INSTITUT NATIONAL DE RECHERCHE EN INFORMATIQUE ET EN AUTOMATIQUE

Project-Team DEMAR

Artificial movement and gait restoration

Sophia Antipolis - Méditerranée

Theme : Computational Medicine and Neurosciences

Table of contents

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2. Overall Objectives

2.1. Introduction

Functional Electrical Stimulation (FES) has been used for about 30 years in order to restore deficient physiological functions. At the beginning, only surface stimulation was possible and thus only used in a clinical context due to the low reliability of electrode placements. In the early eighties, implanted FES appeared through well-known applications: pacemaker, Brindley bladder control, cochlear implant, and more recently deep brain stimulation (DBS).

Currently, FES is the only way to restore motor function even though biological solutions are studied, but not yet successfully tested on humans. Few teams carry out researches on implanted FES and the functional results remain poor. Nevertheless, the technique has proved to be useable and needs enhancements that we address in DEMAR. Regarding technology, complex electrode geometries associated with complex stimulus waveforms provide a way to perform fibre type selectivity and spatial localisation of the stimuli in the nerves. These features are not yet implemented and demand new hardware and software architectures. Several teams in Denmark (SMI U. Aalborg), Germany (IBMT Franhaufer Institute), England (U. College of London), Belgium (U. Catholique de Louvain), United States (Cleveland FES centre), and Canada (Ecole Polytechnique de Montréal), work on multi-polar neural stimulation but mainly on electrode aspect, except Polystim Lab of Montréal.

Such a complex system needs advanced control theory tools coupled with a deep understanding of the underlying neurophysiological processes. This major area of research will be also an important part of the DEMAR objectives.

Besides, experiments are necessary to: improve neurophysiology knowledge, identify and validate models, evaluate control strategies or test neuroprostheses. Our experiments are carried on valid and non-valid individuals in clinical environment, but also on animals. Nevertheless, it really worth the effort in order to bring theory to useable systems.

Finally, industrial transfer is mandatory since we aim at proposing effective solutions to patients. Thus we try to prototype all our findings in order to validate and transfer efficiently our concepts. To be useable in clinical or private environments by the patients themselves, systems need to be certified as an industrial Medical Device.

DEMAR research is organized as follows:

1. Modelling and identification of the human sensory-motor system.
2. Synthesis and control of functions.
3. Interfacing artificial and natural parts through neuroprosthetic devices: both stimulation and recording.

The main applied research fields are then:

- Quantitative characterization of the human sensory-motor system firstly for motor disorders diagnosis and objective quantification, and secondly in order to help the design and the control of neuroprosthetic devices.
- Restoring motor and sensitive functions through implanted FES and neural signal sensing such as lower limb movement synthesis and control for spinal cord injured patients, synergetic control of the deficient limb for hemiplegic patients, bladder control, pain relief...
- Improving surface stimulation for therapy such as active verticalization of paraplegic patients, reduction of tremor, reeducation of hemiplegic post-stroke patients...

2.2. Highlights

- David Guiraud obtained the 2010 prize from "Académie des Sciences" and EADS fundation in Information Technology applied to medical devices.
- David Guiraud obtained the 2010 prize from "Victoires de la Réussite - Club des 500 / prix de la recherche scientifique (Montpellier)".

3. Scientific Foundations

3.1. Modelling and identification of the sensory-motor system

Participants: Mitsuhiro Hayashibe, Christine Azevedo Coste, David Guiraud, Philippe Poignet.

The literature on muscle modelling is vast, but most of research works focus separately on the microscopic and on the macroscopic muscle's functional behaviours. The most widely used microscopic model of muscle contraction was proposed by Huxley in 1957. The Hill-Maxwell macroscopic model was derived from the original model introduced by A.V. Hill in 1938. We may mention the most recent developments including Zahalak's work introducing the distribution moment model that represents a formal mathematical approximation at the sarcomere level of the Huxley cross-bridges model and the works by Bestel and Sorine (2001) who proposed an explanation of the beating of the cardiac muscle by a chemical control input connected to the calcium dynamics in the muscle cells, that stimulates the contractile elements of the model. With respect to this literature, our contributions are mostly linked with the model of the contractile element, through the introduction of the recruitment at the fibre scale formalizing the link between FES parameters, recruitment and Calcium signal path. The resulting controlled model is able to reproduce both short term (twitch) and long term (tetanus) responses. It also matches some of the main properties of the dynamic behaviour of muscles, such as the Hill force-velocity relationship or the instantaneous stiffness of the Mirsky-Parmley model. About integrated functions modelling such as spinal cord reflex loops or central pattern generator, much less groups work on this topic compared to the ones working on brain functions. Mainly neurophysiologists work on this subject and our originality is to combine physiology studies with mathematical modelling and experimental validation using our own neuroprostheses. The same analysis could be drawn with sensory feedback modelling. In this domain, our work is based on the recording and analysis of nerve activity through electro-neurography (ENG). We are interested in interpreting ENG in terms of muscle state in order to feedback useful information for FES controllers and to evaluate the stimulation effect. We believe that this knowledge should help to improve the design and programming of neuroprostheses. We investigate risky but promising fields such as intrafascicular recordings, area on which only few teams in North America (Canada and USA), and Denmark really work on. Very few teams in France, and none at INRIA work on the peripheral nervous system modelling, together with experimental protocols that need neuroprostheses. Most of our INRIA collaborators work on the central nervous system, except the spinal cord, (ODYSSEE for instance), or other biological functions (SISYPHE for instance). Our contribution concern the following aspects:

- Muscle modelling,
- Sensory organ modelling,
- Electrode nerve interface,
- High level motor function modelling,
- Model parameters identification.

We contribute both to the design of reliable and accurate experiments with a well-controlled environment, to the fitting and implementation of efficient computational methods derived for instance from Sigma Point Kalman Filtering.

3.2. Synthesis and Control of Human Functions

Participants: Christine Azevedo Coste, Philippe Fraisse, Philippe Poignet, David Andreu.

We aim at developping realistic solutions for real clinical problems expressed by patients and medical staff. Different approaches and specifications are developped to answer to those issues in short, mid or long terms. This research axis is therefore obviously strongly related to clinical application objectives. Even though applications can appear very different, the problematic and constraints are usually similar in the context of electrical stimulation: classical desired trajectory tracking is not possible, robustness to disturbances is critical, possible observations of system are limited. Furthermore there is an interaction between body segments under voluntary control of the patient and body segments under artificial control. Finally, this axis relies on modelling and identification results obtained in the first axis and on the technological solutions and approaches developped in the third axis (Neuroprostheses). The robotics framework involved in DEMAR work is close to the tools used and developped by BIPOP team in the context of bipedal robotics. There is no national teams working on those aspects. Within international community, several colleagues carry out researches on the synthesis and control of human functions, most of them belong to the International Functional Electrical Stimulation Society (IFESS) community. In the following we present two sub-objectives. Concerning spinal cord injuries (SCI) context not so many team are now involved in such researches around the world. Our force is to have technological solutions adapted to our theoretical developments. Concerning post-stroke context, several teams in Europe and North America are involved in drop-foot correction using FES. Our team specificity is to have access to the different expertises needed to develop new theoretical and technical solutions: medical expertise, experimental facilities, automatic control expertise, technological developments, industrial partner. These expertises are available in the team and through strong external collaborations.

3.3. Neuroprostheses

Participants: David Andreu, David Guiraud, Guy Cathébras, Fabien Soulier, Serge Bernard.

The main drawbacks of existing implanted FES systems are well known and include insufficient reliability, the complexity of the surgery, limited stimulation selectivity and efficiency, the non-physiological recruitment of motor units and muscle control. In order to develop viable implanted neuroprostheses as palliative solutions for motor control disabilities, the third axis "Neuroprostheses" of our project-team aims at tackling four main challenges: (i) a more physiologically based approach to muscle activation and control, (ii) a fibres' type and localization selective technique and associated technology (iii) a neural prosthesis allowing to make use of automatic control theory and consequently real-time control of stimulation parameters, and (iv) small, reliable, safe and easy-to-implant devices.

Accurate neural stimulation supposes the ability to discriminate fibres' type and localization in nerve and propagation pathway; we thus jointly considered multipolar electrode geometry, complex stimulation profile generation and neuroprosthesis architecture. To face stimulation selectivity issues, the analog output stage of our stimulus generator responds to the following specifications: i) temporal controllability in order to generate current shapes allowing fibres' type and propagation pathway selectivity, ii) spatial controllability of the current applied through multipolar cuff electrodes for fibres' recruitment purposes. We have therefore proposed and patented an original architecture of output current splitter between active poles of a multipolar electrode. The output stage also includes a monotonic DAC (Digital to Analog Converter) by design. However, multipolar electrodes lead to an increasing number of wires between the stimulus generator and the electrode contacts (poles); several research laboratories have proposed complex and selective stimulation strategies involving multipolar electrodes, but they cannot be implanted if we consider multisite stimulation (i.e. stimulating on several nerves to perform a human function as a standing for instance). In contrast, all the solutions tested on humans have been based on centralized implants from which the wires output to only monopolar or bipolar electrodes, since multipolar ones induce to many wires. The only solution is to consider a distributed FES architecture based on communicating controllable implants. Two projects can be cited: Bion technology (main competitor to date), where bipolar stimulation is provided by injectable autonomous units, and the LARSI project, which aimed at multipolar stimulation localized to the sacral roots. In both cases, there was no application breakthrough for reliable standing or walking for paraplegics. The power source, square stimulation shape and bipolar electrode limited the Bion technology, whereas the insufficient selection accuracy of the LARSI implant disqualified it from reliable use.

Keeping the electronics close to the electrode appears to be a good, if not the unique, solution for a complex FES system; this is the concept according to which we direct our neuroprosthesis design and development, in close relationship with other objectives of our project-team (control for instance) but also in close collaboration with medical and industrial partners.

Our efforts are mainly directed to implanted FES system but we also work on surface FES architecture and stimulator; most of our concepts and advancements in implantable neuroprostheses are applicable somehow to external devices.

4. Application Domains

4.1. Objective quantification and understanding of movement disorders

One main advantage of developping a model based on a physical description of the system is that the parameters are meaningful. Therefore, these parameters when identified on a given individual (valid or deficient), give objective and quantitative data that characterize the system and thus can be used for diagnosis purposes.

Modelling provides a way to simulate movements for a given patient and therefore based on an identification procedure it becomes possible to analyse and then understand his pathology. In order to describe complex pathology such as spasticity that appears on paraplegic patients, you need not only to model the biomechanics parts - including muscles -, but also parts of the peripheral nervous system - including natural sensors - to assess reflex problems. One important application is then to explore deficiencies globally due to both muscles and peripheral neural nets disorders.

4.2. Palliative solutions for movement deficiencies

Functional electrical stimulation is one possibility to restore or control motor functions in an evolutive and reversible way. Pacemaker, cochlear implants, deep brain stimulation (DBS) are successful examples. DEMAR focuses on movement disorder restoration in paraplegic and quadriplegic patients, enhancements in hemiplegic patients, and some other motor disorders such as bladder and bowel control. Nevertheless, since some advances in neuroprosthetic devices can be exploited for the next generation of cochlear implants, the team also contributes to technological and scientific improvements in this domain.

The possibility to interface the sensory motor system, both activating neural structure with implanted FES, and sensing through implanted neural signal recordings open a wide application area:

- Restoring motor function such as grasping for quadriplegic patient, standing and walking for paraplegic patient, compensating foot drop for hemiplegic patients. These applications can be firstly used in a clinical environment to provide physiotherapist with a new efficient FES based therapy (using mainly surface electrodes) in the rehabilitation process. Secondly, with a more sophisticated technology such as implanted neuroprostheses, systems can be used at home by the patient himself without a clinical staff.
- Modulating motor function such as tremors in Parkinsonian patient using DBS. Techniques are very similar but for the moment, modelling is not achieved because it implies the central nervous system modelling in which we are not implied.
- Sensing the afferent pathways such as muscle's spindles, will be used to provide a closed loop control of FES through natural sensing and then a complete implanted solution. Sensing the neural system is a necessity in some complex motor controls such as the bladder control. Indeed, antagonist muscle's contractions, and sensory feedbacks interfere with FES when applied directly on the sacral root nerve concerned. Thus, enhanced activation waveforms and sensing feedback or feedforward signals are needed to perform a highly selective stimulation.

To achieve such objectives, experimentations in animals and humans are necessary. This research takes therefore a long time in order to go from theoretical results to real applications. This process is a key issue in biomedical research and is based on: i) design of complex experimental protocols and setups both for animals and humans, ii) ethical attitude both for humans and animals, with ethical committee approval for human experiments iii) volunteers and selected, both disabled and healthy, persons to perform experiments with the adequate medical staff.

5. Software

5.1. Software

5.1.1. RdP to VHDL tool

Participants: David Andreu, Grégory Angles.

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

5.1.2. SENISManager

Participants: David Andreu, Grégory Angles, Robin Passama.

We developed a specific software environment called SENISManager allowing to remotely manage and control a network of DSUs, i.e. the distributed FES architecture. SENISManager performs self-detection of the architecture being deployed (Fig.1; left). This environment also allows the manipulation of micro-programs from their edition to their remote control (Fig.1; right). The software was delivered to TIME european project consortium.

5.1.3. STIMWare

Participants: David Andreu, Robin Passama.

We designed and partially developed a software environment allowing the management and control of a heterogeneous technology based external FES architecture. This software environment eases the configuration and exploitation of the external FES platform since it ensures the interoperability of the heterogeneous entities implied within the platform. It is based on a middleware and a set of modules organized according to two-layer software architecture: the interaction layer and the control layer. The interaction layer directly pilots stimulators and sensors used in the platform, ensuring the communication with these entities according to their specific protocol stacks. Its middleware contains a scheduler in charge of the scheduling, the activation and the monitoring of the corresponding modules. The control layer supports the development of control strategies, potentially based on a set of heterogeneous entities (stimulators and sensors), like closed-loop controllers and/or supervisory controllers. This software is already tested with stimulators used on patient under ethical committee approval.

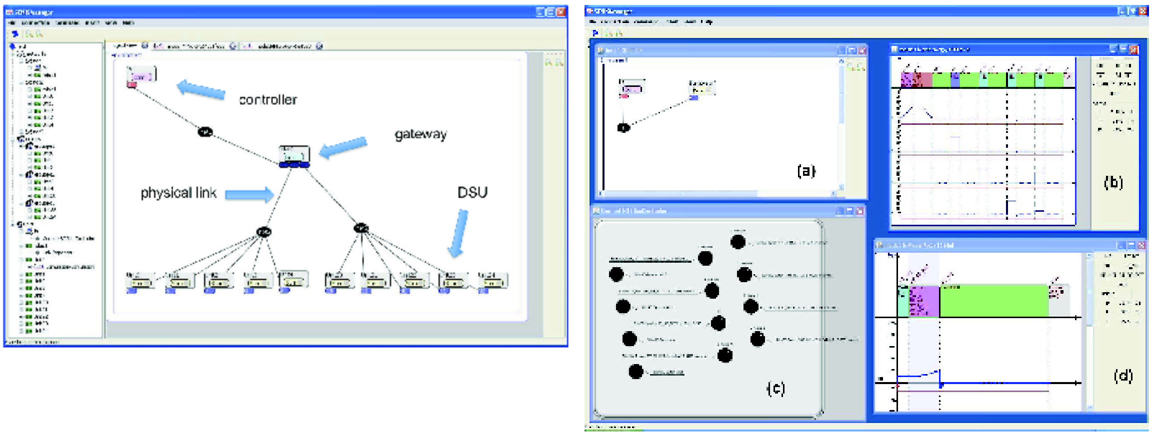


Figure 1. Left) Example of SENIS Architecture managed through SENIS Manager. Right) Some windows available on SENISManager: (a) FES architecture management, (b) graphical editing of micro-programs, (c) console for remote control of the execution of micro-programs of which parameter values are displayed in real-time (d).

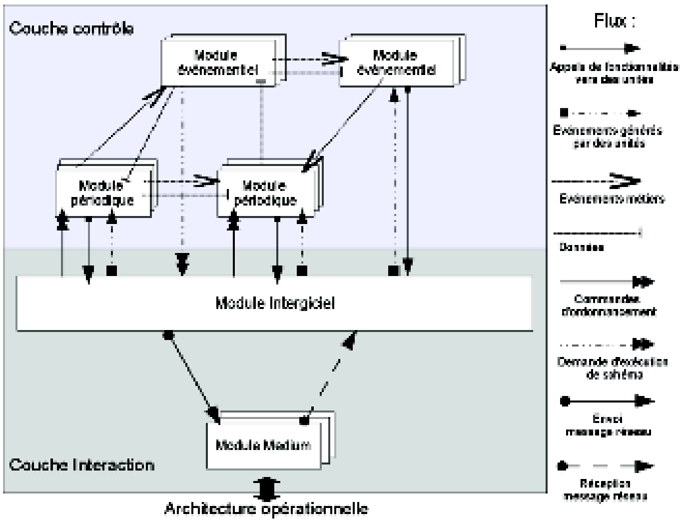


Figure 2. Schematic description of the software environment allowing the deployment of control strategies based on heterogeneous entities

A graphical interface will allow the end-user to manipulate the FES architecture (software entities and their associated hardware), at greater abstraction level.

5.1.4. gOM2N

Participants: Jérémy Laforêt, David Guiraud.

We have developped a software tool chain to simulate electrode-nerve interface. It involves two different softwares (OpenMEEG and Neuron) and three ways of interaction: command line, Python scripts, and editing makefiles. To enable the use of this tool-chain by non specialist we designed a graphical interface. It is based only on free software technologies: Python, gtk and glade. It enables the user to define the model parameters and run the simulations. It takes into account the intermediate steps and thus can resume previous simulations or use part of them as basis for new ones.

5.1.5. Planning and Fast Re-Planning of safe motions

Participants: Sébastien Lengagne, Philippe Fraisse, Nacim Ramdani.

This algorithm allowing to generate optimal safe motion in term of balance is based on interval analysis. It can be downloaded at: http://safemotions.sourceforge.net/.

5.1.6. FES muscle modeling in Opensim framework

Participants: Mitsuhiro Hayashibe, Philippe Fraisse, David Guiraud, Emel Demircan, Oussama Khatib (INRIA Equipe Associée).

In FES context, movement synthesis and control remain challenging tasks due to the complexity of whole body dynamics computation and the nonlinearity of stimulated muscle dynamics. The characteristics of each muscle and each patient are quite different, and mathematical model of muscle dynamics and whole body biomechanics are prerequisites to enable unified subject specific FES control. As a first step, we have implementated a muscle model representing electrically stimulated muscle into the Stanford Opensim framework. Opensim is an open source package for biomechanical analysis.

Originally, our FES physiological muscle model was developed in Matlab. For the integration with Stanford platform for whole body dynamic computation, it was essential rewrite it in C++ and in Opensim structure.

A FES muscle class was implemented and integrated within Opensim platform. FES muscle activation was tested in simple dynamic situation with two muscles as shown in Fig.3. Blue lines show the path of muscle and the gray block was fixed on the floor then middle cube was pulled with the identical muscle stimulated synchronously. The right plots show activation level, developed muscle force and the contracted muscle length respectively. The result in this isometric test showed the same result as the numerical integration in Matlab. The implementation of FES muscle class allows us to easily develop the plug-in to be used with whole body musuculoskeletal model. Originally Opensim model was embedded with Hill muscle model designed to represent voluntary muscle contractions. Through plug-in feature in Opensim environment, all muscles could be replaced with FES muscle models.

6. New Results

6.1. Modelling and Identification

6.1.1. Nonlinear identification method corresponding to muscle property variation

Participants: Mitsuhiro Hayashibe, Mourad Benoussaad, David Guiraud, Philippe Poignet, Charles Fattal.

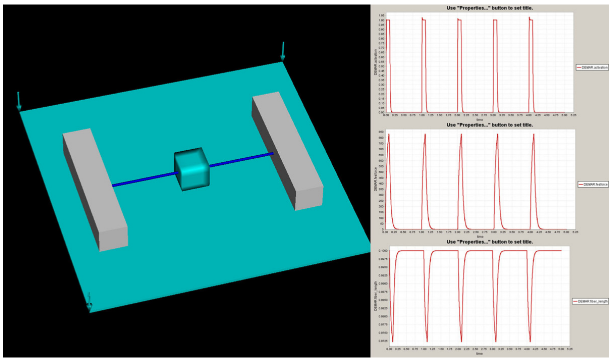


Figure 3. FES muscle activation test in simple dynamic situation with two muscles. The right plots show activation level, developed muscle force and the contracted muscle length respectively.

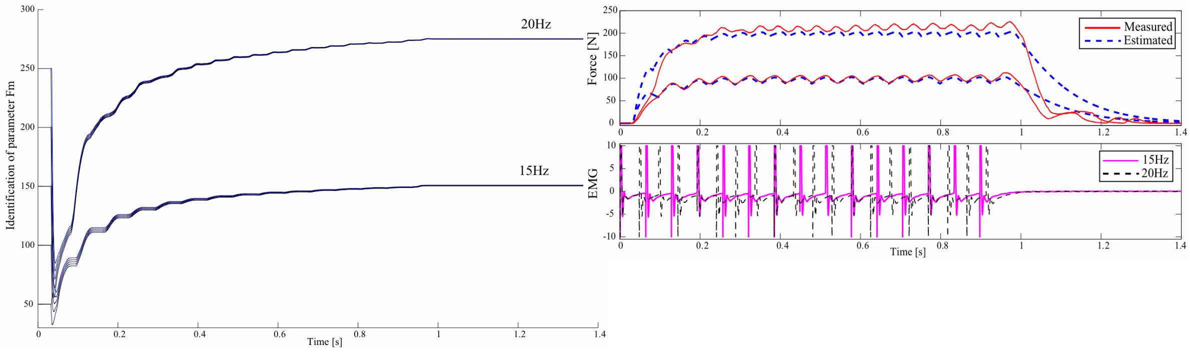
A model-based FES would be very helpful for adaptive movement synthesis of spinal-cord-injured patients. The nonlinearity of the neuromuscular system can be captured through modeling and identification process. However, there are still critical limitations in FES: rapid muscle fatigue and time-varying property. In order to minimize fatigue intermittent stimulation is usually adopted. In this case, fatigue and recovery occur in sequence. Thus, the time-varying muscle response is really difficult to be predicted for FES force control. We have proposed an identification method in order to identify unknown internal states and maximal force parameter which are inside the nonlinear differential equation. Among the internal parameters of muscle model, maximal force Fm should be mainly changed corresponding to the current muscle condition. Muscle fatigue and recovery are difficult to be modeled and predicted. However observing muscle input-output information will allow for adaptive estimation of changes due to fatigue or other unknown metabolic factor of human system.

Experiments were conducted on three male subjects, who have complete paralysis ASIA A of lower extremity. An authorization from the local ethical committee and an agreement from each subject were obtained. Muscle force responses were measured respectively in 15Hz and 20Hz stimulation frequency. The identification was executed by Sigma Point Kalman Filter estimator to obtain parameter F_m with different initial values as in Fig.4. The stable identification result could be obtained with every initial value in SPKF. The estimation with the identified model can be confirmed with the measured force as direct validation in Fig.4. The normalized root mean squared deviation (NRMSD) between the model estimations and measured values in force plateau was 4.87 percent in average. The detailed result of cross validation can be found in [20].

6.1.2. *Torque Prediction Using Evoked EMG during Different Muscle Fatigue States*

Participants: Qin Zhang, Mitsuhiro Hayashibe, Maria Papaiordanidou, Philippe Fraisse, Charles Fattal, David Guiraud.

Muscle fatigue is a major limitation of the application of FES. The detection and compensation of muscle fatigue is essential to avoid movement failure and achieve desired trajectory. This work aims to predict ankle plantar-flexion torque using stimulus evoked EMG (eEMG) during different muscle fatigue states. Five spinal cord injured patients were recruited for this study. An intermittent fatigue protocol was delivered to triceps surae muscle in isometric condition. A Hammerstein model was used to capture the muscle contraction dynamics to represent eEMG-torque relationship. The prediction of ankle torque was based on measured eEMG and past measured or past predicted torque. The latter approach makes it possible to use eEMG as a synthetic force sensor when force measurement is not available in daily use. Some previous researches suggested to use eEMG information directly to detect and predict muscle force during fatigue assuming a fixed relationship between eEMG and generated force. However, we found that the prediction became less precise



Direct validation: n

Figure 4. Identification of parameter F_m with different initial values.

with the increase of muscle fatigue when fixed parameter model was used. Therefore, the torque prediction was carried out with an adaptive parameter using the latest measurement. The prediction of adapted model showed an improvement of 16.7%-50.8% compared to the fixed model in all subjects. Fig.5 illustrates the result obtained in one of the subjects [26].

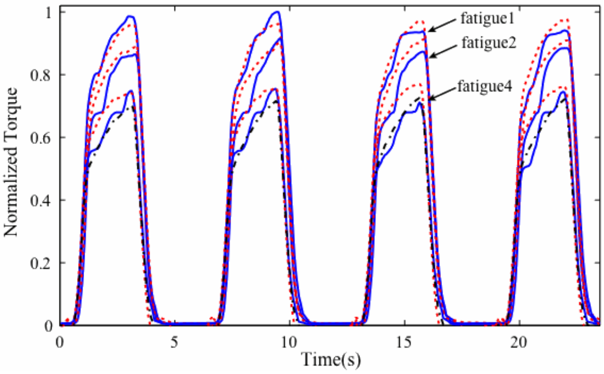


Figure 5. The measured and predicted torque obtained by eEMG-torque model with fatigue-inducing protocol (subject3). The blue solid line indicates the measured torque. The red dotted line represents the corresponding predicted torque based on fixed model. The black dashdotted line represents the torque prediction of fatigue4 based on adapted model. All the torques are normalized with the maximal measured torque of fatigue1.

6.1.3. Torque Prediction in Fatiguing Muscle Toward Advanced Drop Foot Correction

Participants: Qin Zhang, Mitsuhiro Hayashibe, Bertrand Sablayrolles, Christine Azevedo Coste.

Electrical stimulation (ES) has been applied since 1961 for the correction of hemiplegic drop foot. One main drawback of the technique is the occurrence of early fatigue. Therefore, it is essential to predict force generation for precise ES closed loop control when the stimulated muscle becomes fatigued. This work aims to predict ankle torque using stimulus evoked EMG (eEMG) during different muscle fatigue states. Five healthy subjects participated in our study. Conventional stimulation protocol for drop foot correction was applied by surface stimulation in sitting position. The results show that the long-term stimulation yields muscle fatigue leading to torque decline, the muscle myoelectrical activity (eEMG) performs quite differently in different fatigue levels. In this work, we carried out the torque prediction with an adapted parameter model according to muscle fatigue states by reidentification using the latest measurement. The prediction showed an improvement of 21%-90.9% comparing to the fixed parameters model in all subjects. Fig.6 illustrates the prediction performance obtained in one of the subjects [27]. The results revealed a promising approach to use evoked EMG for fatigue compensation in the application of drop foot correction.

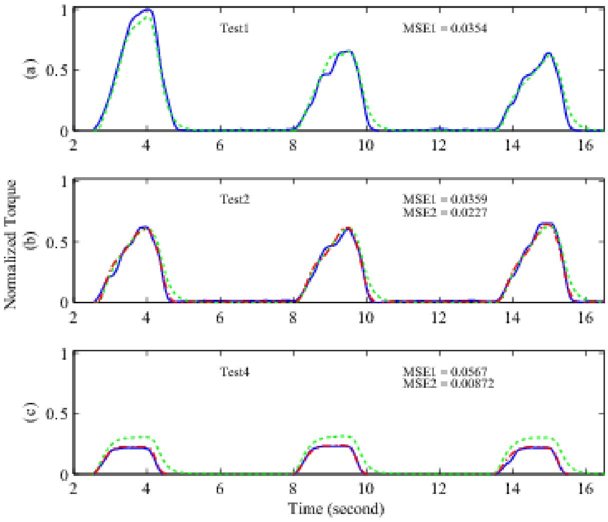


Figure 6. The measured torque and predicted torque based on evoked EMG in different muscle fatigue states in subject2. The measured torque (blue), the predicted torque with fixed model (green dotted) and the predicted torque with adapted model (red dashdotted) are shown. The results are normalized by the maximum value in the whole test.

6.1.4. Does central fatigue exist under low-frequency stimulation of a low fatigue-resistant muscle?

Participants: Maria Papaiordanidou, David Guiraud, Alain Varray.

The aim of the present study was to determine whether central fatigue occurs when fatigue is electrically induced in the abductor pollicis brevis (APB) muscle. Three series of 17 trains (30 Hz, 450us, 4s on/6s off, at the maximal tolerated intensity) were used to fatigue the muscle. Neuromuscular tests consisting of electrically evoked and voluntary contractions were performed before and after every 17-train series. Both the force induced by the stimulation trains and maximal voluntary force generation capacity significantly decreased throughout the protocol (-27% and -20%, respectively, at the end of the protocol, $P < 0.001$). These decreases were accompanied by significant impairment in the muscle contractile properties ($P < 0.05$), as assessed by the muscle mechanical response (Pt), and a failure in muscle excitability ($P < 0.01$), as assessed by the muscle compound action potential (M-wave or Mmax). Central fatigue indices (level of activation, RMS/Mmax and H reflex) were not significantly changed at any point in the protocol. This gives evidence of preserved motor command reaching the motor neurons and preserved spinal excitability. The results indicate that this low-frequency stimulation protocol entails purely peripheral fatigue development when applied to a low fatigue-resistant muscle [9].

6.1.5. Neuromuscular fatigue development during intermittent electrical stimulation of the triceps surae in spinal cord-injured patients.

Participants: Maria Papaiordanidou, Alain Varray, Charles Fattal, David Guiraud.

The aim of the present study was to examine neuromuscular fatigue development under intermittent electrical stimulation applied to complete spinal cord-injured subjects. The triceps surae was fatigued using a 30-Hz ES protocol (50% duty cycle) composed of three series of five trains. Spinal excitability (assessed by the H reflex), muscle excitability (assessed by the M-wave) and muscle contractile properties (assessed by mechanical response parameters) were tested before and after every five-train series. Torque evoked by ES significantly decreased throughout the protocol ($P < 0.001$). This decrease was accompanied by a significant increase in M-wave amplitude ($P < 0.001$), while H reflex and the Hmax/Mmax ratio were not significantly modified by the protocol. The contraction properties (contraction time and rate) of the mechanical response were improved ($P < 0.05$), while the amplitude of the mechanical response was significantly altered during the ES protocol ($P < 0.05$). The results indicated high fatigue development that could be attributed to alterations taking place only distally to the muscle membrane. Significance: These results may help clinicians to develop stimulation strategies for optimal stress of the patients' musculoskeletal system, by designing strengthening programs aiming at enhancing muscle contractile properties.

6.1.6. Fatigue tracking in spinal-cord injury using a physiology-based muscle model

Participants: Maria Papaiordanidou, Mitsuhiro Hayashibe, Alain Varray, Charles Fattal, David Guiraud.

Muscle fatigue is a complex phenomenon that limits the application of FES, used to activate skeletal muscle in order to perform functional movements. The purpose of the present study was to track the development of neuromuscular fatigue under intermittent FES applied to the triceps surae muscle of 5 subjects paralyzed by Spinal Cord Injury (SCI). Experimental results gave evidence of neuromuscular fatigue development attributed to muscle contractile properties impairment. Classical parameters representing muscle contractile properties (peak twitch, Pt and twitch contraction and relaxation parameters) significantly decreased at the end of the protocol. These experimental data were used to identify the parameters of a previously developed physiological mathematical model describing all possible contractive states occurring in a stimulated muscle. The sigma-point Kalman filter was used for the identification of the model parameters and simulation results prove that the model was capable to track fatigue and under the present stimulation conditions even predict muscle contractile behavior. This work reinforces clinical research with a tool allowing clinicians to monitor the current state of the stimulated muscle for its optimal solicitation.

6.1.7. A Computational Model of the Primary Auditory Neuron Activity

Participants: Christophe Michel, Jérôme Bourien, Régis Nouvian, Christine Azevedo Coste, Jean-Luc Puel.

The mechanosensory hair cells of the cochlea (inner hair cells, IHC) convert the incoming sound stimulation into neurotransmitter release. The time and intensity coding of sound require a fast and coordinated release of glutamate, the neurotransmitter of the IHC, onto the afferent auditory nerve fibers. At the presynaptic side, vesicles are clustered around an electron-dense body, the synaptic ribbon (see Fig.7 A). Patch-clamp recordings from the auditory afferent terminal and non-stationary fluctuations of IHC exocytic capacitance measurements demonstrated a coordinated release of synaptic vesicles. This multivesicular release is associated with fast excitatory post-synaptic current (EPSCs) carried by AMPA type glutamate receptors (Glowatzki, Nat. Neurosci., 2002). Presumably, EPSCs yielded at the afferent terminal trigger action potential firing along the axon of the auditory neuron (see Fig.7 B).

Despite cell physiology studies have added important insights into the synaptic mechanisms underlying fidelity and reliability of sound coding, the whole processing from transmitter release to action potential initiation is still lacking. Therefore, the aim of this study is to design a computational model of the first auditory synapse. This implies to compute EPSCs properties at the afferent terminal and action potential firing (Woo, IEEE Trans. Biomed., 2009) at the axon (see Fig.7 C). Beside simulation of action potential firing as a function of the input, this model will enable to unravel auditory synaptic disorders such as the synaptopathy [23].

6.2. Function control and synthesis

6.2.1. Model-based synthesis of FES patterns for rehabilitation: Experimental results

Participants: Mourad Benoussaad, Philippe Poignet, David Guiraud, Mitsuhiro Hayashibe, Charles Fattal.

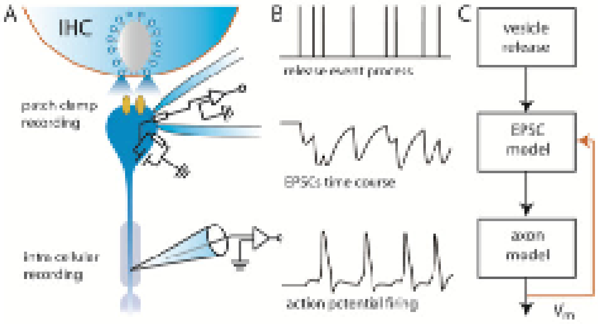


Figure 7. Electrophysiology and modeling of the primary auditory neuron. A. The IHC ribbon (gray) accumulates glutamate vesicles at the synapse in front of the AMPA glutamate receptors (yellow). EPSCs and action potential can be measured with patch-clamp and intracellular recording techniques, respectively. B. Each coordinate release of vesicles evokes an EPSC which triggers action potential firing in the primary auditory neurons. C. Block diagram of the proposed computational model. The parameters of the EPSCs model are continuously regulated by the membrane potential (Vm).

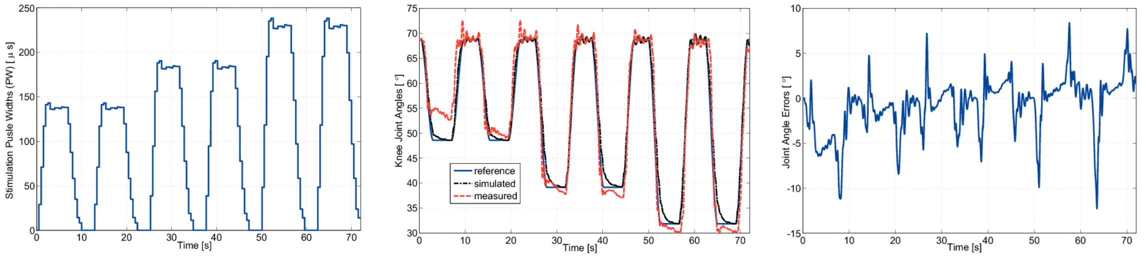
In rehabilitation context, the FES patterns are often empirically chosen, which can lead to an excessive level of muscular activation and an inappropriate use of musculoskeletal system capacities. We investigated an optimization methods based on a musculoskeletal physiological model to synthesize the best FES patterns which ensuring any functional task restoration. To illustrate the approach, a knee joint activated by its stimulated quadriceps and hamstring muscles has been used.

The first part of this study was done in simulation and consisted of the investigation of several optimization criteria and their effects on muscular energy consumption and on the co-contraction phenomenon. It also include a comparison based on an energetic and on a co-contraction criteria. The comparison highlights a high level of both co-contraction and muscular energy consumption when following an imposed trajectory which may accelerate muscular fatigue. In the future works, a compromise should be find between co-contraction level, which is useful for joint stability, and minimization of muscular fatigue. The second part of our work was aimed at validating synthesizing FES patterns on SCI subjects. Four patient were using surface stimulation and one patient has an implanted FES system. The test was made in dynamical condition, where the knee joint angles were measured using the mounted electrogoniometer (Fig.8-(a)) and recorded through an acquisition chain (Fig.8-(b)).

(a) (b)

Figure 8. Experimental setup in dynamical conditions: Equipments for measurements (a) and acquisition chain (b).

The experimental results show good agreement (Fig.9(b)) between a desired trajectory, the simulated trajectory with the model and the measured one obtained under a synthesized FES patterns (Fig.9(a)). The difference between the desired and the measured trajectories are quantified through the angle errors presented in Fig.9(c). It highlights a small errors except some peaks which are probably due to the musculoskeletal system delay. These experimental results are encouraging and presents a first step of using efficiently FES in rehabilitation of paralyzed limbs. In the future works the system will be completed with an antagonistic muscle in order to use all the musculoskeletal system capacities.



(a) Stimulation PW (b) Knee angles (c) Angle errors

Figure 9. Experimental validation of FES synthesis

6.2.2. Signal-based segmentation of human locomotion using embedded sensor network

Participants: Maud Pasquier, Bernard Espiau, Christine Azevedo Coste, Roger Pissard-Gibollet (SED INRIA), Guillaume Chelius.

We introduce a simple approach to segment in homogeneous phases a long-duration record of locomotion data consisting of body segment acceleration and foot pressure information. Two cases are considered: walk and run around an indoor running track and outdoor marathon (Fig.10). The association of acceleration norms with impact detections allows us to successfully apply K-means algorithm in order to automatically classify the locomotion in terms of walking and various running speeds. The method is validated on experimental data : one subject, equipped with inertial measurement units (IMU) and foot pressure units was asked to successively walk and run around an indoor running track. The algorithm was able to detect the different types of motions (Fig.11). In collaboration with the Salomon company, a second experiment was conducted at a large scale: a wireless network of measurement units was embedded on a runner during the 26th Sultan Marathon Des Sables (MDS). The MDS is a 6 stage foot race over a distance of about 240km in the Morocco desert. Each participant carries his/her own backpack containing food, sleeping gear and other material.

Due to the severe environmental and running conditions, several problems occurred at the connector level, leading to loss of data. Nevertheless, processing of a full stage was possible, and, for example, a good correlation between step period and hearth rythm was demonstrated.

6.2.3. The HumanPost project: motion control in the elderly population.

Participants: Emel Demircan (PhD, Stanford Univ.), Oussama Khatib (Pr. Stanford Univ.), Philippe Fraisse, Michele Vanoncini (LIRMM), Thierry Keller (Fatronik), Nacim Ramdani (Pr. IUT Bourges).

HumanPost is a joint research project involving the Lirmm, the Research Centre Fatronik-Technalia (with main headquarters in San Sebastian, Spain, and in Montpellier, France) and Stanford University through @Walk project. A first visit to Stanford was organized in order to participate to a workshop on the software package Opensim; a second visit was then organized in order to establish a working relationship with Emel Demircan, a PhD student at the AI laboratory. Both objectives are closely related to the HumanPost project, as explained later in this document (see sections Opensim workshop and EMG informed CMC project).

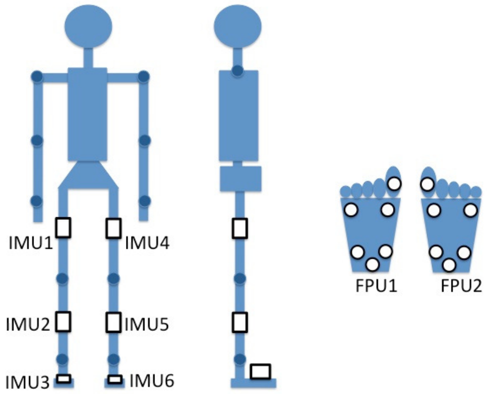


Figure 10. IMUs positioning on the subject.

The aim of the Humanpost project is to study motion control in the elderly population, and in particular during sit-to-stand transfers. The ageing process induces physiological changes which have detrimental effects on postural coordination and stability control; understanding and modelling such effects has potential impact on clinical practice and humanoid robotics. In clinical practice, such knowledge can lead to the development of more reliable testing procedures for fall prevention in the elderly population, and allow the development of more effective post-traumatic rehabilitation procedures. In humanoid robotics, it will guide the development of better human-machine interfaces for robotic devices aimed at providing mobility assistance for the frail eldelry during daily activities, possibly interacting with their carers. Following this vision, the project focuses on the Sit-To-Stand (STS) transfer, since it is a pre-requisite for independent living, and is at the base of several test procedures used in clinical practice. The experimental work conducted for the project consisted in collecting biomechanical data (movement, forces exerted on the ground, and muscle electrical activity) during STS transfers performed by a total of 37 volunteers, divided in 2 age groups (young and elderly). Each volunteer was asked to perform STS movements at different velocities and with eyes open or closed; imposing more challenging conditions than those encountered in everyday activities was expected to magnify differences between the two age groups in the movement strategies adopted.

The software Opensim was used to perform several steps of the data elaboration procedure, to compute meaningful variables for a comparison of the STS in the two age groups. The workshop organized at Stanford University allowed us to improve our usage of this software tool.

Opensim is a free-to-the-user software package for the simulation of the human body, providing tools for the elaboration of typical sets of experimental data collected in movement laboratories. The software is developed and maintained at the Simbios National NIH Center for Biomedical Computing, based at Stanford University, and it is being adopted as a working tool by a growing community of research scientists all over the world. The workshop organized in Stanford brought together users from different research institutions, and focused on the particular applications proposed by the participants. We consider the participation to the workshop as an invaluable experience, since it allowed us to deepen our knowledge of the software by talking directly to the developers. This enhanced our awareness of its potentialities and of its limitations, which is essential for a critical analysis of the results of my study. We are using Opensim to compute the values of the physiological joint angles of the human body (ankle, knee, hip, etc) from the data collected with a motion capture system; furthermore, it allows to compute the joint torques needed to accomplish the STS movement, and to estimate the muscle contractions required to produce such torques. However, the estimate is

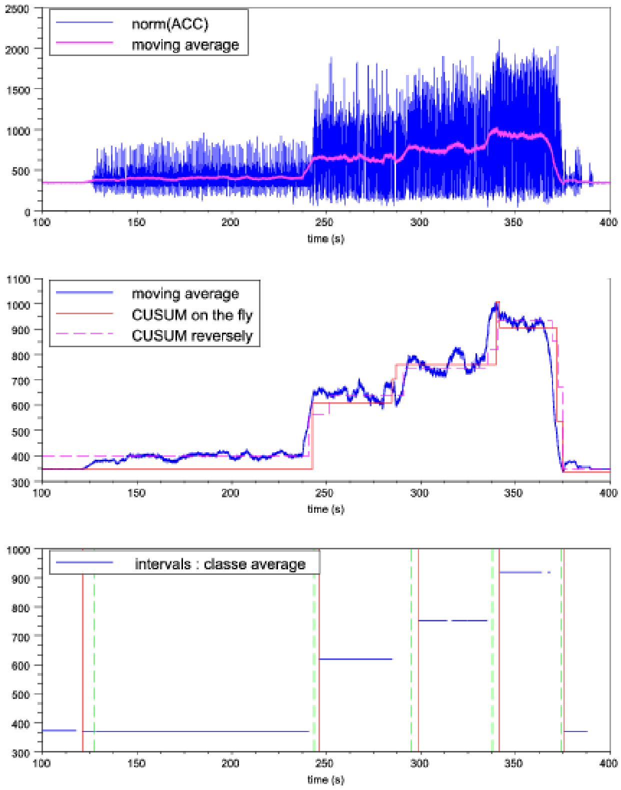


Figure 11. Classification result for IMU1 sensor (right thigh). ***Top:*** *Raw and filtered acceleration norm of IMU1.* ***Middle:*** *bidirectional break-point detection.* ***Bottom:*** *Dashed vertical lines represent the rhythmic changes guessed from signal visual observation. Solid vertical lines indicate the frontier between classes obtained with K-means. Horizontal lines indicate to the mean-value of the corresponding class.*

based on mechanical models of the biological tissues (tendons,ligaments and muscles) which have only been validated for a population of young adults. This may limit the results currently obtainable from experimental data collected on the elderly population. The EMG informed CMC project tries to address this issue.

The EMG informed CMC project aims at using electromyographic signals (EMG) as an additional source of information for the estimation of the muscle control activations (Computed Muscle Control), which are currently estimated on the basis of measured movement and force exerted on the ground. The new concept has been implemented as a software plug-in for Opensim by Emel Demircan (Stanford University), and has been tested on a limited set of experimental data, collected during a walking cycle. The EMG informed CMC project aims at validating and improving the new tool, by testing it on the data collected during STS movements. Our visit to Stanford gave us the opportunity to work with E. Demircan the specific aims of the project, and to plan the research work. It is envisaged that the improved estimation of the muscle activations provided by the new software will serve as a tool for a more appropriate comparison of young and elderly subjects than what is possible at the present time. In fact, the modifications of the musculoskeletal system due to ageing (decrease in force and velocity of contraction of the myofibers, changes in the mechanical properties of the tendons, etc.) have been widely investigated and measured for specific cases (e.g. flexion/extension of the ankle joint). However, a generalization of this work of quantification remains difficult, and hence it is impossible to include age related modifications in a full body model of the human body. Therefore, biomechanical studies in gerontotechnology are usually conducted considering a model validated for the young population. This may induce a bias in the results, typically in the estimation of the muscle activations required to perform a chosen movement. The EMG informed CMC project proposes a method to improve the estimation of muscle activations which takes into account the effects of the ageing process, since these are reflected by the EMG recordings. The research will not involve the development of a model of the elderly, which would require more time and resources; nonetheless it will allow to estimate the error which is committed when using a « young model » to estimate muscle activations in the elderly. This information will allow to judge the urgency of the development of biomechanical model for the elderly [4].

6.2.4. Correction of drop-foot in post-stroke hemiplegic patients

Participants: Christine Azevedo Coste, Roger Pissard-Gibollet (SED INRIA), David Andreu, Bernard Espiau (INRIA RA), Jérôme Froger (Rehab. Centre, Grau du Roi, CHU Nîmes).

Hemiplegia is a condition where one side of the body is paretic or paralyzed; it is usually the consequence of a cerebro-vascular accident. One of the main consequences of hemiplegia is the drop-foot syndrome. Due to lack of controllability of muscles involved in flexing the ankle and toes, the foot drops downward and impede the normal walking motion. Today, there are commercially available assistive systems that use surface electrodes to stimulate Tibialis Anterior (TA) muscle and prevent drop-foot. The efficiency of drop-foot stimulators depends on the timing of stimulation and functionality of dorsiflexion motion. Classically, available stimulators use footswitches to detect foot on/off events. These discrete events allow only for triggering the stimulation and/or playing with the duration of the stimulation pattern, but does not allow for precise online modification of the pattern itself. We have developed algorithms to monitor the ongoing walking cycle by observing the valid limb movements. In order to ensure legs coordination during walking, the CPG (Central Pattern Generator) concept was introduced, and we proposed a robust phase estimation method based on the observer of a nonlinear oscillator. We have modified a commercial stimulator, ODSTOCK, in order to be able to trigger it using our own wireless sensors and algorithms. Agreement from Nîmes CPP (ethical committee) was obtained in June 2010 to run tests on patients. [2], [28], [16], [33]

6.2.5. Sit-to-stand

Participants: Jovana Jovic, Christine Azevedo Coste, Philippe Fraisse, Roger Pissard-Gibollet (SED INRIA), Charles Fattal.

Rising from sitting to standing position is a common daily activity in valid humans. Individuals experiencing rising difficulties have problems living independently. Paraplegic patients cannot perform this postural task due to their lower limbs paralysis. Rising in paraplegic patients can be achieved using functional electrical stimulation of lower limbs. If there is no coordination between healthy limbs under patient control and impaired limbs under FES control, the result of the stimulation can be undesired motion and increased upper body support. Also, if rising process is not optimized, muscle fatigue appears sooner and following activities of the patient are compromised.

We developed the system which coordinates upper and lower body in FES-assisted sit-to-stand motion in order to reduce the arm efforts and muscle fatigue. The proposed approach is based on the observation of trunk acceleration in sagittal plane during rising motion and a detection algorithm, which triggers a pre-programmed stimulation pattern. Trunk acceleration is measured using one-axis wireless accelerometer positioned on the T3 anatomical level of the subjects. Detection algorithm is based on Pearson correlation coefficients which compare acceleration of measured sit to stand trial with a referent signal. Referent signal is build by calculating the mean value of previously recorded trunk acceleration for same subject, defining a time window which terminates when the stimulator should be triggered. (Fig.12)

We validated the algorithm by testing the feasibility of triggering stimulation at the moment when trunk acceleration is maximal, 100 ms and 200 ms before maximal trunk acceleration in valid subjects. We also compared trunk acceleration signal in sagittal plane from healthy and paraplegic subjects and concluded that signal pattern looks the same for both groups [1][29]. Agreement from Montpellier CPP (ethical committee) was obtained in October 2010 to run tests on patients [32].

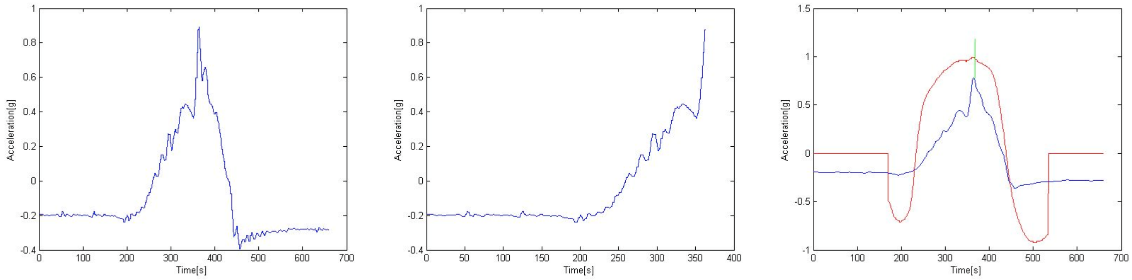


Figure 12. Top: Average trunk acceleration signal for one subject. Middle: example of time window for same signal, terminated at the time when the stimulator should be triggered. Bottom: Blue line represents trunk acceleration signal. Red line represents correlation coefficients. Green line represents beginning of stimulation.

6.2.6. Active tremor compensation using FES to modulate joint impedance

Participants: Antonio Bo, Christine Azevedo Coste, Philippe Poignet, Christian Geny, Charles Fattal.

The main goal of the TREMOR Project is to evaluate the use of FES in the active compensation of pathological tremor. It is one of the most common movement disorders and its incidence is higher on the upper limbs.

We first develop pathological tremor and voluntary motion modeling and online estimation algorithms for active compensation ([3]). Additionnally, a new strategy to attenuate tremor was evaluated. In our experiments, FES was used to induce co-contraction in pair of antagonist muscles that actuate on the trembling joint. Regulating the stimulation level, it was possible to modulate the contribution of FES-controlled muscles to joint impedance, without disturbing the subject's voluntary motion.

In a first series of experiments, this strategy was evaluated in 7 tremor patients diagnosed with Essential Tremor (ET). A commercial stimulator was used in those tests, and stimulation level was controlled manually. The results confirmed the feasibility of the approach, as illustrated by the motion data recorded from the experiments (Fig.13). However, the performance of the system was not consistent, i.e., performance in tremor reduction was not regular between different trials.

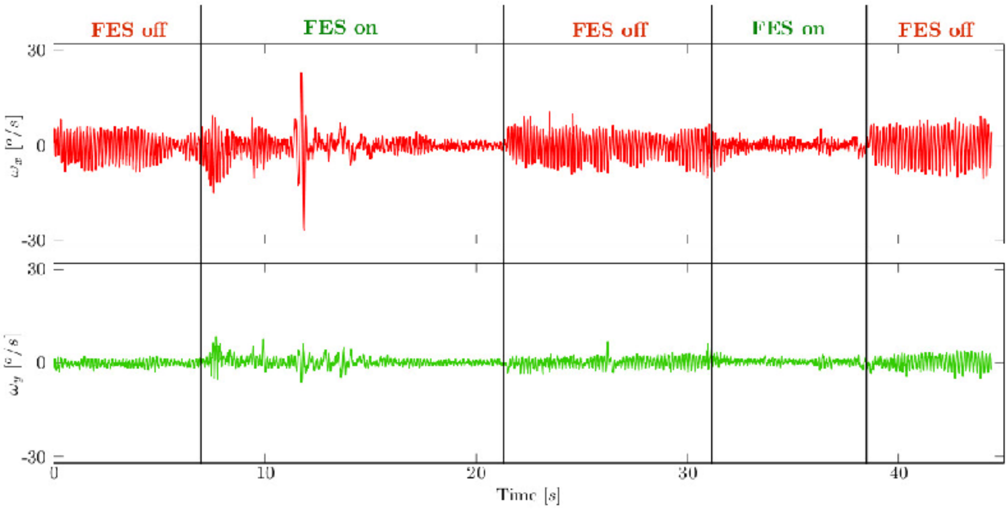


Figure 13. Tremor attenuation results from tremor patient.

In order to improve the current experimental setup, a closed-loop tremor compensation strategy using FES was designed ([19]). The approach was again based on the concept of impedance control by co-contracting antagonist muscles. In this case, however, the corresponding stimulation levels are computed automatically based on the tremor intensity, which is estimated online using portable inertial sensors. The new compensation strategy was tested on 2 healthy subjects whose tremor was produced by an additional stimulator and the results obtained were promising.

6.3. Neuroprostheses

6.3.1. External wireless FES system dedicated to clinical rehabilitation

Participants: Mickael Toussaint, David Andreu, Philippe Fraisse.

Wireless external stimulator and/or bio-feedback units have been transferred end of 2009 to our industrial partner Vivaltis and it has been commercialized in 2010 as PODs integrated within the "PhenixLiberty" product (http://www.vivaltis.com/). In order to exploit this new technology in a closed-loop control based FES, we realized a network metrology in terms of network's performances characterization like transmission delays, lost frame rate in given contexts, reception signal levels, etc (Table 6.3.1 indicates some Round Trip Times measured for given requests). Indeed the wireless network has to be taken into account while designing the control, both from automatic and communication points of view. A control law is thus studied for the control of a joint by FES, over our wireless network architecture. RTT measurements (comprising request transmission, execution and acknowledgment):

Stimulation Operations	Mean RTT (ms)	Standard deviation (ms)
Configuration	12.19	0.016
Start	5.92	0.011
Set amplitude	6.68	0.018
Stop	5.99	0.009

We wish to control the co-contraction of the muscles actuating the joint (see work of Mohammed et al. in DEMAR ACTIVITY REPORT 2005), by modulating the stimulation parameters according to the joint angle measurement. We thus developed a wireless unit embedding a 2-axes angle sensor (goniometer), deployed within our architecture, as the feedback of our closed-loop control. Performances of the network have now to be integrated to the control law, as an image of the network quality of service [25], [24], to ensure the system stability and the patient's safety.

6.3.2. ENG recording

Participants: Olivier Rossel, Fabien Soulier, Serge Bernard, Guy Cathébras.

In the context of FES, neural recording is one of the most promising research area. Artificial control of human limbs needs to know the position of the different parts of the human body. Natural sensors (like neuromuscular spindles and Golgi tendon organs) can bring information about the stretching, velocity and force of the muscles. This information is carried on afferent peripheral nerves and can be recovered from electroneurogram (ENG). We propose to investigate the topic of extracellular action potential (AP) composing ENG, in order to design a new kind of electrode and the associated micro-electronics to create an implantable acquisition system.

Last year, we were considering the spatial shape of an AP taking into account the activity of the nodes of Ranvier (NoR) on a single active fiber. We show that the extracellular AP exhibits high spatial frequencies and that this is directly linked to the position of the NoR. Moreover, this phenomenon only exists for the sub-millimetric distance between electrode and fiber. This means that if it is possible to extract this component, the signal will be the image of the activity on the close area of the electrode. In other words, an electrode sensitive to this phenomenon will be very spatially selective.

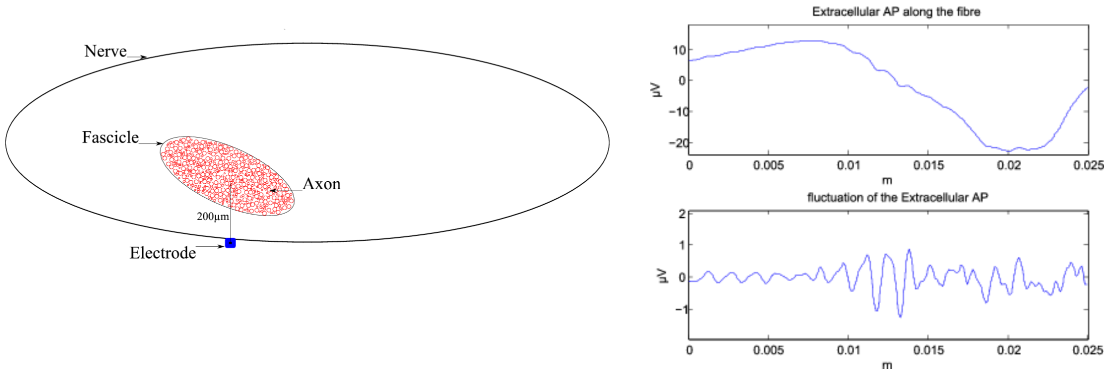


Figure 14. Fascicle model and extracellular potential computed for 500 fibers firing at the same time at a distance of $200\ \mu\mathrm{m}$ *from the electrode.*

This year, we decided to model a whole nerve fascicle. We show that high spatial frequencies also exist in the compound AP (Fig.14). On the same figure, one can see the expected output signal of the electrode presented in the last-year report.

The challenge will be to extract this component, because despite the superposition of AP this signal stays around the micro-volt level, compared to the global signal of about $30\,\mu\mathrm{Vpp}$. This simulation results will be used to dimension the electronic amplifier, in term of gain, noise level and bandwidth. Thanks to this, it will be possible to design the entire electrode, and to select the contact material according to is own noise level.

Experiments have been done to validate this theory.

The presence of high spatial frequencies in the AP signal means that the amplitude of a measured AP depends on the electrode position. In other words, electrodes spaced by some hundreds micrometers one from each other on the longitudinal axis of the nerve should get different measures. A first experiment was made using a worm because this simple animal model exhibits giant axons analogous to some extent to mammalian myelinated fibers. A second one was made using a database of rabbit intra-fascicular recordings to prove this postulate.

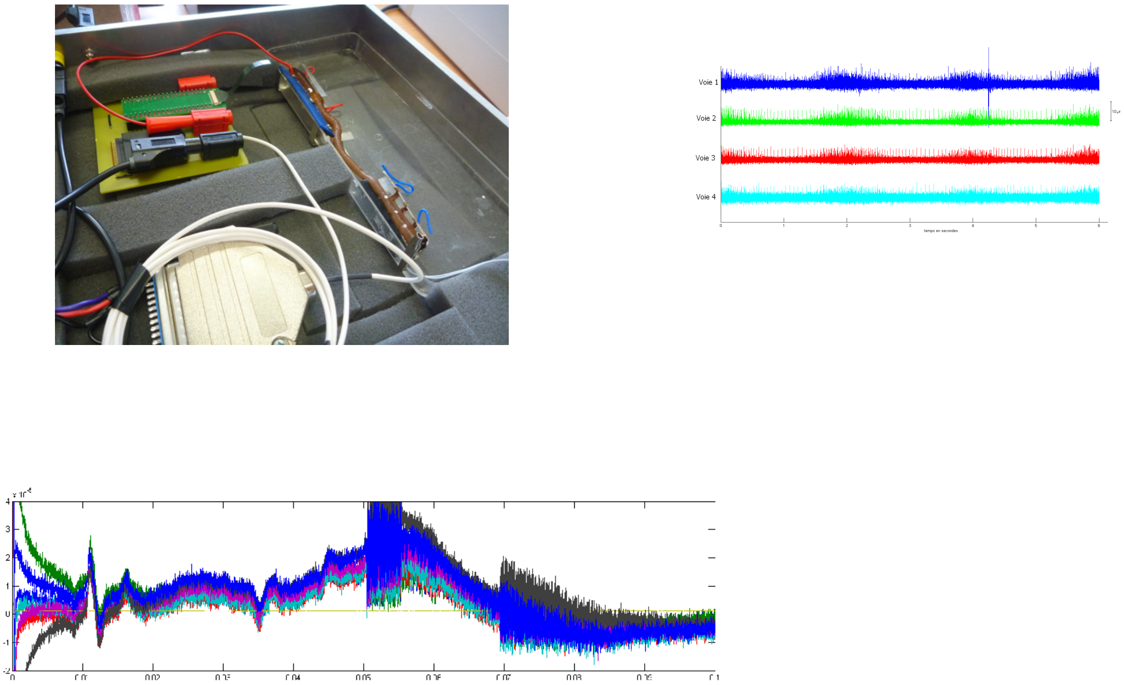


Figure 15. Experimental setup for animal experiments, and resulting measured signals.

Eight electrodes were used in the experimentation on the worm, and four for the rabbit. The results tend to prove that there is actually some differences on the measured amplitude of an AP according to the electrode location (Fig.15). Unfortunately, it was difficult to positively conclude due to the noise level of the signal.

Nevertheless, thanks to these preliminary experiments, we can conclude that the number of recording channels has to be increased and the noise level has to be lowered as much as possible. The solution is the design of a 32-channel high-gain and low-noise amplifier.

Different structures were studied in order to design the ENG amplifier. In the experimental setup, a preamplifier with a gain of 10 was already used. Thus the proposed amplifier simply use one amplification stage and high-order filtering. The Fig.16 shows a single-channel prototype used to validate the design.

Table 2. Main characteristics of the 32-channel ENG amplifier for animal experiments.

Gain	1000
Input noise	$15\,\mathrm{nV}/\sqrt{\mathrm{Hz}}$
Bandwidth	$20\,\mathrm{kHz}$
Output dynamic range	$\pm 3.7\,\mathrm{V}$

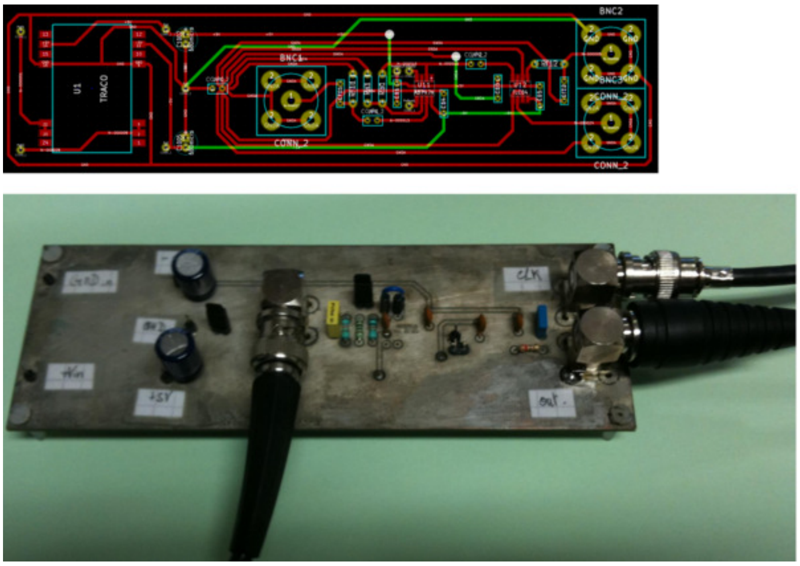


Figure 16. Single-channel prototype used to validate the design of the 32-channel ENG amplifier.

A bio-potential sensor is characterized both by the electronic device and by the electrode properties. So before doing the experiment it is important to characterize the electrode.

The electrode impedance has to be measured and characterized. The electrode noise level was also measured and compared to the attended signal. A potentiostat-type measure was realized to study the impedance of electrode. This impedance is the ratio between the voltages on the electrode-solution interface and the current flowing through it. The measure was done for a very wide bandwidth. The results (amplitude and phase) are plotted as functions of the frequency in the Fig.17.

6.3.3. Implant dependability

Participants: Fanny Le Floch, Fabien Soulier, Serge Bernard, Guy Cathébras.

The safety of the patient has to be guaranteed: once the implant is embedded, the risk and the complexity of a new surgery to replace a defective implant have to be avoided. One of the issues is to develop a highly reliable and robust system which will last the entire patient's life. Unfortunately, the dependability for implanted medical devices is more recent as in aeronautics, space or automotive fields. Furthermore, the transcription of methods used in those fields to the medical domain isn't enough, due to its own specificity. The respect of basic directive and standard gives us some guidelines to follow and helps us to start with the certification of the implant. We have already defined a global strategy for risk management at level system for FES implant [15] in order to estimate their robustness towards every possible fault. If a failure occurs, the consequences can be devastating. So, to avoid any disaster, the micro-circuit is used as a safety part for the entire system, by integrating specific Built-In-Self-Test and Built-In-Self-Repair solutions. This year, this work has led us to focus on a sensitive and essential part of the implant: the level shifter; responsible for shifting data about the stimuli (in terms of duration, amplitude, shape) from low voltage to high voltage (the front end). If any error appears in this critical circuit, it will have catastrophic and unpredictable consequences during the stimulation, and thus for the patient (Fig.18).

6.3.4. ASIC analog design

Participants: Jérémie Salles, Guy Cathébras, Serge Bernard, Fabien Soulier, Laurent De Knyff.

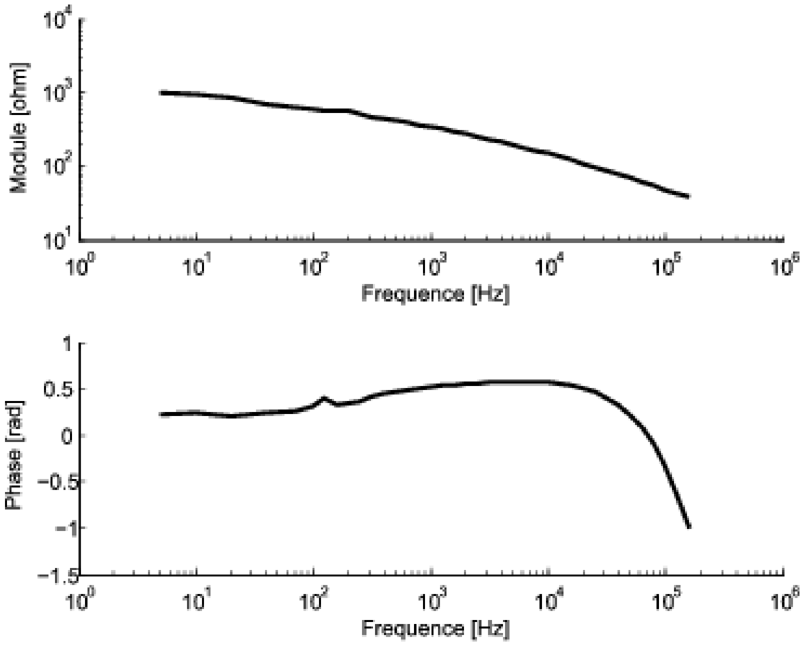


Figure 17. The measured impedance of the electrode placed in a Ringer solution.

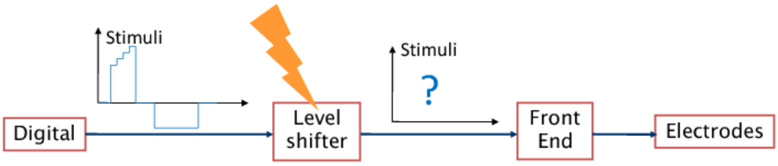


Figure 18. The sensitivity of the stimuli through the level shifter.

The microstimulator can be divided into two main parts: a controller (digital) and an active part (analog). In the active part, the output stage gets its input current from an external DAC converter which sets the maximum stimulation amplitude. This current is then distributed to a twelve-pole stimulating electrode. A pole can be set in four different states: anode, cathode (both current controlled), open (high impedance) or shunt (voltage-controlled). A digital block controls the evolution of the pole states and the ratio of the stimulation current on each pole.

A first version of the output stage was developed in 2006 and a prototype (ASIC) was fabricated. Some faults were observed while carrying out the circuit characterisation. These faults were of four main kinds:

- asymmetry between poles (up to $108\,\mu$A),
- input/output non-linearities (over $4\,$LSB),
- over-consumption on idle state,
- erratic level-shifter[1] behavior.

Since 2006, some researchs and experiments were carried out and few subcircuits were developed to fully access its faults and correct them. Finally, a corrected version was designed this year. The new IC offers three structural modifications and better layout techniques to improve our stimulator characteristics. Some simulation results are presented in the following pictures. The Fig.19 shows an improvement of the symmetry between poles (down to $39\,\mu$A) while Fig.20 highlights a non-linearity reduction to $0.66\,$LSB. The command structure was also modified to get rid off the over-consumption. Finally, the level-shifter parts were designed anew.

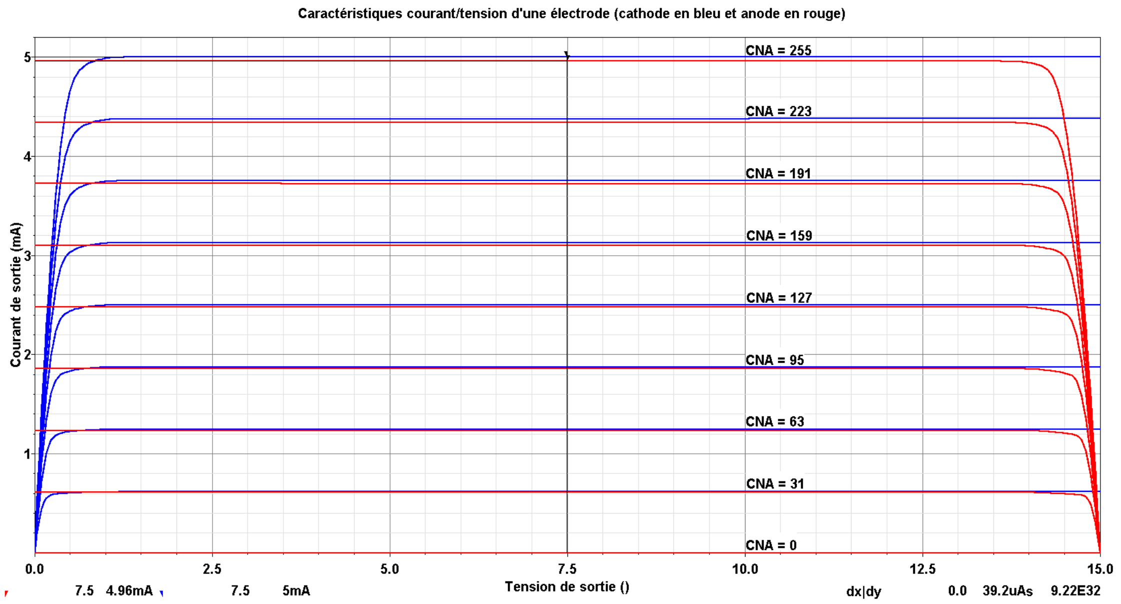


Figure 19. Simulated voltage/current characteristics of CAFE12

The corrected ASIC manufacturing process is scheduled to start on November for a circuit release three months later.

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[1] The level-shifters are the part of the circuit in charge of transmitting control bits from a voltage domain to another.

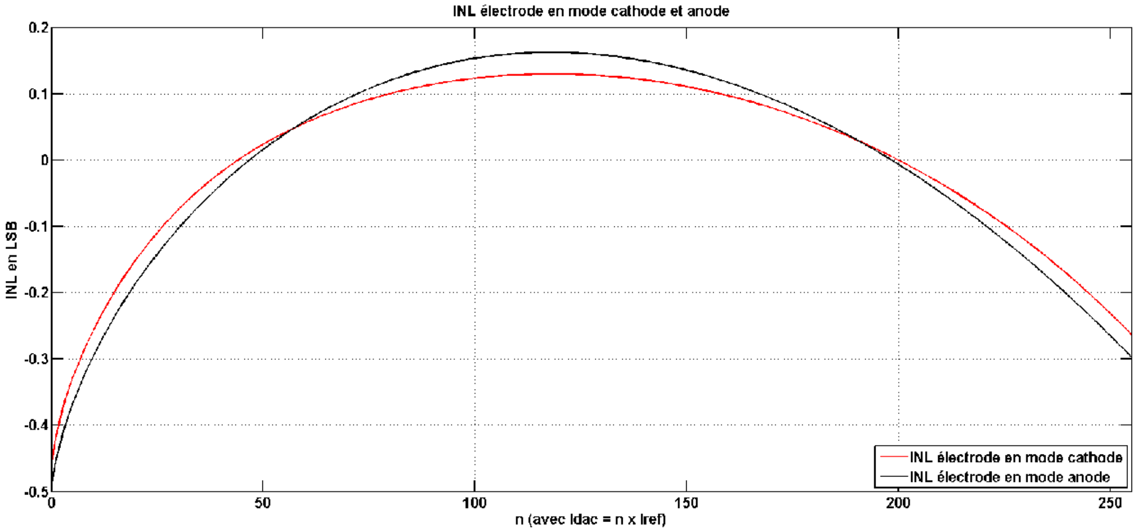

Figure 20. Simulated non-linearities of a typical electrode (cathode in red and mode anode in black)

In 2009, an ASIC was developed within the team to measure in-vivo the electrode impedance. The circuit was released in January. A circuit board (Fig.21) was designed and in-house manufactured to test this integrated circuit. The board allows the test and the characterisation of the:

- embedded logic,
- amplifier,
- I/O pads,
- current mirror,
- AD converter,
- circuit consumption.

A *Xilinx* development board (*Spartan 3*) is used to control the ASIC and to test it while a RS232 serial port is used to program the FPGA. Currently, the circuit logic has been tested but its other parts are still under test.

6.4. Contracts

An industrial technological transfer contract is ongoing with the MXM company that develops cochlear implant and artificial lens implant. MXM can perform also Ethylene Oxyde sterilization necessary for all our experimental setups used during surgery. Two DSU prototypes (named Stim'3D and Stim'nD) and the associated programming environment (SENIS Manager, cf. section 5.1.2) have been developed within this frame.

A contract has been signed with Vivaltis company that is specialized in the development of external stimulators. We commonly aim at new advanced external FES system dedicated to clinical rehabilitation; a first wireless external stimulator has been manufactured.

6.5. International Initiatives

6.5.1. Associated team

Participants: Philippe Fraisse, Oussama Kathib.

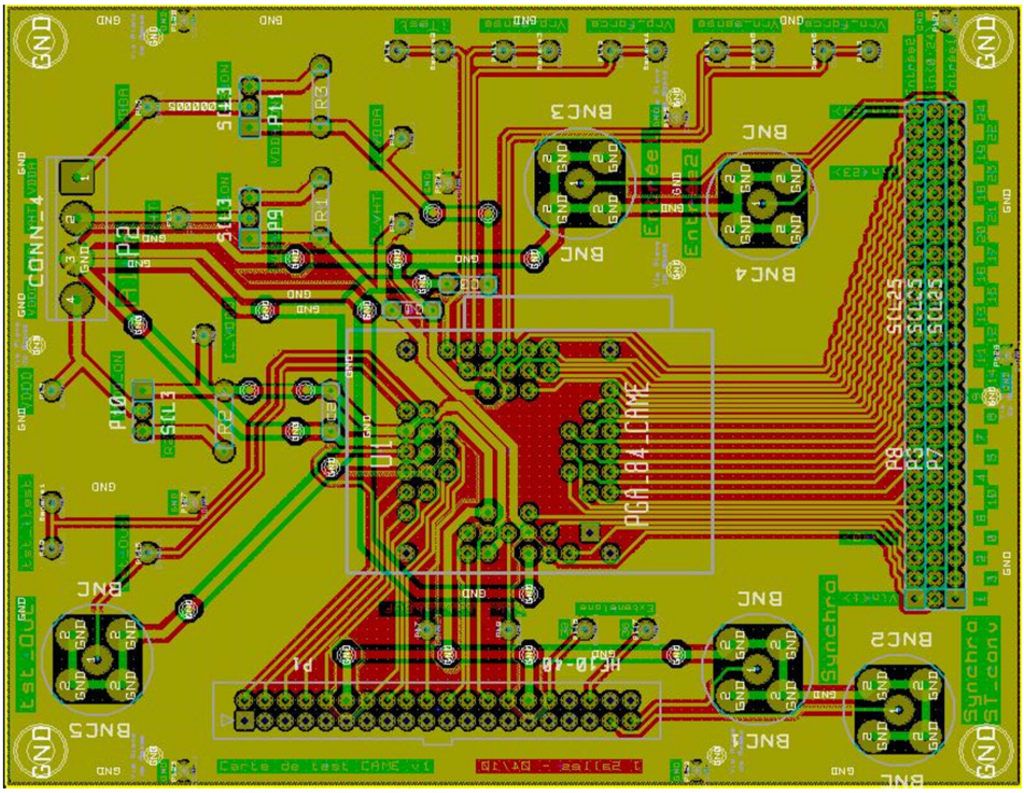

Figure 21. Printed circuit board

An associated team between DEMAR and Stanford's robotic labs has been launched to cooporate on Opensim software development and modeling of the movement of deficient persons in particular elderly.

6.5.2. Merlion program

Participant: Philippe Poignet.

LIRMM scientific leader for Merlion program with NTU, Singapore. Junior and senior Researcher exchange (2009-2010).

6.5.3. Japan-France Integrated Action Program "SAKURA and AYAME Junior"

Participant: Mitsuhiro Hayashibe.

"Modele Neuromusculaire du Corps Humain et ses Applications pour la Rehabilitation par la Stimulation Electrique Fonctionnelle", Funding for exchange supported by JSPS and INRIA 2010-2011.

6.6. National Initiatives

6.6.1. Cosinus ANR

Participants: Philippe Poignet, Philippe Fraisse, David Guiraud, Mitsuhiro Hayashibe, Christine Azevedo-Coste.

Project SoHuSim on modeling muscle tissue during contraction in 3D movements using SOFA software and functional modeling of the organs. 150 kE. Partners: INRIA Evasion, Tecnalia, HPC, CHU Montpellier (Oct. 2010 - Oct. 2014).

6.6.2. PsiRob ANR

Participants: Philippe Poignet, Charles Fattal, Christine Azevedo-Coste.

Project TREMOR on pathological tremor compensation using FES, 243 kE. Partners: MXM, Propara, CHU Montpellier (Oct. 2006 - Oct. 2009 - 1 year extended). This project is jointly conducted with the DEXTER team at LIRMM.

6.6.3. DGE Neurocom

Participants: David Guiraud, David Andreu, Fabien Soulier, Serge Bernard, Guy Cathébras.

DGE Neurocom, (2007-2010). 475keuros, '*Implant Cochléaire 'tout implanté' pour la restauration des surdités sévères et profondes*'. Partners : MXM-Neurelec, ELA-Sorin group, APHM Hopitaux de Marseille, CHU Montpellier.

6.6.4. ADT SENSAS - SENSBIO

Participants: Christine Azevedo-Coste, Bernard Espiau, David Andreu.

6.7. Actions Funded by the EC

6.7.1. European project Time

Participants: David Guiraud, David Andreu, Fabien Soulier.

(2008-2012). 375keuros, "*Transverse, Intrafascicular Multichannel Electrode system for induction of sensation and treatment of phantom limb pain in amputees*". Partners : AAU (Aalborg, Denmark), MXM (Vallauris, France), SSSA (Pisa, Italy), IMTEK (Freiburg, Germany), UAB (Barcelona, Spain), UCBM (Roma, Italy), IUPUI (Indianapolis, USA).

6.8. Animation of scientific community

- D. Guiraud
  1. Associate editor at EMBC 2010 and track chair "Neural Rehabilitation Technologies"
  2. Member of steering committee of INSERM Institut des Technologies pour la Santé (ITS)
  3. Chair and organizer of a special session "Recent and Emerging Rehabilitation Approaches"
- C. Azevedo-Coste
  1. Board member of IFESS society (international functional electrical stimulation society)
  2. Associate Editor of Paladyn Behavioral Robotics Journal
- Mitsuhiro Hayashibe
  1. IEEE BIOROB2010 Mitsuhiro Hayashibe was Exective Program Committe and associate editor, third IEEE/RAS-EMBS International Conference on Biomedical Robotics and Biomechatronics, September, 26-29, 2010, Tokyo, Japan.
- D. Andreu:
  1. D. Andreu was member of the Program Committee of CAR'2010
- B. Espiau:
  1. directeur scientifique adjoint en charge du domaine de recherche "Mathématiques appliquées, calcul et simulation".
- P. Fraisse:
  1. Co-leader of the french working group on Humanoid Robotics of the GdR Robotique
  2. Head of Robotic Department (LIRMM)
  3. Program Committee Member of IEEE Humanoid 2009
- P. Poignet:
  1. Co-organizer of the french working group on Medical Robotics of the GdR Robotique (http://www.gdr-robotique.fr/index.php)
  2. Member of the IFAC T2.3 technical committee on Nonlinear Control Systems
  3. Member of the CNU 61 (2008-2012)
  4. Member of the evaluation comittee of ANR TECSAN
  5. Responsible for the 'Spécialité Doctorale' in Micro-electronics and Control System (about 80 PhD students) - (http://www.edi2s.univ-montp2.fr/)
  6. Responsible for the Licence Professionnelle par Apprentissage - Métiers de la Mesure et de l'Instrumention
  7. Member of the scientific comittee of the LIRMM
  8. Associate editor of JESA

6.9. Teaching

- David Guiraud, Master SMH, electrophysiology of striated muscles, modelling and control of electrically stimulated muscles 16h/y
- David Guiraud is responsible for the UE5 module in the "parcours TIC et Santé IT-Montpellier", Medical devices and medical robotics. He teaches 5h/y and he is member of the educational committee.

- David Andreu, Assistant Professor, 200h/y, Engineering school Polytech Montpellier and Master degree, Software engineering, real time OS, Petri Net.
- Guy Cathébras, Professor at Polytech'Montpellier (Electronics, Robotics and Industrial Informatics (ERII) Department), teaches: Mathematics and Signal theory for 3rd year ERII students; Analog integrated circuits: "An introduction to electronics: designing with Bipolar transistors", for 3rd year ERII students; "CMOS Analog integrated circuits design" CAD practical works for 4th year ERII students; "CMOS standard cells design" CAD practical works for 4th year ERII students.
- Philippe Poignet Professor at IUT Montpellier Applied Physics teaching automatic control and signal processing.
- Philippe Fraisse, Professor at Polytech'Montpellier (ERII) teaching automatic control and networks.
- Fabien Soulier, assistant professor at Polytech'Montpellier (ERII) teaching electronics and signal processing.
- Christine Azevedo-Coste, "parcours TIC et Santé IT-Montpellier", neurophysiology, 2h/y.
- The team organised a half day course for a group of 8 nurses from Nîmes nurse school in May 2010.

6.10. Organization of seminars

- Maura Whittaker (Vancouver, Canada) was invited to give a talk in PROPARA clinical centre, September 16th 2010. "Clinical applications of electrical stimulation"

6.11. Participation in seminars and workshops

- Christine Azevedo-Coste was invited to present her research results at LAAS (Robotics and Artificial Intelligence Lab), Toulouse. March 15th 2010. "Assistance fonctionnelle : exploiter les fonctions résiduelles du système sensori-moteur déficient."
- Christine Azevedo-Coste gave a keynote lecture during the annual meeting of Club de la Locomotion et de la Motricité Rythmique, September 17th 2010, Montpellier. "Analyse et contrôle de la posture saine, assistée ou robotisée."
- Christine Azevedo-Coste presented her research work during a seminar at IT (Institut Telecom). Brest, July 2010.
- Mitsuhiro Hayashibe was moderator during the France-Japan Meeting on Technologies for Helping People with Physical Disabilities, Thursday, September 30th, 2010, Embassy of France in Japan, Tokyo.
- Mitsuhiro Hayashibe presented his work during a Seminar presentation at Intelligent Systems Research Institute, National Institute of Advanced Industrial Science and Technology (AIST), October 5th, 2010, Tsukuba, Japan.
- Mitsuhiro Hayashibe presented his work during a Seminar presentation at GV lab and Morishima lab, Tokyo University of Agriculture and Technology, October 1st, Tokyo, Japan.
- Mitsuhiro Hayashibe presented his work during a Seminar presentation at Nakamura lab, University of Tokyo, October 15th, 2010, Tokyo, Japan.
- David Guiraud was invited for a talk at "robotic rehabilitation workshop" in Montpellier, faculté de médecine, 18th of october.

6.12. Theses and Internships

6.12.1. Thesis Defenses

1. David Andreu defended his HDR.

2. David Guiraud and Alain Varray supervise **Maria Papaiordanidou**,*Nature périphérique et centrale de la fatigue musculaire.* defended oneht 8th of october in Montpellier.

6.12.2. *Ongoing theses*

1. David Andreu and Philippe Fraisse co-supervise **Mickael Toussaint**, *Conception et réalisation d'une architecture de stimulation musculaire externe distribuée et sans-fil : Application au contrôle de mouvement d'une articulation*, Thesis CIFRE VIVALTIS, 2008-2011.
2. Philippe Poignet supervises **Antônio Bo**, *Compensation active du tremblement pathologique du membre supérieur via la stimulation électrique fonctionnelle.*", Thèse CIFRE MXM ? Neuromedics 2007-2010
3. Serge Bernard, Guy Cathébras co-supervise **Fanny Le Floch**, *Sûreté de fonctionnement des circuits implantables dans le corps humain.*, MENRT.
4. Guy Cathébras and Fabien Soulier co-supervise **Olivier Rossel**, *Circuits intégrés de recueil et d'interprétation des signaux nerveux*, Axa fundation.
5. Jérôme Bourien (INM, Montpellier) and Christine Azevedo-Coste, co-supervise **Christophe Michel**, *Modélisation de l'efférence latérale du système auditif périphérique*, CIFRE MXM.
6. Christine Azevedo-Coste and Bernard Espiau co-supervise **Maud Pasquier**, *Observation et contrôle de mouvements non cycliques des membres inférieurs et supérieurs en assistance fonctionnelle.*, ANM.
7. Mitsuhiro Hayashibe and Philippe Fraisse co-supervise **Qin Zhang**, *FES modelling and control with on-line update of time-varying muscular property based on Evoked EMG.*, Oversea PhD Study Scholarship, awarded by China Scholarship Council in Ministry of Education.
8. Christine Azevedo-Coste, Philippe Fraisse and Charles Fattal co-supervise **Jovana Jovic**, *Maintien prolongé de la station debout équilibrée fonctionnelle chez le patient paraplégique*, BDI Région-INRIA.

6.12.3. *PostDoc*

- David Andreu supervised Jean-François Pineau, "Ordonnancement dans un système de stimulation électro-fonctionnelle" (1 year contract, Neurocom project), 2009-2010.
- Christine Azevedo Coste and David Andreu supervise Pawel Maciejasz, "Selective neural electo-stimulation" (1 year contract, TIME project), 2010-2011.

6.12.4. *Internships*

6.12.5. *Contract Engineers*

- David Andreu supervised Robin Passama on "Configuration, programmation et contrôle à distance d'une unité de stimulation ; aspects logiciels", Computer Science Engineer (1 year contract, TIME financial support).
- David Andreu supervises Grégory Angles. "Conception et réalisation d'un environnement logiciel, basé sur Eclipse, pour le prototypage rapide sur composants électroniques programmables (HILECOP)". Computer Science Engineer, INRIA ODL contract (2 years contract, INRIA financial support).
- Guy Cathébras, Serge Bernard and Fabien Soulier co-supervise Jérémie Salles "Correction de la version 2 et développement de la version 3 de l'ASIC de stimulation 12 pôles" Microelectronics Design Engineer (1 year contract, NEUROCOM financial support)

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Publications of the year

Articles in International Peer-Reviewed Journal

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[2] C. AZEVEDO COSTE, R. HÉLIOT, R. PISSARD-GIBOLLET, P. DUSSAUD, D. ANDREU, J. FROGER, I. LAFFONT. *MASEA : Marche Assistée par Stimulation Électrique Adaptative. D'un déclenchement événementiel à un contrôle continu de la stimulation électrique pour la correction du syndrome de pied tombant chez l'hémiplégique*, in "Sciences et Technologie pour le Handicap", 2010, vol. Numéro Spécial Handicap et Mouvement, n^{o} 4/1, 22.

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[5] M. DJILAS, C. AZEVEDO COSTE, D. GUIRAUD, K. YOSHIDA. *Spike Sorting of Muscle Spindle Afferent Nerve Activity Recorded With Thin-Film Intrafascicular Electrodes*, in "Computational Intelligence and Neuroscience", 2010, vol. Special Issue "Signal Processing for Neural Spike Trains", 10.

[6] M. HAYASHIBE, Q. ZHANG, D. GUIRAUD, C. FATTAL, P. FRAISSE. *Modeling and Experimental Identification for Muscular force Estimation Based on Evoked EMG in FES*, in "Journal of Biomechanics (Orthopaedic Biomechanics, CAS)", Jun 2010, vol. 43, sup.1, S66.

[7] R. HÉLIOT, C. AZEVEDO COSTE, L. SCHWIRTLICH, B. ESPIAU. *Gait Spectral index (GSI): a new quantification method for assessing human gait*, in "Health", Jan 2010, vol. 2, n^{o} 1, p. 38-44.

[8] S. KRUT, C. AZEVEDO COSTE, P. CHABLOZ. *Secured Microprocessor-Controlled Prosthetic Leg for Elderly Amputees: Preliminary Results*, in "journal of Applied Bionics and Biomechanics", 2010, vol. Special Issue on Assistive and Rehabilitation Robotics, 8.

[9] M. PAPAIORDANIDOU, D. GUIRAUD, A. VARRAY. *Does Central Fatigue Exist Under Low-Frequency Stimulation of a Low Fatigue-Resistant Muscle ?*, in "EUROPEAN JOURNAL OF APPLIED PHYSIOLOGY", Jul 2010, vol. Online preview, p. 1-9.

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[11] J. VAN DOORNIK, C. AZEVEDO COSTE, J. USHIBA, T. SINKJAER. *Positive Afferent Feedback to the Human Soleus Muscle during Quiet Standing*, in "Muscle and Nerve", 2010, 10, to appear.

[12] D. ZHANG, P. POIGNET, F. WIDJAJA, W. ANG. *Neural Oscillator Based Control for Pathological Tremor Suppression via Functional Electrical Stimulation*, in "Control Engineering Practice", 12 2010, vol. Accepted 30 August 2010, http://dx.doi.org/10.1016/j.conengprac.2010.08.009.

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[15] F. LE FLOCH, G. CATHÉBRAS, S. BERNARD, F. SOULIER. *Dependability: A Challenge for Electrical Medical Implant*, in "32nd Annual International IEEE EMBS Conference", Argentine Buenos Aires, Aug 2010, 4.

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[16] C. AZEVEDO COSTE, J. FROGER. *Correction du syndrome de pied tombant par stimulation électrique fonctionnelle*, in "ISPO'10: International Society for Prosthetics and Orthotics Conference", France, Oct 2010.

[17] S. BERNARD. *Applications and Challenges of Electrical Medical Implants*, in "DTIS'10: Design and Test of Integrated Systems in Nanoscale ERA", Tunisie, 03 2010, 104.

[18] S. BERNARD, P. CAUVET. *Test and Dependability of Microsystems*, in "DTC'10: European Nanoelectronics Design Technology Conference", France, 06 2010, p. 210-216.

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[22] J. LAFORÊT, C. AZEVEDO COSTE, D. ANDREU, D. GUIRAUD. *Modeling and simulation of bladder artificial control*, in "IEEE BioRob 2010", Japon Tokyo, Sep 2010.

[23] C. MICHEL, R. NOUVIAN, C. AZEVEDO COSTE, J. PUEL, J. BOURIEN. *A Computational Model of the Primary Auditory Neuron Activity*, in "EMBC'2010: 32nd IEEE Engineering in Medicine and Biology Conference", Argentine Buenos Aires, Aug 2010, 6.

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[28] C. AZEVEDO COSTE, R. PISSARD-GIBOLLET, B. ESPIAU, D. ANDREU, J. FROGER, I. LAFFONT. *Observation en continu de la marche hémiplégique pour la stimulation électrique des muscles releveurs de pied*, in "HANDICAP", France, Jun 2010, 5.

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