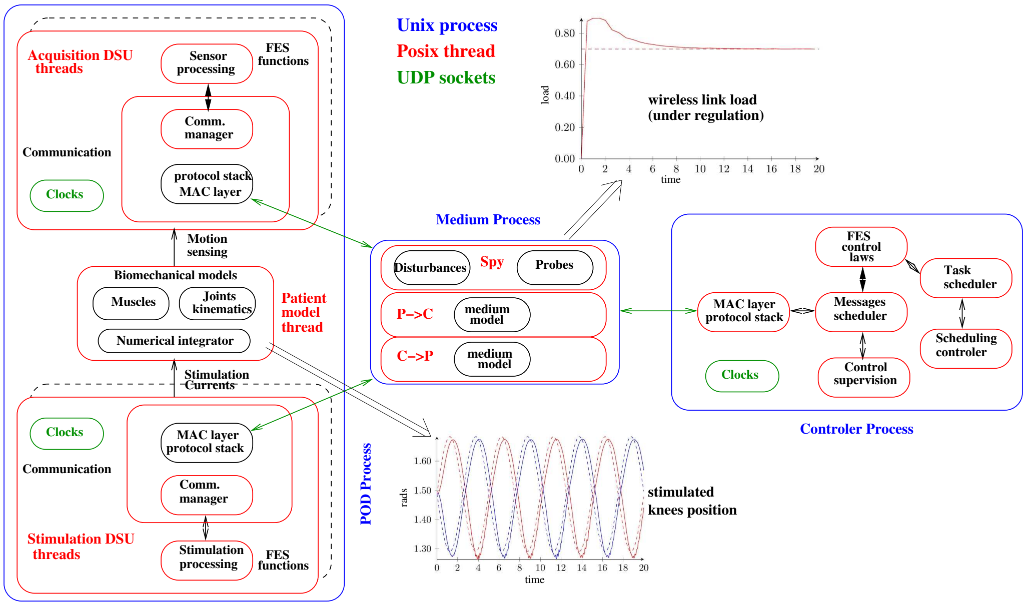


Figure 27. Real-time hybrid simulation architecture

to the hybrid nature of the simulation tool, the effect of the enhanced protocol can be directly observed on the controller output (e.g., concurrent controllers running to control several joints).

Another use is for the evaluation of closed-loop controllers acting on the execution resources of the distributed system. This approach provides adaptability and robustness, allowing for the design of fault-tolerant systems against varying and uncertain operating conditions [48]. It is especially usefull for embedded systems where these resources are scarce and fragile, as for the limited bandwith of wireless links between controllers and stimulation probes. Hence, a simple PI controller has been applied to the (m,k)-firm scheduling policy of control messages sent over the wireless link between the control device and the stimulation probes. It has been observed that such simple scheduling controller is able to jointly regulate both the communication load and the joints control quality.

8. Bilateral Contracts and Grants with Industry

8.1. Bilateral Contracts with Industry

FUI MMCD (Multifunctions Modular Cockpit Display) [2014-2017] Labels : Pegase, ASTech
The MMCD project (Multi Functions Modular Cockpit Display) aims at designing a mechatronic architecture that is modular, certifiable and evolutive in terms of embedded GPU. This project will contribue to Avionics 2020 by developping a mock-up of new cockpit display system, allowing easy to manage GPU evolution.
Our contribution concerns formal design and prototyping of embedded supervisory functions, using the HILECOP methodology and tool.

8.2. Bilateral Grants with Industry

CIFRE phd financial support with Axonic (PhD grant), Wafa Tigra, 2013-2016, restoration of grasping using FES and selective stimulation

9. Partnerships and Cooperations

9.1. Regional Initiatives

- LABEX NUMEV (postdoc):

  Participants: Mitsuhiro Hayashibe, Denis Mottet (EUROMOV).

  A 1-year postdoc was funded by the NUMEV Labex on "Control of Arm Synergies After a Stroke (CASAS)".
- LABEX NUMEV (PhD grants co-fundings): Participants: Christine Azevedo, David Andreu, Benoit Sijobert.
  Participants: Sofiane Ramdani, François Bonnetblanc, Anthony Boyer.

9.2. National Initiatives

- BCI-LIFT: an Inria Project-Lab Participants : Mitsuhiro Hayashibe, Saugat Bhattacharyya.

  BCI-LIFT is a large-scale 4-year research initiative (2015-2018) which aim is to reach a next generation of non-invasive Brain-Computer Interfaces (BCI), more specifically BCI that are easier to appropriate, more efficient, and suit a larger number of people. We work on BCI-FES study for promoting motor learning.
- ADT PersoBalance2

  Participants : Mitsuhiro Hayashibe, Philippe Fraisse.

  A half-year engineer was funded by Inria ADT on "Personalized Balance Assessment in Home Rehabilitation, version2 (PersoBalance2)".

9.2.1. Excellence intitiative, PSPC

- Project INTENSE 2012-2018
- Leader: LIVANOVA
- Partners: LTSI, INRA Rennes, CEA LETI, HEGP, CHU Rennes, MXM-Axonic, 3D+
- the aim of the project is to treat severe obesity and cardiac failure through Vagus Nerve Stimulation (VNS). Our contirubution concerned the development of innovative hardware and software architecture to allow for selective stimulation. We developped the models that were used to optimize the settings of the stimulators taking into account the geometry of the 12-pole neural electrode. The selectivity and the efficacy of the stimulation were also improved through the study of original stiumulus waveforms. As a whole the idea was to further enhance the therapy while limiting the side effects that VNS my induce.
- the cardiac application stops end of august due to internal decisions at LIVANOVA but the obesity application continues to be investigated.

9.3. European Initiatives

9.3.1. FP7 & H2020 Projects

Program: FP7

Project acronym: EPIONE

Project title: Natural sensory feedback for phantom limb pain modulation and therapy

Duration: 2013-2017

Coordinator: AAU (Aalborg, Denmark)

Other partners: Ecole polytechnique fédérale de Lausanne (EPFL), IUPUI (Indianapolis, USA), Lund University (LUNDS UNIVERSITET), MXM (Vallauris, France), Novosense AB (NS), IMTEK (Freiburg, Germany), UAB (Barcelona, Spain), Aalborg Hospital, Universita Cattolica del Sacro Cuore (UCSC), Centre hospitalier Universitaire Vaudois (CHUV)

Abstract: http://project-epione.eu/. The aim of the project is to treat phantom limb pain. CAMIN is only involved in the invasive approach using intrafascicular electrodes. We developed certified software with EPFL and AAU, co-supervised animal tests and data processing with UAB, provide support to clinical trials with IMTEK and UCSC and developped a new stimulator with MXM.

9.4. International Initiatives

9.4.1. Inria Associate Teams Not Involved in an Inria International Labs

9.4.1.1. NEUROPHYS4NEUROREHAB

Title: Development of neurophysiological test setup for customizing and monitoring patient-specific non-invasive electrical stimulation-facilitated neurorehabilitation.

International Partners (Institution - Laboratory - Researcher):

IITH (India) - Centre for VLSI and Embedded Systems Technology - Shubhajit Roy Chowdhury

IIT Gandhinagar (India) - Department of Electrical Engineering- Uttama Lahiri

Start year: 2014

See also: https://team.inria.fr/nphys4nrehab/

Stroke presents with heterogeneous patient-specific impairments in motor, sensory, tone, visual, perceptual, cognition, aphasia, apraxia, coordination, and equilibrium where the functional limitations following stroke are varied, including gait dysfunction, fall risk, limited activities of daily living, difficulties in swallowing, reduced upper extremity function, altered communication, besides others. These heterogeneous patient-specific impairments make planning of the neurorehabilitation therapy challenging. Here, it may be important to stratify the stroke survivors for restorative neurorehabilitation based on the prognosis and the ability of the stroke survivor to undergo therapy depending on their cardiovascular and neuromuscular capacity besides psychological factors such as motivation where the therapy needs to be tailored to individual health condition. The WHO International Classification of Functioning (ICF) model recommends intervention at multiple levels (e.g., impairment, activity, participation) where environment and personal factors can play an important role in resource-limited India. In fact, deconditioned chronic stroke survivor will need to recondition their cardiovascular endurance, metabolic fitness, and muscle conditions with a gradual increase in the intensity (number of hours per day) and frequency (number of days per week) of therapy, providing a higher level as they improve their function. Towards that overarching goal in a low-resource setting, we propose development of neurophysiological screening and monitoring tools using low-cost sensors.

9.4.1.2. CACAO

Title: Lower limb electrical stimulation for function restoration

International Partner (Institution - Laboratory - Researcher):

UNB (Brazil) - NTAAI - FACHIN-MARTINS Emerson

UNB (Brazil) - LARA - Padilha-Bo Antonio

Start year: 2016

See also: https://team.inria.fr/cacao/

Electrical stimulation (ES) can activate paralyzed muscles to support rehabilitation. ES applied to fully or partially paralyzed muscles artificially induces muscle contraction substituting or completing the normal volitional control. In CACAO team we will join our efforts and specific expertise to develop approaches of lower limb function restoration in spinal cord injured individuals. Two main applications will be addressed: 1) Functional Electrical Stimulation (FES) to assist SCI individuals to perform pivot transfers and 2) FES-assisted cycling (we already jointly prepared and participated to CYBATHLON'16). We aim at proposing solutions that can have an effect on patients' quality of life, thus our choices intend to be realistic form a practical point of view. We will take care in evaluating both functional and psychological effects of our solutions and to constrain technical choices to be acceptable by final user. CACAO project will be a good opportunity to combine "bioengineer" (DEMAR) and "physiology/rehabilitation" (NTAAI) visions and knowledges towards solutions for clinical applications.

9.5. International Research Visitors

9.5.1. Visits to International Teams

9.5.1.1. France-Stanford program

The Executive Committee of the France-Stanford Center for Interdisciplinary Studies supported our collaboration (§7.1.1) with Prof. Jessica Rose (Department of Orthopaedic Surgery, Stanford University). As part of the collaboration, Professor Rose presented a keynote lecture on Artificial Walking Technologies for Neuromuscular stimulation-assisted Gait for children with cerebral palsy at the International Functional Electrical Stimulation Society (IFESS) conference hosted by CAMIN. In July, a Benoît Sijobert spent 2 weeks in July 2016 to setup the experiment and Christine Azevedo Coste 1 week to run experiments.

9.5.1.2. Asgard program

From may 5 to may 13, François Bonnetblanc visited The Endestad Brain Imaging Group, the Institute of Basic Medical Sciences, Akershus universitetssykehus HF, Sunnaas Sykehus HF, UiO Department of Psychology, and the Norwegian School of Sport Sciences in Norway thanks to the Asgard programme. (http://www.france.no/if/oslo/cooperation/sciences/programmes-sciences/asgard/)

A shared project about the closed-loop stimulation of urinal control of pigs has been proposed with the Institute of Basic Medical Sciences in the framework of Aurora (followup of Adgard).

9.5.1.3. Research Stays Abroad

Christine Azevedo Coste spent 2,5 months (November 2015-February 2016) at Brasilia University as an invited researcher in collaboration within Emerson FACHIN-MARTINS responsible of the NTAAI (Nucléo de Tecnologia Assistiva, Acessibilidade e Inovacão) initiative.
Brazilian program: Science without borders (Ciencías sem fronteiras) CAPES. She spent 10 days in May 2016 together with Charles FATTAL to perform experiments.

Mitsuhiro Hayashibe was invited to participate to JSPS Program: Program for Advancing Strategic International Networks to Accelerate the Circulation of Talented Researchers. (PI Prof. Hitoshi Hirata, Dep. of Med. Nagoya Univ.)(Feb. 2016)

Mitsuhiro Hayashibe was visiting Researcher at EPFL, BIOROB supported by Swiss National Science Foundation (Sep.-Oct. 2016)

10. Dissemination

10.1. Promoting Scientific Activities

10.1.1. Scientific Events Organisation

10.1.1.1. General Chair, Scientific Chair

Christine Azevedo Coste was general chair of IFESS conference. http://ifess2016.inria.fr

M. Hayashibe is Co-Chair of IEEE Technical Committee on Human Movement Understanding at Robotics and Automation Society with E. Demircan (Univ. of Tokyo), D. Kulic (Univ. of Waterloo) and D. Oetomo (Univ. of Melbourne). https://sites.google.com/site/ieeehmu/

10.1.1.2. Member of the Organizing Committees

François Bonnetblanc, Mitsuhiro Hayashibe were membres of the IFESS organizing committee;

We organized the third European Computational Motor Control Summer School, June 26- July 2, 2016, Montpellier (Nicolas Schweighofer, Denis Mottet, Mitsuhiro Hayashibe) and Mitsuhiro Hayashibe organized Hands-on seminar for Friday July 1st. Motor Synergies. (AM : Andrea D'Avella, PM: Mitsuhiro Hayashibe)

10.1.2. Scientific Events Selection

10.1.2.1. Member of the Conference Program Committees

- David Guiraud was associate editor of Theme 6 (rehabilitation Engineering) at IEEE EMBC conference
- David Guiraud was member of the IFESS program committee
- François Bonnetblanc was member of the IFESS program committee
- David Andreu was member of the IFESS program committee
- Mitsuhiro Hayashibe was member of the IFESS program committee
- Daniel Simon, ETFA 2016 and ICINCO 2016
- Mitsuhiro Hayashibe was Associate Editor of IEEE ICRA'17 (International Conference on Robotics and Automation) in charge of handling reviews on 6 papers in Nov.2016.

10.1.2.2. Reviewer

- Christine Azevedo was reviewer for IFESS and Engineering in Medicine and Biology Conference conferences
- David Guiraud was reviewer for IFESS, IEEE EMBC conferences
- François Bonnetblanc was reviewer for the IFESS and IEEE EMBC conferences;
- Daniel Simon was reviewer for the ETFA, ICINCO and MED conferences;
- Karen Godary-Dejean was reviewer for the IROS conference

10.1.3. Journal

10.1.3.1. Member of the Editorial Boards

M. Hayashibe is member of the Editorial Board of the International Journal of Advanced Robotic Systems, in Rehabilitation Robotics. David Guiraud is member of the editorial board of Journal of Neural Engineering (JNE) M. Hayashibe is member of the Editorial Board of ROBOMECH Journal.

10.1.3.2. Reviewer - Reviewing Activities

- François Bonnetblanc was reviewer for Cerebral Cortex, Neuropsychologia, and for the Journal of Neurophysiology;
- David Guiraud was reviewer for IEEE TNSRE, IEEE TBME, JNE, MEP, IEEE TBIOCAS, JNER, IEEE TCSC, journals
- Christine Azevedo was reviewer for Gait and Posture, IEE Transactions on Robotics (TRO), Artificial Organs, IEEE Journal of Biomedical and Health Informatics, IEEE Transactions on Biomedical Engineering (TBME) and IEEE Transactions on Neural Systems and Rehabilitation Engineering (TNSRE) Journals

10.1.4. Invited Talks

Mitsuhiro Hayashibe gave 2 talks on "Personalized Neuroprosthetics" and " Synergetic Learning Control" for LSRO and BIOROB labs, EPFL respectively at October 2016 (Lausanne, Switzerland).

Mitsuhiro Hayashibe gave a talk on "Synergetic Learning Control Paradigm - Computational Motor Control Principle" at Workshop Human Motor Control and Learning (EUROMOV, Montpellier) on November 21th 2016. In this workshop, Prof. Mark L. Latash (Pennsylvania State University, USA) and Dr. Yen-Hsun Wu were also invited.
Christine Azevedo gave a talk on "Neuroprosthetics in functional assistance: from observation to artificial control of movement" at EUROMOV, Montpellier on November 10th 2016.
Christine Azevedo gave a lecture at the International Symposieum on Electrical Stimulation Applied to Assistive technologies at Brasilia University in May 2016
Christine Azevedo gave a lecture at Genoploys center in June 16th ithin RUREKA cycle of conferences

10.1.5. Leadership within the Scientific Community

Christine Azevedo Coste is member of the board of International Functional Electrical Stimulation Society.

10.1.6. Scientific Expertise

Karen Godary-Dejean is member of COSTI «Acquisition de données traitement et visualisation de données numériques – Mécatronique » at Transfert LR, and member of the tranfer commission at LIRMM.

10.1.7. Research Administration

Christine Azevedo Coste is member of Inria Evaluation Committee.
She is involved in the working group for DEFROST and CHROMA Inria teams creation.
David Guiraud is involved in the working group for BIOVISION Inria team creation.

10.2. Teaching - Supervision - Juries

10.2.1. Teaching

- Master : Christine Azevedo, Ethics consideration in bioengineering research, 3h, M1, Master STIC SANTÉ, Montpellier University, France
- Master: Mitsuhiro Hayashibe, Neuroprotheses I and II (module coordinator), EMG and EEG signal processing and other rehabilitation modeling issues, 12h, Master STIC pour la Sante, Univ. de Montpellier, France;
- Master: Karen Godary-Dejean, computer engineering: embedded network, real time, DES (Discrete event system) modeling and control, dependability, formal validation, 230h, Polytech Montpellier.
- Master: David Guiraud, FES and Neuroprosthesis, M2 SMH, 12h, M1 and M2 Stic Santé 6h
- Master : D. Andreu, Software engineering, real time OS, discrete event systems, control architectures, networks, neuro-prosthesis, 200h, master and engineers degrees, Polytech Montpellier, France;

The team is leading 2 modules in Master Stic-Santé in Montpellier: Neuroprosthesis I (HMSN216) and II and (HMESN321). The objective is to initiate students to techniques used for the design of neuroprotheses in order to compensate for sensory motor deficiencies. This course aims at: investigating uses and needs for basic medical systems, as well as active and implantable ones and teaching of theoretical tools required for theirs understanding, settings and their conception (command, signal processing of physiological and physical signals, physical interfacing between living and artificial systems, bases in neurophysiology). Students will have to learn the following skills: electro- and neurophysiology bases required to understand active medical implantable systems, bases in signal processing, bases in embedded informatics and electronics, knowledge about sensory-motor functions and their deficiencies, bases on simulations and closed loop control for living and artificial systems.

10.2.2. Supervision

PhD defended on December 14th 2016 : Wafa Tigra, Assistance à la préhension par stimulation électrique fonctionnelle chez le patient tétraplégique, 01/10/2013, Christine Azevedo Coste, David Guiraud,

PhD defended on December 9th 2016 : Thomas Guiho, Évaluation de l'efficience de la stimulation électrique médullaire en vue de la restauration des fonctions urinaires et intestinales chez le patient lésé médullaire, 01/10/2013, David Guiraud, Christine Azevedo Coste

PhD in progress : Antony Boyer, Neuroplasticité et récupération dans les structures corticales et sous corticales distantes suite à une chirurgie éveillée des gliomes infiltrants de bas grades, 01/09/2016, François Bonnetblanc and Sofiane Ramdani.

PhD in progress : Marion Vincent, Mesures des potentiels évoqués par la stimulation électrique directe lors de la chirurgie éveillée des gliomes infiltrants de bas grades vers une compréhension des effets électrophysiologiques, 01/12/2013, François Bonnetblanc, David Guiraud and Hugues Duffau.

PhD in progress : Maxence Blond, Commande et modélisation d'un véhicule sous-marin, 18/01/2016, Daniel Simon, Vincent Creuze (LIRMM) and Ahmed Chemori (LIRMM).

PhD in progress : Ibrahim Merzoug, Validation formelle pour les systèmes embarqués critiques, Since Oct. 2014, K. Godary-Dejean and D. Andreu.

PhD in progress : Mélissa Dali, modèles de génération et de propagation de potentiel d'action neurla en condition de stimulation sélective multipolaire, since october 2014, David Guiraud and Olivier Rossel (up to july 2016).

PhD in progress : Benoît Sijobert, Stimulation électro-fonctionnelle pour l'assistance aux mouvements des membres inférieurs dans les situations de déficiences sensori-motrices, Since Dec. 2015, Christine Azevedo Coste and D. Andreu.

PhD in progress: Victor VAGNE, "Couplage de la Spectroscopie en proche infrarouge et de la stimulation Transcrânienne (NIRS-tDCS) à courant continu dans l'Evaluation diagnostique de l'ischémie cérébrale lors d'un AVC", Oct. 2016, M. Hayashibe, D. Guiraud, Vincent Costalat (CHU Montpellier) and Emmanuelle Le Bars (CHU Montpellier)

10.2.3. Juries

Daniel Simon was reviewer and member of the PhD jury of Wael Zouaoui (LAAS Toulouse, january 15, 2016).

Karen Godary-Dejean was member of the PhD jury of Louis Marie Givel,École Centrale de Nantes, december 16, 2016.

David Guiraud was reviewer of 2 PhD thesis at UTC and Univ. Of Toulon.

David Guiraud was member of the selection committee, CNU61, for an assistant professor position at the university of Nantes.

Christine Azevedo was member of the selection committee, Inria, Young graduate scientist ("CR2") in Paris.

David Andreu was reviewer and member of the PhD jury of Nicolas Gobillot, INPT Toulouse, april 29, 2016, and member of the PhD jury of Lotfi Jaiem, University of Montpellier, november 21, 2016.

10.3. Popularization

- Large cover in general media (radio, TV, newspapers) of Cybathlon project http://freewheels.inria.fr/
- Christine Azevedo presented Cybathlon project at DIRCOM Inria, Rocquencourt, in the context of Handicap national week.

- Christine Azevedo presented Freewheels experience at Carrefour du Pôle EUROBIOMED (Marseille).
- Christine Azevedo presented the job of researcher in secondary school Collège Léon Cordas (Montpellier)

11. Bibliography

Major publications by the team in recent years

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Publications of the year

Doctoral Dissertations and Habilitation Theses

[11] T. GUIHO. *Étude de stratégies de stimulation électrique de la moelle épinière pour la restauration des fonctions vesico-sphinctériennes*, I2S, Université de Montpellier, Dec 2016

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