RESEARCH CENTRE Sophia Antipolis - Méditerranée

2021 ACTIVITY REPORT

Project-Team CAMIN

Control of Artificial Movement & Intuitive Neuroprosthesis

DOMAIN Digital Health, Biology an<u>d Earth</u>

THEME

Computational Neuroscience and Medicine

Contents

Pr	Project-Team CAMIN 1			
1	Team members, visitors, external collaborators 2 Overall objectives 3 Research program 4 3.1 Exploration and understanding of the origins and control of movement			
2				
3				
4	Application domains4.1Movement Assistance4.2Movement Analysis4.3Evoked electrophysiology	6 6 6		
5	Social and environmental responsibility5.1 Impact of research results	6 6		
6	Highlights of the year	6		
7	New software and platforms7.1New software7.1.1NeuroPrehens7.1.2IMUSEF7.1.3ID-IMU7.1.4ANT4ROTOR7.2New platforms7.2.1Exofinger: an orthotic solution to restore key-grip function in a user with tetraplegia7.2.2Monitoring tremor in ecological conditions : PARaKeet	6 7 7 7 8 8 8 8 9		
8	New results	11		
	 8.1 AGILIS: Implanted multi-contact epineural stimulation to restore hand function in complete upper-limb paralysis. 8.1.1 A method based on wavelets to analyze overlapped and dependant M-Waves 8.1.2 Influence of the H reflex on the selectivity of recruitment using multi-contact epineural stimulation 8.1.3 IMU activation of a neuroprosthesis for individuals with tetraplegia 8.1.4 EMG activation of a neuroprosthesis for individuals with tetraplegia 8.1.4.1 Primary experiments: frequency-domain sEMG analysis and classification results 8.1.4.2 EMG/IMU ongoing experimental protocols and data analysis 	11 13 13 14 15 15 18		
	 8.2 Hybrid neuroprosthesis for individuals with central nervous system disorders	18 18 18 19 20 21		
	8.3 Direct electrical stimulation (DES) of the Brain and measurement of evoked potentials for on-line guidance of Neurosurgery: a combined simulation and experimental approach	22		
	 8.4 Spinal cord stimulation (SCS) 8.4.1 SCS for rehabilitation of bladder, bowel and sexual functions in spinal cord injury – SPINSTIM Project 8.4.1.1 Systematic review on Sacral Anterior Root Stimulation (SARS) 8.4.1.2 Pig experiment campaign 	23 23 24		

		8.4.2	Investigation of cervical spinal cord stimulation (SCS) on upper limb functions in	
				25
				26
	8.6			26
				26
				28
	8.7	Ongo	ing experimental protocols with human participants	28
9	Bila	teral c	ontracts and grants with industry	29
10	0 Par	tnersh	ips and cooperations	29
	10.1	Interr	national initiatives	29
		10.1.1	Inria associate team not involved in an IIL or an international program	29
			10.1.1.1 CACAO associate team	29
			11 0	29
		10.1.2	1 0	30
				30
	10.2			30
		10.2.1		30
				30
		10.2.2		30
				30
				31
	10.4	Regio	nal initiatives	31
1		semina		32
	11.1		0	32
		11.1.1	0	32
			0 0	32
		11.1.2		32
			1 0	32
		11.1.3		32
				32
			0	32
				32
			1	33
			Scientific expertise	
	11.0		Research administration	
	11.2		ing - Supervision - Juries	
			0	33 34
				34 34
	11 2		· · · · · · · · · · · · · · · · · · ·	34 34
	11.3	-		34 34
1:				35
			The second s	35
	12.2	Public Public	cations of the year	36

Project-Team CAMIN

Creation of the Project-Team: 2019 March 01

Keywords

Computer sciences and digital sciences

- A1.2.6. Sensor networks
- A1.3. Distributed Systems
- A2.3. Embedded and cyber-physical systems
- A2.5.2. Component-based Design
- A4.4. Security of equipment and software
- A4.5. Formal methods for security
- A5.1.4. Brain-computer interfaces, physiological computing
- A5.9.2. Estimation, modeling
- A5.10.5. Robot interaction (with the environment, humans, other robots)
- A6.1.1. Continuous Modeling (PDE, ODE)
- A6.3.2. Data assimilation
- A6.4.1. Deterministic control
- A6.4.6. Optimal control

Other research topics and application domains

- B1.1.9. Biomechanics and anatomy
- B1.2.1. Understanding and simulation of the brain and the nervous system
- B2.2.1. Cardiovascular and respiratory diseases
- B2.2.2. Nervous system and endocrinology
- B2.2.6. Neurodegenerative diseases
- B2.5.1. Sensorimotor disabilities
- B2.5.3. Assistance for elderly

1 Team members, visitors, external collaborators

Research Scientists

- Christine Azevedo Coste [Team leader, Inria, Senior Researcher, HDR]
- Francois Bailly [Inria, Researcher, from Oct 2021]
- François Bonnetblanc [Inria, Researcher, HDR]
- Charles Fattal [USSAP Perpignan, Researcher, Medical Doctor in Physical Medicine, HDR]
- Thomas Guiho [Inria, Starting Research Position]
- David Guiraud [Inria, Senior Researcher, HDR]
- Benoît Sijobert [Institut Saint Pierre]

Post-Doctoral Fellows

- Lucas Oliveira Da Fonseca [Inria]
- Fernanda Rodrigues Ferreira Lopes [Univ de Montpellier, from Oct 2021]
- Thekla Stefanou [Inria]

PhD Students

- Vincent Iampietro [Univ de Montpellier, until Sep 2021]
- Ronan Le Guillou [Centre hospitalier universitaire de Toulouse]
- Helene Moron [Centre hospitalier universitaire de Nîmes]
- Felix Schlosser-Perrin [Univ de Montpellier, from Sep 2021]
- Clement Trotobas [Inria]
- Lucie William [Inria]

Technical Staff

- Arthur Hiairrassary [Neurinnov, Engineer, from Mar 2021 until Sep 2021]
- Olivier Rossel [Inria, Engineer, from Sep 2021]

Interns and Apprentices

- Rodolfo Bettencourt Pereira Cerqueira [Université du Minho Portugal, until Mar 2021]
- Sam Durand [Inria, from Feb 2021 until Jul 2021]
- Marie Ghekiere [Inria, from Aug 2021]
- Luis Miguel Marques Martins [Université du Minho Portugal, until Mar 2021]
- Mylene Pistre [Inria, from Apr 2021 until Aug 2021]
- Felix Schlosser-Perrin [Institut du Cerveau et de la Moelle Epinière, from Mar 2021 until Aug 2021]
- Clotilde Turpin [Inria, from Apr 2021 until Aug 2021]

Administrative Assistant

• Annie Aliaga [Inria]

Visiting Scientists

- Nadia Nasri [Université d'Alicante-Espagne, until Apr 2021]
- Fernanda Rodrigues Ferreira Lopes [Universidade Federal de Minas Gerais Brésil, until Sep 2021]

2 Overall objectives

CAMIN research team 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 patients quality of life. 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 (Figure 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.

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 spinal cord injury (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 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 is 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.

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**.

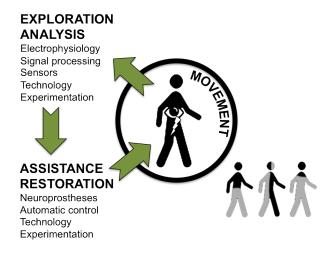


Figure 1: Overview of CAMIN general scientific approach.

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 Direct Electrical Stim-

ulation (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). Real-time adaptation of the stimulation

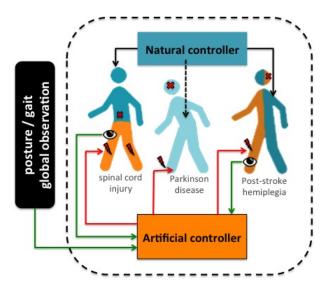


Figure 2: FES assistance should take into account the coexistence of artificial and natural controllers. Artificial controllers should integrate both global (posture/gait) and local (limb/joint) observations.

patterns is an important challenge in most of the clinical applications we consider. The modulation of ES parameters to adapt to the occurrence of muscular fatigue or to environement changes needs for advanced adaptive controllers based on sensory information. A special care in minimizing the number of sensors and their impact on patient motion should be taken.

Application domains 4

Movement Assistance 4.1

CAMIN develops neuroprosthetic solutions dedicated to restore or assist movements of paralyzed limbs. Among the considered functions we can cite: pedalling, grasping, walking. Different users are considered: individuals with post-stroke hemiplegia, people with spinal cord lesions, persons with Parkinson disease. We have also started to develop skills in orthosis design.

4.2 Movement Analysis

For the purpose of assisting movement, CAMIN has developped an important expertise in movement interpretation using a large range of sensors: inertial measurement units, MOCAP systems, encoders, goniometers... Various Classification methods are used depending on the objective.

This knowledge is applied in other applications than movement assistance, like in MEDITAPARK project were we developped an application (PARAKEET) embedded in a smartwatch to monitor hand tremor in persons with parkinson disease.

Evoked electrophysiology 4.3

CAMIN develops solutions to trigger, record and process electrophysiological signals evoked by electrical stimulation applied to various neural tissues. These evoked responses are used to control the activity of the excitable tissue, to probe its electrophysiological status for diagnostic purposes and to investigate the conductivity/connectivity between the stimulation and the recording sites (electrophysiological mapping).

These neural engineering procedures can be applied to muscle, nerve, spinal cord and brain, in animals and humans.

For instance, electrical stimulations can be applied externally and non-invasively on muscles to induce muscle contractions as well as invasively on the human brain in order to guide neurosurgeries.

5 Social and environmental responsibility

5.1 Impact of research results

CAMIN research is clearly dedicated to applications which intend to improve quality of life and/or self esteem of individuals with sensori-motor deficiencies.

We give a very important place to ethics of our work. Christine Azevedo is a member of INRIA ethical committee INRIA.

Highlights of the year 6

- An agreement has been signed for Charles Fattal (medical doctor at USSAP Perpignan) and Benoît Sijobert (HumanLab Manager ISP Palavas) who are now officially attached to the team.
- François Bailly obtained a permanent position as Research Scientist in CAMIN team.
- Thomas Guiho obrained an INRIA Starting Research Position in the team for 3 years.

7 New software and platforms

Let us describe new software/platforms.

7.1 New software

7.1.1 NeuroPrehens

- Keywords: Python, Qt, GUI (Graphical User Interface), Medical, Medical applications, Real-time application
- **Functional Description:** Python application using a framework of input as EMG, IMU, Foot switchs, Camera etc. for controlling a Functional Electrical Stimulation neuroprosthesis in real time closed loop for prehension restoration in hemiplegic stroke patients.

Contact: Christine Azevedo Coste

Participants: David Gasq, Ronan Le Guillou, Christine Azevedo Coste

Partner: CHU de Toulouse

7.1.2 IMUSEF

Keywords: Inertial module unit, Movement analysis, Software platform, Embedded systems

- **Scientific Description:** Modular embedded framework for real-time control of Functional Electrical Stimulation in closed loop with sensor feedback.
- **Functional Description:** IMUSEF allows to acquire data from inertial sensors in order to estimate a segment orientation or a joint angle. From this, an event can be defined to be used to control an electrical stimulator.
- Release Contributions: 1.0: First fully functional version application focused with stimulator control, sensor data acquisition and analysis and decisional algorithm (https://www.mdpi.com/545320).
 2.0: Full rework as a modular framework, allowing selection of decisional algorithm, stimulator system, sensors etc. and optional communication and control in real time from a remote fully featured Graphical User Interface through autonomous hotspot wifi.

News of the Year: New major version (2.0).

URL: https://gitlab.inria.fr/CAMIN/imusef/imusef_app

Publication: limm-02305548, version 1

Contact: Christine Azevedo Coste

Participants: Benoît Sijobert, Ronan Le Guillou, Christine Azevedo Coste, Martin Schmoll

Partner: Université de Montpellier 2

7.1.3 ID-IMU

Name: Intention Decoder based on IMU

- **Keywords:** Inertial module unit, Classification, Movement analysis, Recognition of human movement, Artificial intelligence
- **Scientific Description:** The software process IMU data (accelerometer and gyroscope, 3 axes each) by differentiating it at each new data point, and band-pass filtering it. Then, in a moving window fashion, it extract the following features: rms (root mean square), average, and psd (power spectrum density). Finally, it uses these features as input for training or classifying detected movements. Movements are detected based on a threshold applied to the resultant movement data in the window. The classifier is a nu-SVM (nu-support vector machine) with linear kernel. Most parameters are editable in the parameters.json file.

- **Functional Description:** Users can wear movement sensors (IMUs) on different parts of their bodies and train the system to identify specific and arbitrary movements. These can then be used to activate or trigger other devices, such as neuroprostheses, or robots. As is, this software can read and classify movement data stored in files according to the AGILIS standards by the time of its publication. The real time reading of sensor data and device actuation is out of scope.
- **Release Contributions:** This versions adds a feature for saving data at intermediate steps, in addition to the final classification results.

URL: https://gitlab.inria.fr/luolivei/movementclassification-cpp

Contact: Christine Azevedo Coste

Participants: Lucas Oliveira Da Fonseca, Christine Azevedo Coste

7.1.4 ANT4ROTOR

Name: ANT+ communication for Rotor 2INPOWER

Keywords: Motion analysis, Communicating devices, Power monitoring, Monitoring

- **Functional Description:** Based on the ANT+ communication protocol's Python library, this project unlocks the low frequency limits (4Hz) from the default ANT+ protocol to allow acquisition of the ROTOR "Fast Mode" data streaming (50Hz) through ANT+. This enables data acquisition and monitoring of crank angle, cadence, average power, torque applied on the left and right side independently and more, at frequencies sufficient to analyse the pedalling dynamics inside of a turn rather than having a simple overview of it.
- **Release Contributions:** Version 1 : Complete and functional project. Tested on ROTOR 2INPOWER only, with a RPI 3B.

URL: https://gitlab.inria.fr/CAMIN/ant4rotor

Contact: Christine Azevedo Coste

Participants: Martin Schmoll, Ronan Le Guillou, Christine Azevedo Coste

7.2 New platforms

7.2.1 Exofinger: an orthotic solution to restore key-grip function in a user with tetraplegia

Participants:	Marie Ghekiere, Clément Trotobas, Christine Azevedo, Benoît Si-
	jobert, Christophe Braillon [SED Grenoble], Roger Pissard-Gibollet
	[SED Grenoble], Laurence Boissieux [SED Grenoble]

In 2020, we participated to the Fabrikarium 2020 organized by My Human Kit¹ and Ariane Group. A Fabrikarium is a 3-day prototyping workshop dedicated to disabilities that brings together 9 people around a project holder with a disability². The EXOFINGER project aimed at developping a hand orthosis for the project holder: a user with complete C6 tetraplegia who expressed the need to grasp objects in key grip.

During the event, two prototypes were produced. Both were cable driven and worked on the same principle: when a button is activated, the control unit triggers the linear motor. The linear motor pulls or releases a cable connected to the thumb, closing the grasp. One of the prototypes was made of a custom made textile glove; the cable passes through a sheath and then through sleeves on the glove. For this, a

¹myhumankit.org/le-humanlab/

²www.ariane.group/fr/actualites/bienvenue-au-fabrikarium-2020/



Figure 3: Exofinger Device

DC motor coupled with a V-coil placed on the forearm of the user wind a nylon cable attached to his thumb (fig. 3). This causes a tension on his thumb which closes on his index finger.

We have continued to improve the Exofinger orthosis within the Exploratory Action HumanLab Inria³. The improvements made are mainly mechanical to increase the thumb-tightening stroke and make the prototype more usable on a day-to-day basis (wireless button module, Android App...(fig. 4)).

Moreover, an experimental protocol for the validation of the functional characteristics of the Exofinger orthosis has been developed and submitted to Coerle. We expect to identify the potential users of such a solution and validate the preliminary design.

7.2.2 Monitoring tremor in ecological conditions : PARaKeet

Participants: Ronan Le Guillou, Christine Azevedo, Christian Geny [CHU Montpellier, France], Gregory Baptista [Montpellier Mindfulness Centre, France].

As part of a preliminary study on the effects of Mindfulness meditation on participants with Parkinson's Disease (PD) (10.3 Partnerships and Cooperations : National Initiatives : LABEX NUMEV - MED-ITAPARK), an application was developed to monitor at home tremor occurrence using a smartwatch Samsung Gear S3 and its newer model, the Samsung Galaxy Watch (fig.5). A Python program has been developed to process and format the recorded data, extract specific features and present the characteristics of the Parkinson tremors under a user friendly and comprehensible format for clinicians. This was finalized this year through a comprehensive rewriting where precision and accuracy of data processing was improved. Furthermore, the ease of use of the automatized data processing and the automatic generation of reports on the patient's detected tremors were completed and improved upon, compared to the previous versions. The goal of this system being to identify Parkinson's tremors characteristics qualitatively and quantitatively to highlight global tendencies and help objectively determine effectiveness of diverse treatments against PD tremors. This system was tested again and validated through visual confirmation using acquired tremor data coupled to videos of the watch on a volunteering participant. The different levels of tremor severity were calibrated through data/video comparison with the clinical assessment provided by Dr. Christian Geny.

A one day sample of acquisition is presented in a hourly format displaying the evaluation of the quantity of displacement generated by parkinson tremors during each hour as well as the average severity estimation of the related tremors (fig.6). The created system allows the qualification of tremors in punctual clinical check-ups in the Hospital as well as quantitative formatting of daily tendencies. This

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Figure 4: Exofinger Android application

system should now allow to highlight the evolution of several characteristics from Parkinson's tremors throughout the MBSR (Mind-fullness Based Stress Reduction) meditation program which has now started in November 2021. This clinical protocol aims to evaluate the impact of Mind-fulness Based Stress Reduction on PD tremors. Acquisition of the data pre-MBSR program was concluded successfully for the first session of the protocol. The ClinicalTrial.gov ID of this protocol is : NCT05168046. The software APP of this platform can be found here as the PARa-Keet Project with the Bil Id: Software_3565.



Figure 5: Smartwatch Samsung Galaxy used for long duration recordings of wrist movement by acquisition of accelerometer data from Parkinson tremors, autonomously starting and stopping at predefined hours of the day.

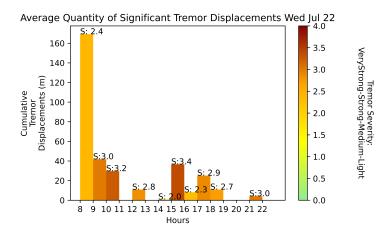


Figure 6: One day data sample from a week long acquisition that allowed us to validate the Tremor severity indicator and improve robustness and ease of use of the system.

8 New results

8.1 AGILIS: Implanted multi-contact epineural stimulation to restore hand function in complete upper-limb paralysis.

Participants: Lucie William, Lucas Fonseca, Christine Azevedo, David Guiraud, Charles Fattal, Jacques Teissier [Clinique St Jean Sud de France], Antoine Geffrier [AP-HP Paris, France], Arthur Hiairassary, David Andreu [Neurinnov, France].

Two multi-contact neural cuff electrodes were placed around radial and median nerves of 2 subjects with high tetraplegia C4, AIS A, group 0 of the International Classification for Surgery of the Hand in Tetraplegia (NCT04306328). The electrodes were maintained during 28 days. The purpose was to study the safety and capability of these electrodes to generate synergistic motor activation and functional movements and to test control interfaces that allow subjects to trigger pre-programmed stimulation sequences. The device consisted of a pair of epineural electrodes and percutaneous cables with two extracorporeal connection cables inserted during a surgical procedure and removed after 28 days (see Fig.7). Continuity tests of the electrodes, selectivity of movements induced, motor capacities for grasping and gripping, conformity of the control order, tolerance and acceptability were assessed. Neither of the 2 participants showed general and local comorbidity. Acceptability was optimal. None of the stimulation configurations generated contradictory movements. The success rate in task execution by the electrostimulated hand exceeded the target of 50%. The compliance rate of the control orders in both patients was \geq 90% using motion IMU-based detection and using EMG-based detection. These results support the relevance of neural stimulation of the tetraplegic upper limb with a more selective approach, using multi-contact cuff electrodes with 9 and 6 contact points for the median and radial nerve respectively.

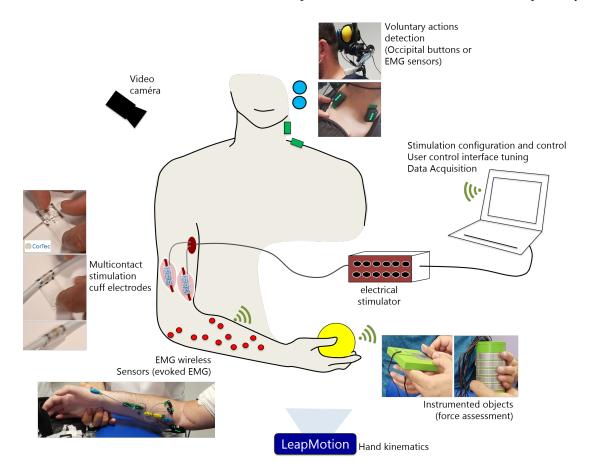


Figure 7: Setup description. An experimental platform was developed to control the stimulation delivered to 2 neural cuff electrodes implanted around the median and radial nerves. Evoked electromyography, video, evoked movement kinematics and grasping forces were recorded. The participants used voluntary muscle contractions or occipital buttons to trigger different stimulation configuration.

8.1.1 A method based on wavelets to analyze overlapped and dependant M-Waves

Participants: Lucie William, Mélissa Dali, Christine Azevedo, David Guiraud.

Implanted multi-contact epineural stimulation could restore hand movement in patients with complete spinal cord injuries. However, assessing the response by surface evoked EMG recordings wass challenging because the forearm muscles are small and overlapping. Moreover, M-waves were dependent because they were induced by a single stimulation paradigm. We hypothesized that the M-waves of each muscle has a specific time-frequency signature (Fig.8) and we have developed a method to reconstruct the muscle recruitment curves using the energy of this specific time-frequency signature. Orthogonal wavelets are used to analyze individual M-waves. As the selection of the wavelet family and the determination of the time-frequency signature were not trivial, the impact of these choices was evaluated. First, we were able to discriminate the 2 relevant M-waves related to the studied muscles thanks to their specific time-frequency representations. Second, the Meyer family, compared to the Daubechies 2 and 4 families, is the most robust choice against the uncertainty of the time-frequency region definition. Finally, the results are consistent with the semi-quantitative evaluation performed with the Medical Research Council (MRC) scoring. The Meyer wavelet transform combined with the definition of a specific area of interest for each individual muscle allows us to quantitatively and objectively evaluate the evoked EMG in a robust manner.

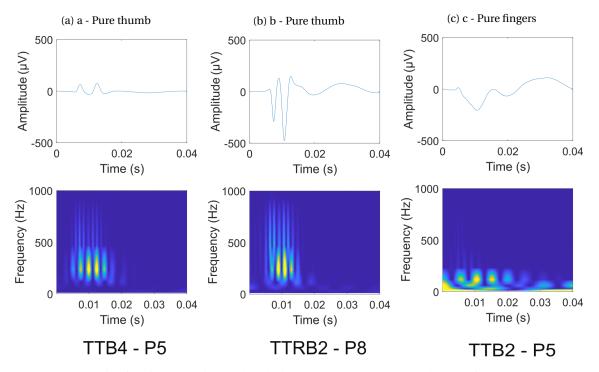


Figure 8: Example of scalograms obtained with the Meyer continuous wavelet transform on two participants that are pure muscle contractions. **a**) and **b**) two thumb flexions - that look very similar -, **c**) fingers flexion - clearly with a different aera of interest-. It further shows that the discrimination in the time domain is not possible due to overlapping.

8.1.2 Influence of the H reflex on the selectivity of recruitment using multi-contact epineural stimulation

Participants: Lucie William, Christine Azevedo, David Guiraud, Charles Fattal.

In AGILIS project during multi-contact epineural stimulation, it was possible to induce involuntary the Hoffman reflex (H-reflex). As the motoneurons have the largest axon diameter, they are usually activated first during the epineural stimulation. However, during the stimulation, it is possible to activated first the axon of sensory Ia afferents because of their large axon diameter. The signal spreads, passes through the spinal cord and activates the α -motoneurons which induces the muscle contraction. Taking into consideration this reflex is important in the context of selective stimulation. The H-reflex was observed for one muscle (the pronator teres, resposible for the pronation movement, see Fig.9,a) on the five recorded. The other muscles recorded were the flexor carpi radialis (FCR) responsible for the wrist flexion, the flexor digitorum superficialis (FDS) responsible for the digit (except thumb) flexion, the flexor pollicis longus (FPL) responsible for the thumb flexion and the abductor pollicis brevis (APB) responsible for the thumb abduction. The impact of this phenomenon on the muscle order of recruitment, the recruitment curves (see Fig.9,b and c) and the selectivity was investigated (see Fig.9,d). Thus, taking into consideration the possibility to evoke this reflex is important to have a selective stimulation inducing a functional movement and in our particular case increasing the range of intensity that can be used by possibly blocking it with anodal block.

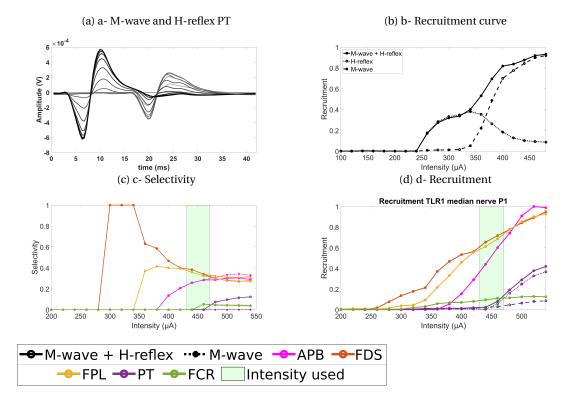


Figure 9: Investigation of the H reflex on the recruitment curves and selectivity of the stimulation. a) Evoked EMG obtained with the configuration TLR3 all intensities of current, PT channel, the intensity of the colour increases with the intensity of the stimulation and b) recruitment curve for the configuration TLR3 with taking into consideration both H-reflex and M-wave or only one of the two, c) the selectivity for the configuration TLR1 d) recruitment for the configuration TLR1.

8.1.3 IMU activation of a neuroprosthesis for individuals with tetraplegia

Participants: Lucas Fonseca, David Guiraud, Arthur Hiairrassary, Charles Fattal, Christine Azevedo.

Assistive technologies may improve autonomy of persons with complete tetralegia but needs for ergonomic interfaces for the user to pilot these device still persist. Despite the paralysis of their arms, people with tetraplegia may retain residual shoulder movements. In this work we explored these movements as a mean to control these devices. We captured shoulder movements with a single inertial sensor and, by training a support vector machine based classifier, we decoded such information into user intent. The setup and training process take only a few minutes and so the classifiers can be user specific. We tested the algorithm with 10 able body and 2 spinal cord injury participants. The average classification accuracy was 80% and 84%, respectively.

The proposed algorithm is easy to set up, its operation is fully automated, and achieved results are on par with state-of-the-art systems. *Significance:* Assistive devices for persons without hand function present limitations in their user interfaces. Our work present a novel method to overcome some of these limitations by classifying user movement and decoding it into user intent, all with simple setup and training and no need for manual tuning. We demonstrate its feasibility with experiments with end users, including persons with complete tetraplegia without hand function.

This interface was used in AGILIS protocol.

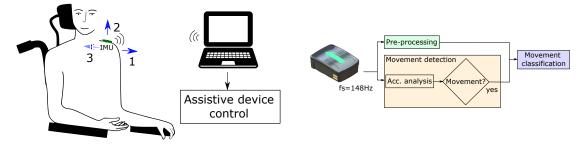


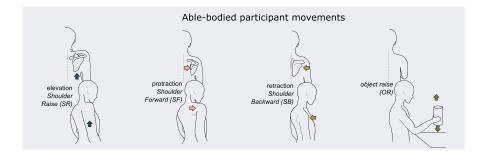
Figure 10: Left: Setup of the experiment. The IMU is illustrated by the green object over the participant shoulder. Participants were asked to perform movements forward (label 1), upward (label2), and backward (label 3, dashed arrow). Data was streamed wirelessly to a computer. Right: Global data flow diagram. The IMU streams 3D accelerometer and gyroscope data at 148*Hz*. Data pre-processing, in green, and movement detection, in yellow, are done in parallel. If a movement is detected, classification, in blue, is performed.

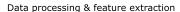
8.1.4 EMG activation of a neuroprosthesis for individuals with tetraplegia

Participants: Thekla Stefanou, Lucas Fonseca, David Guiraud, Charles Fattal, Christine Azevedo.

Human-machine interfaces are a crucial part of assistive, prosthesis and rehabilitation devices. It is essential to correctly identify the user's intent or orders to properly control such devices. We are specifically focusing on the activation of an upper-limb neuroprosthesis developed for individuals with complete tetraplegia (lesions at C4-C6) as in AGILIS protocol using surface electromyography signals (sEMG). We seek to understand, decode and classify surface electromyography (sEMG) signals in order to distinguish between the movements that may be used to activate a neuroprosthesis (AGILIS project) and other every day actions that involve the activation of similar muscles.

8.1.4.1 Primary experiments: frequency-domain sEMG analysis and classification results





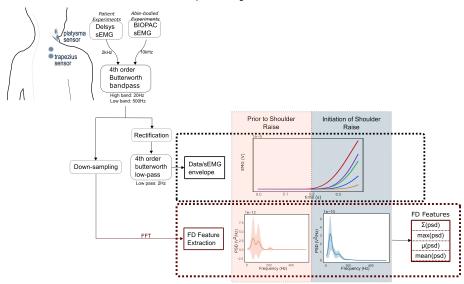


Figure 11: Top: The movements attempted by the able-bodied participants in Protocol A. Bottom: The flow diagram demonstrates the processing of the data leading to the extraction of the frequency domain features.

We analysed surface electromyography (sEMG) signals of the trapezius and platysma muscles, that will be used to activate the neuroprosthesis, in ten able-bodied participants (Protocol A) and two participants with tetraplegia (Protocol B / Agilis protocol). Turning cross-talk to our advantage we demonstrated how one can recognise multiple motions or muscle contractions using a single sEMG channel. Protocol A involved the performance of shoulder raise (*SR*), shoulder forward (*SF*), shoulder backward (*SB*), shoulder raise-and-hold (*SRH*) and object raise (*OR*). In Protocol B individuals with tetraplegia performed shoulder raise and platysma contraction.

Figure 11 demonstrates the sEMG signal processing and feature extraction. Parametric algorithms were used to classify these features. This included decision trees (when a large amount of data were available) and applying thresholding on the features using the median values. Some interesting findings included:

- · a muscle's activity has a specific frequency signature depending on the movements performed
- as a result of cross-talk, classification of *SF* and *SB* is also feasible using the trapezius sensor data despite having different agonists,
- the sEMG sensor placed on the platysma muscle contains information on both platysma muscle contraction and shoulder raise.

We attempt to promote a more optimal use of sEMG signal to better fit a future "home use" system. Single-channel sEMG control could simplify a system or provide contingencies in more complex systems.

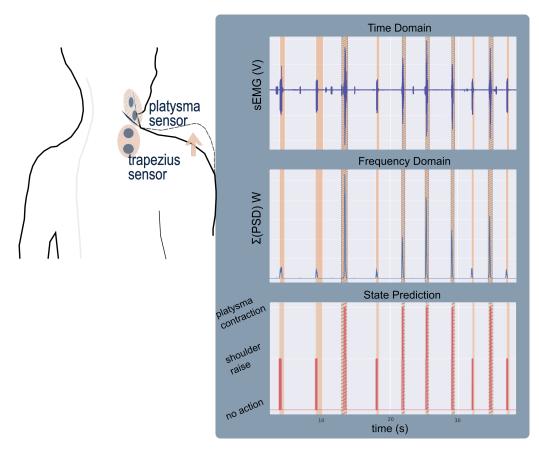


Figure 12: From top to bottom: The filtered EMG readings, the power of the signal and the state-prediction results from a data sample. The shaded regions represent the event occurrences; the hatched shaded regions indicate a *platysma contraction* and the non-hatched ones a *shoulder raise*.

8.1.4.2 EMG/IMU ongoing experimental protocols and data analysis

We are currently in the process of performing an experimental protocol validated by COERLE with able-bodied individuals. For these experiments we have written a script that integrates the Delsys sEMG system with the XSens IMU sensors and created a practical and engaging graphical user interface for the participants. The sEMG and IMU sensors are attached to the participants who are asked to perform a variety of actions such as different shoulder, arm and head movements, as well as laughing. The first stage of experiments is currently helping us develop classification algorithms in order to produce an robust neuroprostheses activation system while the upcoming second stage will mainly be used for the validation of the system.

8.2 Hybrid neuroprosthesis for individuals with central nervous system disorders

Hybrid Robotic Systems (HRS) are an innovative approach to neurological rehabilitation. They combine the advantages of muscle activation using Functional Electrical Stimulation (FES) with the repetitive muscle practice provided by Robot-Assisted Therapy (RT). This technology can potentially result in a device that is overall lighter (and thus more portable) than a non-hybrid robotic device and, on the other hand, can produce greater forces and have more precise control than FES alone.

8.2.1 User requirements for upper limb hybrid neuroprosthesis

Participants:	Fernanda Ferreira, Lucas Fonseca, Christine Azevedo, Clément Tro-	
	tobas, Ronan Le Guillou, Charles Fattal, David Gasq [CHU Toulouse,	
	France], Claysson Vimieiro [UFMG, Brazil], Adriana Valladao [UFMG,	
	Brazil].	

A multicenter pilot study is being conducted in different countries, mainly France and Brazil, on health care professionals and people with neurological disorders. An online questionnaire has been developed by Inria, which included a risk analysis with the data privacy organization of INRIA. The objective is to investigate the essential requirements (needs, preferences, and expectations) of potential users that need to be met during the development of upper limb hybrid neuroprosthesis. This will promote a higher level of compliance, acceptance, and satisfaction with the use of the device, as well as to minimize user abandonment.

The questionnaire was developed with the contribution of 9 professionals from a clinical and engineering multidisciplinary research team composed of medical doctors in physical medicine, occupational therapists and engineers from Brazil and France (USSAP Perpignan and CHU Toulouse). As a pre-test, a small pilot study was conducted on 10 participants (5 in Brazil and 5 in France) in order to ensure relevance and validate the questions, to check that the questions are clear and easily understandable. The questionnaire is currently being widely disseminated on a secure platform at Inria that can be found online.

To our knowledge, this is the first study that investigates user needs for the development of upper limb hybrid neuroprosthesis.

8.2.2 Hybrid neuroprosthesis for rehabiliation in post-stroke hemiplegia

Participants:FernandaFerreira,LucasFonseca,ChristineAzevedo,Claysson Vimieiro [UFMG Brazil],Adriana Valladao [UFMG Brazil].

A portable robotic exoskeleton for upper limb rehabilitation of post-stroke individuals, called Pinotti Portable Robotic Exoskeleton (PPRE) was developed at the Bioengineering Laboratory (Labbio) at the Federal University of Minas Gerais (UFMG). It was improved by adding Functional Electrical Stimulation (FES), transforming it into a hybrid robotic exoskeleton. Fernanda Rodrigues spend 1 year in CAMIN team while she was a UFMG PhD student to work on this topic. The PPRE was segmented into two functional modules: hand and elbow. The elbow module is responsible for flexing and extending the elbow and the hand module is responsible for extension of the second to fifth fingers. Both are motor-driven from Maxon Motors[™]. To improve the device, modifications were made to the hand module by removing the motor and mechanical structures and adding FES, transforming it into a Hybrid FES-Robotic Orthosis. A computer program was developed using Python to integrate the different drive systems (motor and FES), and a new graphic interface was created to facilitate the operation by users. Thus, it was possible to increase the number of movements provided by the equipment from one (extension of the 2nd to the 5th finger) to five (extension and flexion of the 2nd to the 5th finger, thumb extension, adduction and abduction with thumb opposition), enabling the execution of other types of grasps and amplifying the repertoire of possible activities. In addition, the mechanical structure was simplified, the volume decreased, the total weight was reduced and, consequently, greater portability was achieved. Furthermore, it enables direct activation of the paretic muscles, thus reducing the user's passive posture and favoring increased motor control, which should promote functional recovery.

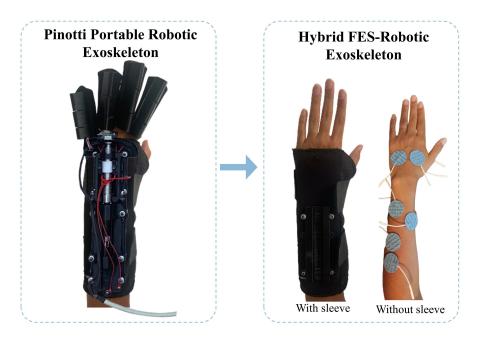


Figure 13: Comparison of the hand module of the Pinotti Portable Robotic Exoskeleton (PPRE) and the resulting Hybrid FES Robotic Exoskeleton

The equipment was tested through experimental tests and it was observed that the system proved to be effective in performing tasks of reaching and grasping different objects with the combination of movements of the elbow and hand modules, indicating that it can be used to perform functional activities. Furthermore, the correct functioning of the system was verified in 2 healthy participants, stimulating with efficiency the desired muscles. In the future, tests will be carried out on individuals with upper limb motor impairment as a result of stroke to ratify these results. This project was approved by the Research Ethics Committee of the Federal University of Minas Gerais (CAAE Registry: 22207213.5.0000.5149).

8.2.3 Systematic review on upper limb hybrid neuroprostheses for rehabilitation of neurological disorders

Participants:FernandaFerreira,LucasFonseca,ChristineAzevedo,Claysson Vimieiro [UFMG Brazil],Adriana Valladao [UFMG Brazil].

Previous studies indicate that hybrid systems may be more effective in improving motor control and

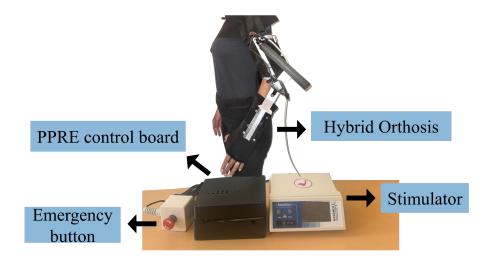


Figure 14: Hybrid FES Robotic Exoskeleton

functional skills compared to robotic therapy alone in patients with hemiparesis after chronic stroke and compared to traditional physical therapy in individuals with acute stroke. However, although studies prove the potential benefit of this technology, few randomized controlled trials have been conducted so far and no systematic literature review has been carried out. Systematic reviews are necessary because it is the most appropriate and current method for summarizing and synthesizing evidences about the effectiveness and effects of interventions. Therefore, this project is investigating systematically the effects of HRRS on central injuries upper limb recovery based on each of the International Classification of Functioning, Disability and Health (ICF) domains. This study will contribute to the development of new hybrid neuroprostheses that are proven to be effective for upper limb rehabilitation. This systematic review is currently underway with the participation of physicians, occupational therapists and engineers. It is registered in PROSPERO under protocol CRD42021227548 [23].

8.2.4 Orthyb: an assistive hybrid orthosis for upper limb function

Participants: Clément Trotobas, Christine Azevedo, Fernanda Rodrigues Ferreira Lopes, Andrew Murray [DimLab Dayton], Roger Pissard-Gibollet [SED Grenoble].

The goal of this project is to give functional mobility to paralyzed hand and wrist of people in order to hold an object in palmar grasp. The context is not rehabilitation as in PPRE device but an assistive solution for daily tasks execution. The challenge is to explore novel technologies to propose a light and modular solution. The device to be developed is a hybrid orthosis composed of a mechanical orthosis and a stimulator. The wrist and finger movements will be generated by muscle contractions through functional electrical stimulation (FES) while the guiding and locking are mechanical. This locking would make it possible to limit early muscle fatigue while maintaining the grip.

A first mechanical orthosis was developed by the startup Aufratech based on CAMIN team specifications in order to assess the general principles of the approach. It includes two DC motors, one for extension and flexion of the wrist, and one for all fingers (fig. 15). It is a cable driven orthosis meaning that motors pull or release cables, moving the limbs. Although the mechanical orthosis is already developed, it lacks drivers and control unit. To date, the driver used is a L298N and the control board is a Adafruit feather nRF52840 express. Moreover, cited participants are the first to test over several months this orthosis and some modifications could be planned. The orthosis can be controlled via keyboard inputs; it is possible to set and move the orthosis to wanted positions and move by increments.

The electrical stimulator chosen is the Vivaltis Phoenix for its portability. Application Programming

Interfaces (APIs) have already been developed in Matlab, C++ and Python. Even if an updated of the API is necessary, the Python version has been chosen for the ease of developing an Graphical User Interface (GUI).

The GUI is currently being developed. It includes both orthosis and stimulator setup and control (fig. 16).

To validate experimentally the approach, a protocol will be carried at the Federal University of Minas Gerais (UFMG) in Brazil. A protocol has been edited and proposed to the local Ethics Committee.





Figure 15: Aufratech orthosis and a pod from Vivaltis Phoenix stimulator (two channels)

Aufra	tech orthosis	Vivaltis	stimulator
Connect to COM 16	Connect	Connect to COM 17	Connect
Hand 🔲 yes	Wrist 🗆 no	First pod 🗌 no 🔳 yes	Activate both
Set up	Set up	Frequency (Hz) 5	0 0
Flexion Extension			
Increment value 10 0		Channel: green Phase width (µs) 250	Channel: yellow Phase width (µs) 250
Flexion max Set position		Intensity (mA) 6	Intensity (mA) 6
Extension max	Set position Flexion max Extension max	Test channel	Test channel
Go to position			
Extension max		Frequency (Hz) 5	
Hand only		Channel: green	Channel: yellow
	Grasp	Phase width (µs)	
		Intensity (mA) 6	
		Test channel	Test channel
			Activate

Figure 16: Design of the GUI for the Orthyb project

8.2.5 Modular Elbow-Forearm Orthosis

Participants: Clément Trotobas, Christine Azevedo, Andrew Murray [DimLab Dayton], Marie Ghekiere. The goal of this project is to imagine novel light and wearable orthotic solutions for upper-limb movements assistance. The objective is to give functional mobility of paralyzed elbow and forearm. The device to be developed would be an hybrid orthosis composed of a mechanical orthosis and a stimulator. The elbow and forearm movements will be generated by muscle contractions through functional electrical stimulation (FES) while the guiding and locking are mechanical. This locking would make it possible to limit early muscle fatigue while maintaining a position.

Disability can be very different from an individual to another and the approach of *one size fits most* is questionable. Thus, the orthosis is intended to be modular with both pods from Vivaltis Phoenix stimulator (fig. 15) and mechanical modules close to the one developed for Exofinger (fig. 17). It would include control board with bluetooth low energy (BLE), batteries, DC motors coupled with coils to wind cables to move limbs. These modules, including Vivaltis pods, could be placed on straps enabling a position and a number fitting the wearer's needs.



Figure 17: Example of mechanical module including power storage, actuation and control unit with bluetooth communication

8.3 Direct electrical stimulation (DES) of the Brain and measurement of evoked potentials for on-line guidance of Neurosurgery: a combined simulation and experimental approach

Participants:Felix Schlosser-Perrin, Olivier Rossel, Emmanuel Mandonnet [AP-HP,
France], Hugues Duffau [CHU-Montpellier, France], François Bonnet-
blanc.

In the future, brain connectivity could be assessed on-line to guide the Neurosurgery using the measure of Potentials Evoked by Direct Electrical Stimulation (DES). However, the effects of DES can be complex and remain poorly understood. Here, we test the effects of orienting differently a bipolar probe on white matter tracts. In our approach we combine modeling and experimental studies with in-vivo measurements. The modeling is performed in two stages. First, it includes the calculation of the electric fields in the conductive medium via the COMSOL software and then the estimation of the activation on the Ranvier nodes with the propagation of the action potentials along the fiber (thanks to an axon model). The simulations (fig.18) show that during orthogonal positioning of the probe relative to the white matter tract, the central part in the axon section may not be activated, suggesting the prediction that during orthogonal stimulation of the tract, which, at the cortical endings opens in a fan, we should not observe evoked potentials on the middle electrode. This is observed on experimental data (fig.19 and fig.20). More specifically, an activation gap between probes in the orthogonal configuration (fig.18A) for axon tracts is seen but not when the probes where set in a parallel configuration (fig.18B). This may also be observed experimentally on recordings (fig.20). For parallel stimulation, activation is more focal, it activates the major part of the track.

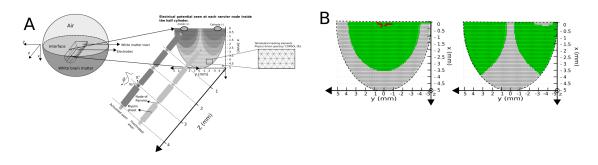


Figure 18: A) represents the built geometry in COMSOL multiphysics (left) and the axon location for the CRRSS model computation (center). Each axon has a computed potential at each of its own Ranvier node according to a pre-determined meshing in COMSOL matching with the in vivo axons sizes. B): activation maps for a 2.5mA bipolar (probe orientation beeing either orthogonal or parallel to the tract), 500 µs phase width balanced square biphasic stimulation of a white matter pathways. Green dots show axons propagating in both direction along the axons (+z -z). Left and right plots, represent parallel and orthogonal stimulation respectively.

The experimental results (fig.20) show that for the parallel configuration the amplitude of the evoked potential is maximum for the contact 15. The adjacent contacts (14 and 16) register evoked potentials of lower amplitude. This confirms a localized epicenter. Conversely, for the orthogonal configuration the amplitude of the evoked potential is minimum for the contact 15, the adjacent contacts (14 and 16) record evoked potentials of higher amplitudes. This confirms that central fibers are not or only slightly activated unlike the fibers located more lateraly and under the stimulation contacts. These preliminary results are in the vein of simulation results, this confirms that simulations have a great interest for the clinical field. This can be of daily use to neurosurgeons, allowing them to be able to accurately track on-line white matter fascicles.



Figure 19: Brain tumor resection with ECoG recording, the probe is positioned orthogonally to the FAT fascicle (vertical orientation). This track is supposed to be connected to the gray matter bellow contacts 14, 15 and 16

8.4 Spinal cord stimulation (SCS)

8.4.1 SCS for rehabilitation of bladder, bowel and sexual functions in spinal cord injury – SPINSTIM Project

Spinal cord injuries have disastrous consequences for individuals, who, in addition to the motor impairments, must deal with sexual, bowel and urinary problems. Beyond their impact on health, these disorders have psychosocial implications that must not be neglected. Regarding lower urinary tract (LUT) function, SCI induces a communication breakdown between supraspinal and spinal levels that not only manifests by the loss of voluntary control of micturition but also by an exacerbation of reflex processes. Adult neurogenic lower urinary tract dysfunction refers to the urological symptoms associated with these disturbances and expresses clinically by two major problems: the disruption of the detrusor activity (detrusor overactivity – DO or detrusor underactivity – DU) and the detrusor sphincter dyssynergia (DSD).

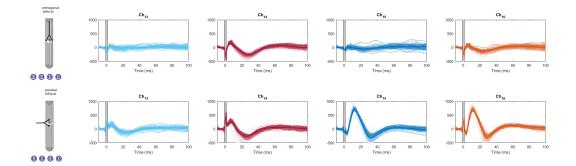


Figure 20: Recorded evoked potentials for contacts 13, 14, 15 and 16 with a 2.5mA intensity, 9Hz frequency, and biphasic stimulation pulse. A) Orthogonal configuration. B) Parallel configuration

8.4.1.1 Systematic review on Sacral Anterior Root Stimulation (SARS)

Participants:	Thomas Guiho, Luc Bauchet [CHU Montpellier, France], Jean-
	Rodolphe Vignes [CHU Bordeaux, France], Claire Delecci [CHU
	Bordeaux, France], Christine Azevedo Coste, Charles Fattal,
	David Guiraud.

In order to restore urinary function, a device based on a strategy of functional electrical stimulation – more specifically, sacral anterior root stimulation (SARS) – was developed 40 years ago: the Brindley-Finetech® implant (or SARS implant). However, the Brindley device does not handle DO by itself as bladder contractions at low filling are still likely induced by the disturbed sacral reflex arch. Sacral deafferentation (i.e., sectioning of the sacral posterior roots, procedure called rhizotomy) is often coupled with SARS implantation to prevent DO – and, consequently, promote bladder compliance – but results in the potentially irreversible loss of spared perineal sensation and function (erection and ejaculation in men, vaginal lubrication in women, defecation). In an article published in World Neurosurgery in September [14], we systematically reviewed (Preferred Reporting Items for Systematic reviews and Meta-Analyses – PRISMA – recommendations) the reports of 40 years of SARS implantation and assessed the medical added-value and limits of this approach through four axes of investigation: i) impact on visceral functions, ii) implantation safety and device reliability, iii) individuals quality of life, and iv) additional information about the procedure. (fig.21)

Despite generally positive results on visceral functions – especially LUT function – the number of Brindley implantation procedures has declined in recent years. Thus, the rehabilitation of visceral functions remains a major concern of individuals with SCI, and we decided to investigate less invasive solutions or alternatives that are likely to offer these persons a dramatic gain in quality of life.

8.4.1.2 Pig experiment campaign

Participants: Thomas Guiho, Jean-Luc Boulland [Oslo University], Christine Azevedo Coste, David Guiraud.

This 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. Two experimental explorations were performed with direct spinal cord stimulation in Oslo in December (on 2 pigs). Experiments were conducted in collaboration

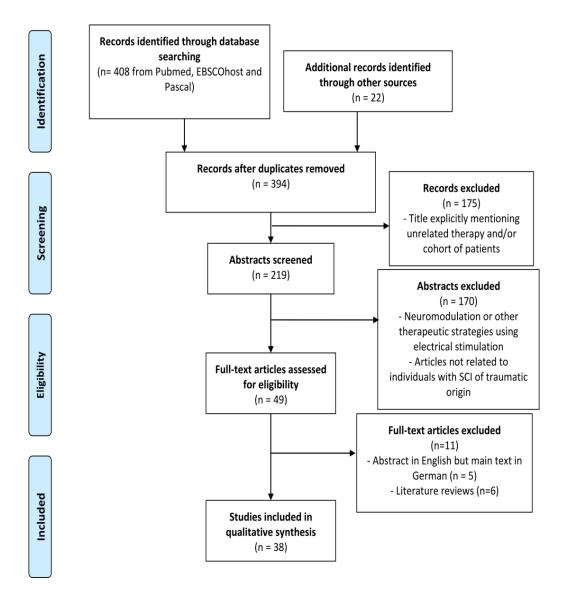


Figure 21: Flow diagram of the literature search

with the University of Oslo and additional experiments are expected in the next few months subject to an improvement of the covid-19 situation. Data will be further processed in the next few months after recruitment of a master student. (fig.22)

8.4.2 Investigation of cervical spinal cord stimulation (SCS) on upper limb functions in rhesus macaques

Participants: Thomas Guiho, Andrew Jackson [Newcastle University].

From January to February 2021, Thomas Guiho was seconded in Newcastle University to investigate the impact of spinal cord stimulation protocols at a cervical level on upper limb functions in rhesus macaques. Both stimulation during sedated and awake sessions were implemented in intact animals while phamacological inactivation of upper limbs was performed to mimic impairments following spinal cord injury. A novel multielectrode cuff was placed around both and ventral surface and multiple stimulation parameters were further investigated in an attempt to highlight the mechanism of action of SCS.

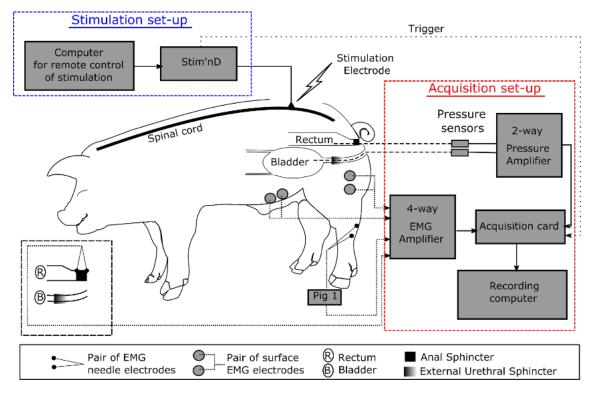


Figure 22: Experimental set-up implemented

8.5 Assisted cycling : CYCLOSEF

Participants: Martin Schmoll, Ronan Le Guillou, Christine Azevedo, Charles Fattal.

Our team has been working for several years on FES-assisted cycling for individuals with spinal cord injury. We intend to improve cycling accessibility to a larger population in order to propose exercising and leisure activity to improve quality of life and self esteem. It has also been shown that FES-cycling of subjects with Spinal Cord injuries (SCI) results in physiological and psychological positive effects such as cardiovascular training, decrease in pressure sores occurrence and self-esteem improvements. However, the use of this technology has often remained restricted to indoor and stationary ergometers in clinical contexts, partly due to the small amount (10–25 W) of power produced and the requirement of experimented users to finely tune the stimulation patterns needed to stimulate lower limb.

Following the conclusion of the CYCLOSEF study, several publications were produced. The benefits of 1-year home training with Functional Electrical Stimulation cycling in paraplegia during the COVID-19 crisis were presented, as well as a novel framework for quantifying accuracy and precision of event detection algorithms in FES-Cycling (fig.23) [13, 16].

Furthermore, as part of the research on this project, experiments from November 2019 in Brasília in collaboration with our associate team CACAO, lead to the publication in January 2021 of a practical approach on standardizing fatigue-resistance testing during electrical stimulation of paralysed human quadriceps muscles [20].

8.6 Post Stroke upper limb rehabilitation

8.6.1 Post Stroke upper limb rehabilitation with tangible BCI : GRASP-IT

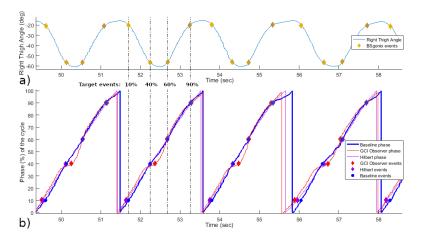


Figure 23: Representative data from subject 1 showing the right thigh angle on the top (a) and the phase estimations on the bottom (b). On the bottom graph, the blue line is the baseline reference, the red line is the GCI Observer output phase interpretation, and finally in purple, the Hilbert phase estimation. Corresponding events detected by the algorithms are shown superimposed on their respective line. Target events from the baseline in the second cycle are highlighted with vertical lines to help visual comparison with the corresponding event detections from the other algorithms.

Participants: Ronan Le Guillou, Christine Azevedo, David Gasq [CHU Toulouse, France], Laurent Bougrain [LORIA, France].

Stroke is a major cause of disability in adults. The GRASP-IT project aims at improving the motor recovery of the upper limb of post-stroke hemiplegic patients by designing and using a gamified system that integrates complementary stimulation modalities (functional electrical, haptic and tangible stimulation) in brain-computer interfaces (BCIs) based on the generation of kinesthetic motor imaginations (KMI) (fig.24).

This project, carried by Laurent Bougrain [LORIA], proposes to design and evaluate the usability (including the effectiveness of the interactions with respect to the stimulation of the motor and somatosensory cortex) and the acceptability of the interface, called GRASP-IT, and of the interactions it induces. This project integrates both the design of the solutions and their evaluation, through an ambitious clinical evaluation including 75 patients in 3 functional rehabilitation centers in France. The GRASP-IT project is planned over 48 months to allow the design and validation of evaluation methods (preliminary and final) within a multicenter clinical protocol.

As collaborators in this project, and one of the clinical centers [CHU Toulouse], in preparation for the clinical experiments to start (expected to be Q3-Q4 2022), we developped a module allowing Functional Electrical Stimulation as a feedback modality for the Grasp-IT project.



Figure 24: Grasp-IT project using practical BCI games and feedback modalities to improve functional recovery in post-stroke patients.

8.6.2 Post Stroke upper limb neuroprosthesis : Projects Prehen-Stroke & Grasp-Again

Participants: Ronan Le Guillou, Christine Azevedo, David Gasq [CHU Toulouse].

The improvement of the grasp abilities remains a challenge in 50% of post-stroke subjects who have not recovered functional grasping due to paralysis of the finger's extensor muscles. Following the ePrehension-Stroke study in 2019-2020 and its informative results, a new study was started. The PHRCi Prehen-Stroke project (ClinicalTrials.gov Identifier: NCT04804384), aims to evaluate the piloting modalities and the functional impact of a grasping neuroprosthesis in the vascular hemiparetic patient. The addition of new features like voice control was completed and inclusions of participants have begun (fig.25). An embedded version of this grasping neuroprosthesis is being developped to further evaluate its functional impact on the grapsing abilities of hemiplegic patients at home. This embedded version is to be used as part of an ancillary study of Prehen-Stroke, named Grasp-Again, which is being written currently.

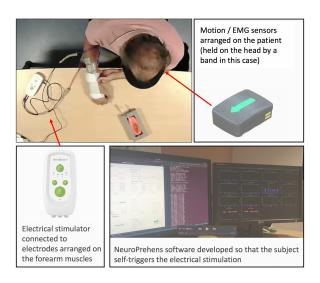


Figure 25: Experimental devices constituting the Prehen-Stroke self-triggered grasping neuroprosthesis.

8.7 Ongoing experimental protocols with human participants

Our activities are associated to an important working load on designing protocols and obtaining authorizations from ethical committees and/or health agencies. We list in the following the protocols that have obtained authorizations and were valid in 2021.

- 1. Assessment of the Functional Impact of a Close-loop Controlled Prehension Neuroprosthesis in Post-stroke Patients (PREHENS-STROKE). Evaluation of optimal piloting modalities and their impact on the grasping capacity in Functional Electrical Stimulation of Finger Extensor Muscles in the Hemiplegic Patient in Chronic Phase. CHU Nîmes, CHU Toulouse. Protocol RCB 2018-A02144-51. ClinicalTrials.gov Identifier: NCT04804384
- 2. Variability of the Unique Fiber Potentials of a Spastic Muscle Treated With Botulinum Toxin (JIT-TOX). CHU Nîmes? Protocol RCB 2019-A01863-52A. ClinicalTrials.gov Identifier: NCT04002843
- Measure of the Potential Evoked by Electric Stimulation (PE & CE). CHU Montpellier. Protocol RCB 2014-A00056-43. ClinicalTrials.gov Identifier: NCT02509442
- Mindfulness-based Intervention for People With Parkinsonian Tremor (MEDITAPARK). CHU Montpellier. ID-RCB: 2020-A01927-32. ClinicalTrials.gov Identifier: NCT05168046

- 5. AGILIS-ML: Development of user control interface based on residual movement for upper limb neuroprostheses in the context of the AGILIS project. The protocol includes experiments with able body subjects and has the approval of COERLE (autorisation nº 2020-09 AGILIS).
- 6. Exofinger: a tool for entering objects. COERLE (autorisation nº 2021-47 Exofinger)
- 7. Vibrosens: Comparative study of electro- and vibro-stimulation. COERLE (autorisation nº 2022-06 Vibrosens)
- 8. Human Upper Body Biomechanics: building an upper body bio-mechanics dataset that can be used for research and development of upper limb assistive devices. COERLE (autorisation nº 2021-28)
- 9. Upper limb hybrid robotic rehabilitation effectiveness aiming at compiling existing knowledge on the use of hybrid robotic devices on the rehabilitation of neurological disorders affecting upper limbs. The systematic review is registered in PROSPERO (protocol CRD42021227548).

9 Bilateral contracts and grants with industry

NEURINNOV startup finances half of the PhD thesis salary of Lucie William.

10 Partnerships and cooperations

10.1 International initiatives

H2020-MSCA-IF-2019. Lucas Fonseca has obtained a Marie Curie Grant for his project: "Neuroprosthesis user interface based on residual motor skills and muscle activity in persons with upper limb disabilities".

10.1.1 Inria associate team not involved in an IIL or an international program

10.1.1.1 CACAO associate team

Title: Lower limb electrical stimulation for function restoration

Duration: 2019 -> 2022

Coordinator: Christine Azevedo

Partners:

- University of Brasilia UnB (Brazil) Emerson Fachin-Martins
- University Federal of Minas Gerais (Brazil) Henrique Resende

Inria contact: Christine Azevedo Coste

Summary: Associate team dedicated to the development of assistive technologies to enhance rehabilitation of individuals with sensory-motor deficiencies. Topics include FES-assisted cycling and transfer and hybrid orthosis for upper-limb.

10.1.1.2 BrEl-Mapping

Title: Electrophysiological brain mapping

Duration: 2021 ->

Coordinator: Riki Mastumoto (matsumot@med.kobe-u.ac.jp)

Partners:

Kobe University Graduate School of Medicine

Inria contact: Francois Bonnetblanc

Summary: Direct electrical stimulation of the brain (DES) helps to inhibit areas of the brain in order to perform anatomo-functional mapping. It is used successfully in clinical practice in the awake surgery of epileptogenic foci and infiltrating brain tumors. It identifies "non-functional" areas that can be resected. Its electrophysiological effects are still very poorly understood because of the complexity of the excited brain structures, and the stimulation modes used remain rudimentary. Understanding these mechanisms is crucial for (1) understanding the relationships between electrophysiology and function (2) neuromodulation of the brain and (3) at longer term for the development of neuroprosthetics for sensorimotor restoration. To better control the practice of DES and its utility in electrophysiological mapping, we will measure its electrophysiological effects through the action potentials (PA) and evoked local field potentials (PE). The clinical objectives are to improve the protocol of DES and the collection of its electrophysiological effects in the awake surgery of low-grade infiltrating gliomas but also for any other type of surgery of tumors practiced under general anesthesia to (1) develop electrodiagnostic approaches and tools that aim to determine the electrophysiological status in real time of neural tissues on and around the tumor and (2) to measure the structural connectivity in vivo and real-time in the peri-lesional area and in particular the subcortical areas to help objectify the boundaries of resection on the white matter bundles during the surgical procedure itself.

10.1.2 Participation in other International Programs

10.1.2.1 RESCUEGRAPH

FLAG-ERA JTC 2021 - Graphene - Applied Research and Innovation

Partner Institution(s): • Universitat Autonoma de Barcelona - Institute of Neurosciences (UAB)

- Catalan Institute of Nanoscience and Nanotechnology Advanced electronic materials and devices group (ICN2)
- Boğaziçi University Institute of Biomedical Engineering (BOUN)
- NEURINNOV company (France)

Date/Duration: 36 months starting December 2021

10.2 International research visitors

10.2.1 Visits of international scientists

10.2.1.1 Other international visits to the team

• Fernanda Rodrigues spent 1 year in the team during her last year of PhD from University Federal of Minas Gerais (Brazil)

10.2.2 Visits to international teams

10.2.2.1 Research stays abroad

- Thomas Guiho spent 2 months in Newcastle in January/February to perform experiments of spinal cord stimulation in monkeys
- Thomas Guiho spent 2 weeks at Oslo University in December to run an experimental protocol with pigs within SPINSTIM project framework.

10.3 National initiatives

Inria AeX HumanLab Inria

https://project.inria.fr/humanlabinria/

Humanlabs are collaborative spaces for digital fabrication or repair of objects, open to people with disabilities to enable them to appropriate technology for their own use. Inria's HumanLab contributes to meeting the needs expressed by individuals with disabilities within the framework of the Humanlabs network or via clinical partners. Our action is part of a frugal and opensource innovation approach and aims to implement the scientific and technological know-how of Inria's staff to meet specific needs.

• ANR Grasp-It (2019-2023)

http://graspit.loria.fr/

The funded ANR project GRASP-IT aims to recover upper limb control improving the kinesthetic motor imagery (KMI) generation of post-stroke patients using a tangible and haptic interface within a gamified Brain-Computer Interface (BCI) training environment.

• Fondation ARC pour la recherche sur le Cancer : Guiding brain tumor surgery in real time using electrophysiology.

François BonnetBlanc, 412k€ pour 3 ans. During the resection of brain tumors, the neurosurgeon has substantial imaging data allowing him/her to plan his gesture upstream. However, during the actual surgical gesture, in real time, this imaging becomes ineffective due to the deformation of the brain (so called brain shift). It is then possible to use direct electrical stimulation of the brain in an awake patient who cooperates with the neurosurgeon to determine the functional areas and those which are not. When patients are under general anesthesia this possibility no longer exists. We have planned to use the electrophysiology evoked by the direct electrical stimulation (DES) of the brain during brain surgery to diagnose and determine the location the tumor and the anatomical connectivity on-line in order to guide the surgery in awake patients or under general anesthesia. This need to go beyond the proof of concept, we have alrealdy performed, and necessitate to address and solve some methodological challenges. At a fondamental level, this will also help to better understand the electrophysiological effect of DES in order to optimize its use.

• LABEX NUMEV - MEDITAPARK project

Collaboration with Montpellier Hospital (Neurology service) and the Montpellier Mindfulness Center to analyze the impact of meditation on upper limb tremor.

10.4 Regional initiatives

- **SPINSTIM** I-SITE MUSE COMPANIES AND CAMPUS grant (ended 31-12-2021) Collaboration with academic local partners (CHU, IES) and NEURINNOV company on the spinal stimulation for bladder and bowel functions restoration. This is linked to an ongoing collaboration with Oslo University (Norway).
- AGILISTIM I-SITE MUSE grant Soutien à la recherche

AGILISTIM proposes to implant 3 epineural electrodes around the median, radial and ulnar nerves, just above the elbow of volunteer participants with complete tetraplegia for 30 days. The multicontact neural stimulation will synergistically activate the forearm muscles to trigger: hand opening, a digito-palmar grip or a functional terminal grip. The project must consolidate and extend the scientific results of the previous work and the innovative technologies which result from it. It should allow to reach a crucial proof-of-concept stage before the development of a unique finalized product responding to an unsolved need in order to improve the quality of life and the autonomy of the users.

11 Dissemination

11.1 Promoting scientific activities

11.1.1 Scientific events: organisation

11.1.1.1 Member of the organizing committees

• Christine Azevedo was member of the organizing committee of 24th Annual IFESS at Virtual RehabWeek 2021.

11.1.2 Scientific events: selection

11.1.2.1 Member of the conference program committees

- Christine Azevedo was member of the program committee and reviewer of 24th Annual IFESS at Virtual RehabWeek 2021.
- David Guiraud was Theme editor (Theme 6) of the IEEE EMB annual conference 2021.

11.1.3 Journal

11.1.3.1 Member of the editorial boards

- David Guiraud is associate Editor at Journal of Neural Engineering
- David Guiraud is associate Editor at Medical and Biological Engineering and Computing
- Christine Azevedo is Review Editor Frontiers Neuroscience Neuroprosthetics
- Christine Azevedo represents Inria in the ERCIM News Journal editorial Board

11.1.3.2 Reviewer - reviewing activities

- Christine Azevedo was reviewer for IEEE TNSRE (Transactions on neural systems and rehabilitation engineering), SENSORS MDPI, Frontiers in Neurorobotics Frontiers in Neuroscience, Journal of NeuroEngineering and Rehabilitation...
- David Guiraud was reviewer for IEEE : TNSRE, TMECH, TBME, RA, TASE, JBHI... and JNE, MEP, JNM, MBEC, CBM...
- Thomas Guiho was reviewer for IEEE TNSRE (Transactions on neural systems and rehabilitation engineering), Journal of Neural Engineering, Journal of Neurotrauma and MBEC (Medical & Biological Engineering & Computing)
- Lucas Fonseca was reviewer for IEEE EMBC (Engineering in Medicine and Biology Society Conference) and JCAE (Journal of Control, Automation and Electrical Systems)

11.1.4 Invited talks

- Thomas Guiho presented his work at the 10th NUMEV scientific days. Talk entitled: "Spinal cord stimulation to restore functions in people with spinal cord injury a highly multidisciplinary challenge"
- Christine Azevedo and Charles Fattal presented AGILIS project at the Cyber Days in Lyon. Talk entitled: "Restoring functional grasping in individuals with complete tetraplegia using neural stimulation." https://lyon-cyber-days.sciencesconf.org/
- David Guiraud presented AGILIS project within livestorm INRIA coferences.

11.1.5 Leadership within the scientific community

Christine Azevedo is member of IFESS society board.

11.1.6 Scientific expertise

- Christine Azevedo reviewed a Research project for Natural Sciences and Engineering Research Council of Canada (NSERC) Discovery Grant proposal.
- Christine Azevedo was expert for the French call for proposals "Appel à Projet RIN RECHERCHE EMERGENTS 2021."
- David Guiraud was reviewer of the ANR-FNS (Switzerland) common call in 2021.

11.1.7 Research administration

- Christine Azevedo is a member of COERLE (Inria Commité d'éthique)
- Christine Azevedo is a member of NICE committee, a subgroup of Sophia teamp projects committee (CEP) 7
- Christine Azevedo participated into the Selection committee of a Professor at ENS de Lyon (April 2021)
- Christine Azevedo participated into the INRIA Selection committee Recruitment campaign for Reserachers with disabilities
- Thomas Guiho is responsible for the "Neuroprostheses" teaching unit. This unit is an option common to all the masters of the ICT for health training package.

11.2 Teaching - Supervision - Juries

11.2.1 Teaching

- Master biology and health: Christine Azevedo, Thomas Guiho, David Guiraud, "Bionic approaches: Electrical stimulation in rehabilitation, sensory feedback restoration and BCI" 4.5h, M2, Montpellier University, France
- Master ICT for Health, Neuroprostheses option: François Bailly, "Biomechanics", 3h, M2, Montpellier University, France
- Master ICT for Health, Neuroprostheses option: Thomas Guiho, "Neuroanatomy", 3h, M2, Montpellier University, France
- Master ICT for Health, Neuroprotheses option: Ronan Le Guillou, "Control basics and signal processing", 9h, M2, Montpellier University, France
- Master ICT for Health, Neuroprotheses option: Olivier Rossel, "Signal processing and experimental set-up", 4.5h, M2, Montpellier University, France
- Master ICT for Health, Neuroprotheses option: Felix Schlosser-Perrin, "Electrophysiological mapping during awake brain surgery", 3h, M2, Montpellier University, France
- Master ICT for Health, Neuroprotheses option: Lucie William, "Spontaneous and evoked muscle activity", 3h, M2, Montpellier, France
- Master Sciences & Numérique pour la Santé (SNS), "Structure et Problématique de Santé" option: Lucie William, "The neuron in its environment", 1.5h, Montpellier University, France.
- David Guiraud was invited to the winter school organized by CNRS on "Interfaces"

11.2.2 Supervision

- PhD in progress : Lucie William, "Selective implanted neural stimulation to recover the prehension for quadriplegic", University of Montpellier-Inria-NEURINNOV, october 2019-March 2023, supervised by David Guiraud and Christine Azevedo
- PhD in progress : Hélène Moron, MD, "Jitter of MUAP measured through needle EMG used as a biomearker of the Botulin toxin effect", University of Montpellier-Inria, october 2019-september 2022, supervised by David Guiraud and Arnaud Dupeyron.
- PhD in progress : Clément Trotobas, "Design of arm assistive technologies", University of Montpellier-Inria-Dayton University, september 2020-september 2023, supervised by Christine Azevedo and Andrew Murray (Dayton Univ)
- PhD in progress : Ronan Le Guillou, "Design of a wearable neuroprosthetic solution for arm rehabilitation in post-stroke hemiplegia", University of Montpellier-Inria-CHU Toulouse, December 2020-December 2023, supervised by Christine Azevedo and David Gasq (CHU Toulouse)
- PhD in progress : Félix Schlosser-Perrin, " Mode'lisation des effets e'lectrophysiologiques de la stimulation e'lectrique sur le cerveau et preuves expe'rimentales en chirurgie des tumeurs ce're'brales : variation de l'intensite', de la distance inter-e'lectrode et la largeur du pulse de stimulation", University of Montpellier, september 2021-september 2024, supervised by François BonnetBlanc and Emmanuel Mandonnet (PU-PH en Neurochirurgie à l'APHP)

11.2.3 Juries

- Christine Azevedo participated in Fernanda Rodrigues (University Federal of Minas Gerais, Brazil) PhD defense, September 30th: "HYBRID ROBOTIC SYSTEM FOR REABILITATION OF THE TOP MEMBER OF POST-STEPHALIC VASCULAR STroke INDIVIDUALS: User-Centered Design.3
- Christine Azevedo participated in Tiago Coelho (University Federal of Minas Gerais, Brazil) PhD Qualification defense, November 25th: "Development and application of a high-capacity Functional Electrical Stimulation system for assisted cycling and the impact of different training programs on the physical conditioning of a subject with paraplegia."

11.3 Popularization

11.3.1 Internal or external Inria responsibilities

Christine Azevedo and Roger Pissard-Gibollet (SED Grenoble) coordinate the HumanLab Inria action https://project.inria.fr/humanlabinria/.

11.3.2 Articles and contents

Christine Azevedo Portrait in A.N.T.S association https://ants-asso.com/vie-asso/portrait/ch ristine-azevedo-coste/

11.3.3 Education

- Christine Azevedo gives sessions of programming initiation with Thymio Robot in a middle school class (Collège Léon Cordas, Montpellier) (8 hours)
- Christine Azevedo presented the job of researcher at Lycée Joliot Curie High School (Sète) during a day dedicated to women en engineering position (6 hours).

11.3.4 Interventions

- Lucie William participated into "Ma thèse en 180s" event and was finalist at the regional level.
- Christine Azevedo and Roger Pissard-Gibollet (SED Grenoble) presented the HumanLab Inria action (September 14) to all members of the institute during a videoconference.

12 Scientific production

12.1 Major publications

- [1] A. Boyer, S. Ramdani, H. Duffau, M. Dali, M. Vincent, E. Mandonnet, D. Guiraud and F. Bonnetblanc. 'Electrophysiological Mapping During Brain Tumor Surgery: Recording Cortical Potentials Evoked Locally, Subcortically and Remotely by Electrical Stimulation to Assess the Brain Connectivity On-line'. In: *Brain Topography: a Journal of Cerebral Function and Dynamics* (2020). DOI: 10.1007 /s10548-020-00814-0. URL: https://hal.inria.fr/hal-03106388.
- [2] C. Fattal, B. Sijobert, A. Daubigney, E. Fachin-Martins, B. Lucas, J.-M. Casillas and C. Azevedo Coste. 'Training with FES-assisted cycling in a subject with spinal cord injury: Psychological, physical and physiological considerations'. In: *Journal of Spinal Cord Medicine* (July 2018), pp. 1–12. DOI: 10.10 80/10790268.2018.1490098. URL: https://hal.archives-ouvertes.fr/hal-01875806.
- [3] T. Guiho, C. Delleci, C. Azevedo Coste, C. Fattal, D. Guiraud, J.-R. Vignes and L. Bauchet. 'Impact of direct epispinal stimulation on bladder and bowel functions in pigs: A feasibility study'. In: *Neurourology and Urodynamics* 37.1 (Jan. 2018), pp. 138–147. DOI: 10.1002/nau.23325. URL: https://hal-lirmm.ccsd.cnrs.fr/lirmm-01539038.
- [4] F. M. Petrini, M. Bumbasirevic, G. Valle, V. Ilic, P. Mijović, P. Čvančara, F. Barberi, N. Katic, D. Bortolotti, D. Andreu, K. Lechler, A. Lesic, S. Mazic, B. Mijović, D. Guiraud, T. Stieglitz, A. Alexandersson, S. Micera and S. Raspopovic. 'Sensory feedback restoration in leg amputees improves walking speed, metabolic cost and phantom pain'. In: *Nature Medicine* 25.9 (Sept. 2019), pp. 1356–1363. DOI: 10.1038/s41591-019-0567-3. URL: https://hal-lirmm.ccsd.cnrs.fr/lirmm-02282558.
- [5] F. M. Petrini, G. Valle, M. Bumbasirevic, F. Barberi, D. Bortolotti, P. Cvancara, A. Hiairrassary, P. Mijovic, A. O. Sverrisson, A. Pedrocchi, J.-L. Divoux, I. Popovic, K. Lechler, B. Mijovic, D. Guiraud, T. Stieglitz, A. Alexandersson, S. Micera, A. Lesic and S. Raspopovic. 'Enhancing functional abilities and cognitive integration of the lower limb prosthesis'. In: *Science Translational Medicine* 11.512 (Oct. 2019). DOI: 10.1126/scitranslmed.aav8939. URL: https://hal-lirmm.ccsd.cnrs.fr /lirmm-02307824.
- [6] O. Rossel, F. Soulier, S. Bernard, D. Guiraud and G. Cathébras. 'A phantom axon setup for validating models of action potential recordings'. In: *Medical and Biological Engineering and Computing* 10.4 (2016), pp. 671–678. DOI: 10.1007/s11517-016-1463-3. URL: https://hal-lirmm.ccsd.cnr s.fr/lirmm-01347422.
- [7] W. Tigra, M. Dali, L. William, C. Fattal, A. Gélis, J.-L. Divoux, B. Coulet, J. Teissier, D. Guiraud and C. Azevedo Coste. 'Selective neural electrical stimulation restores hand and forearm movements in individuals with complete tetraplegia'. In: *Journal of NeuroEngineering and Rehabilitation* 17.1 (May 2020), pp. 66–78. DOI: 10.1186/s12984-020-00676-4. URL: https://hal-lirmm.ccsd.c nrs.fr/lirmm-02613474.
- [8] W. Tigra, B. Navarro, A. Cherubini, X. Gorron, A. Gélis, C. Fattal, D. Guiraud and C. Azevedo Coste. 'A novel EMG interface for individuals with tetraplegia to pilot robot hand grasping'. In: *IEEE Transactions on Neural Systems and Rehabilitation Engineering* 26.2 (2018), pp. 291–298. DOI: 10.1 109/TNSRE.2016.2609478. URL: https://hal.archives-ouvertes.fr/lirmm-01373668.
- [9] H. M. R. Ugalde, D. Ojeda, V. Le Rolle, D. Andreu, D. Guiraud, J.-L. Bonnet, C. Henry, N. Karam, A. Hagege, P. Mabo, G. Carrault and A. I. Hernandez. 'Model-Based Design and Experimental Validation of Control Modules for Neuromodulation Devices'. In: *IEEE Transactions on Biomedical Engineering* 63.7 (June 2016), pp. 1551–1558. URL: https://hal.archives-ouvertes.fr/hal-01337430.
- [10] M. Vincent, O. Rossel, B. Poulin-Charronnat, G. Herbet, M. Hayashibe, H. Duffau, D. Guiraud and F. Bonnetblanc. 'Case report: remote neuromodulation with direct electrical stimulation of the brain, as evidenced by intra-operative EEG recordings during wide-awake neurosurgery'. In: *Clinical Neurophysiology* (Nov. 2015). Letter to the editor, pp. 1752–1754. DOI: 10.1016/j.clinph.2015.11.005. URL: https://hal-lirmm.ccsd.cnrs.fr/lirmm-01237964.

12.2 Publications of the year

International journals

- [11] A. Boyer, S. Ramdani, H. Duffau, M. Dali, M. Vincent, E. Mandonnet, D. Guiraud and F. Bonnetblanc. 'Electrophysiological Mapping During Brain Tumor Surgery: Recording Cortical Potentials Evoked Locally, Subcortically and Remotely by Electrical Stimulation to Assess the Brain Connectivity Online'. In: *Brain Topography: a Journal of Cerebral Function and Dynamics* 34 (5th Jan. 2021), pp. 221– 233. DOI: 10.1007/s10548-020-00814-0. URL: https://hal.inria.fr/hal-03106388.
- [12] A. Boyer, C. Stengel, F. Bonnetblanc, M. Dali, H. Duffau, F. Rheault, M. Descoteaux, D. Guiraud, A. Valero-Cabré and E. Mandonnet. 'Patterns of axono-cortical evoked potentials: an electrophysiological signature unique to each white matter functional site?' In: *Acta Neurochirurgica* (12th Jan. 2021). DOI: 10.1007/s00701-020-04656-4. URL: https://hal.inria.fr/hal-03112263.
- [13] C. Fattal, M. Schmoll, R. Le Guillou, B. Raoult, A. Frey, R. Carlier and C. Azevedo-Coste. 'Benefits of 1-year home training with FES cycling in paraplegia during Covid-19 crisis: case report'. In: *American Journal of Physical Medicine and Rehabilitation* Publish Ahead of Print (29th Sept. 2021). DOI: 10.1097/PHM.00000000001898. URL: https://hal.archives-ouvertes.fr/hal-03 366833.
- [14] T. Guiho, C. Azevedo-Coste, L. Bauchet, C. Delleci, J.-R. Vignes, D. Guiraud and C. Fattal. 'Sacral Anterior Root Stimulation (SARS) and Visceral Function Outcomes in Spinal Cord Injury–A Systematic Review of the Literature Over Four Decades'. In: *World Neurosurgery* (Sept. 2021). DOI: 10.1016/j.wneu.2021.09.041.URL: https://hal.inria.fr/hal-03375512.
- [15] T. Guiho, V. M. López-Álvarez, P. Čvančara, A. Hiairrassary, D. Andreu, T. Stieglitz, X. Navarro and D. Guiraud. 'New Stimulation Device to Drive Multiple Transverse Intrafascicular Electrodes and Achieve Highly Selective and Rich Neural Responses'. In: *Sensors* (29th Oct. 2021). DOI: 10.3390/s 21217219. URL: https://hal.inria.fr/hal-03409467.
- [16] R. Le Guillou, M. Schmoll, B. Sijobert, D. Lobato Borges, E. Fachin-Martins, H. Resende, R. Pissard-Gibollet, C. Fattal and C. Azevedo Coste. 'A Novel Framework for Quantifying Accuracy and Precision of Event Detection Algorithms in FES-Cycling'. In: *Sensors* 21.13 (2021), pp. 1–13. DOI: 10.3390/s21134571. URL: https://hal.archives-ouvertes.fr/hal-03278596.
- [17] X. Lu, C. Azevedo Coste, M.-C. Nierat, S. Renaux, T. Similowski and D. Guiraud. 'Respiratory Monitoring Based on Tracheal Sounds: Continuous Time-Frequency Processing of the Phonospirogram Combined with Phonocardiogram-Derived Respiration'. In: *Sensors* 21.1 (Jan. 2021), p. 99. DOI: 10.3390/s21010099. URL: https://hal.inria.fr/hal-03093720.
- [18] H. Moron, C. Gagnard-Landra, D. Guiraud and A. Dupeyron. 'Contribution of Single-Fiber Evaluation on Monitoring Outcomes Following Injection of Botulinum Toxin-A: A Narrative Review of the Literature'. In: *Toxins* 13.356 (17th May 2021), p. 16. DOI: 10.3390/toxins13050356. URL: https://hal.inria.fr/hal-03227777.
- [19] S. Ramdani, A. Boyer, S. Caron, F. Bonnetblanc, F. Bouchara, H. Duffau and A. Lesne. 'Parametric recurrence quantification analysis of autoregressive processes for pattern recognition in multichannel electroencephalographic data'. In: *Pattern Recognition* 109 (2021), #107572. DOI: 10.1016 /j.patcog.2020.107572. URL: https://hal.archives-ouvertes.fr/hal-02921847.
- [20] M. Schmoll, R. Le Guillou, D. Lobato Borges, C. Fattal, E. Fachin-Martins and C. Azevedo Coste. 'Standardizing fatigue-resistance testing during electrical stimulation of paralysed human quadriceps muscles, a practical approach'. In: *Journal of NeuroEngineering and Rehabilitation* 18.11 (21st Jan. 2021). DOI: 10.1186/s12984-021-00805-7. URL: https://hal.inria.fr/hal-0311 8295.
- [21] B. Sijobert, C. Azevedo Coste, J. Pontier, S. Graf and C. Fattal. 'A Sensor-Based Multichannel FES System to Control Knee Joint and Reduce Stance Phase Asymmetry in Post-Stroke Gait'. In: Sensors 21.6 (Mar. 2021), p. 2134. DOI: 10.3390/s21062134. URL: https://hal.inria.fr/hal-031977 30.

Scientific book chapters

[22] D. Guiraud and M. Dali. 'Handbook of NeuroengineeringChapter: Modeling Peripheral Nerve Stimulation'. In: *Handbook of Neuroengineering*. Springer Singapore, 14th Aug. 2021. DOI: 10.1007 /978-981-15-2848-4. URL: https://hal.inria.fr/hal-03320392.

Other scientific publications

[23] F. M. Rodrigues Martins Ferreira, G. de Paula Rúbio, L. Oliveira Fonseca, C. Fattal, A. M. Valladão Novais Van Petten, C. B. Santos Vimieiro and C. Azevedo Coste. *Effectiveness of hybrid robotic* rehabilitation system on upper limb recovery of people with central injuries: a systematic review with meta-analysis. 21st Jan. 2021. URL: https://hal.inria.fr/hal-03130770.