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Synchronous Multichannel Stimulator with Embedded Safety Procedure to Perform 12-Poles TIME-3H 3D Stimulation

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7.1 Introduction

The human functions are controlled through different ways among which both central and peripheral nervous systems (CNS, PNS) play a major part. Within this complex network, the information code is based on action potential (AP) generation. Then, when a sensory function is deficient, inducing APs provides for a partial restoration of the lost function.

Electrical stimulation (ES) induces APs by depolarization of the membrane of the targeted cell, i.e., axons or muscle fibers. From the fifties, ES has been successfully used in a growing set of applications linked to motor and sensory impairments including pain management.

Attempts to use this approach have been made in movement rehabilitation, such as drop foot syndrome for hemiplegic patients (Liberson et al., 1961) and more complex movements or functions for para- and quadriplegic patients (Kralj et al., 1989; Davis et al., 1997; Kobetic et al., 1997, 1999; Rijkhoff, 2004; Guiraud et al., 2014). In the latter case, the functional results could prove to be substantial, including, for instance, recovery of the grasp function for quadriplegic patients, who might then be able to grab hold of objects, eat, and even, in the best cases, write with a pen (Smith et al., 1998).

In the sensory area, cochlear implants allow to recover sound perception for deep deaf persons. The principle is basically the same as for motor restoration with a set of electrodes that increased from one to more than twenty over the thirty past years, located in the cochlea in order to activate the remaining auditory neural circuits (Djourno et al., 1957). It allowed equipped deaf people to understand speech and in the best case speak as healthy subjects.

However, available implanted stimulators dedicated to humans, remained too limited to explore widely all the possibilities that new techniques could provide (Mastinu et al., 2017). In particular, the selective approach applied to nerves through either multicontact cuff (Schiefer et al., 2008) (Dali et al., 2018) or, in the present work, intra fascicular electrodes, needs for advanced multichannel stimulators. The TIME approach, proved to be quite efficient (Badia et al., 2011) but needs for a synchronous 12 outputs stimulator design. The selectivity was a mandatory feature as the project aims at inducing very specific sensation's feedback whereas the whole nerve obviously contains multiple sensory targets, but also, even unused, motor ones. Moreover, as the stimulator was used on humans, intrinsic safety was further needed. The chapter describes the design, the use and the main important results issued from this first-in-man test with multicontact TIME electrode.

7.2 Bench-top Stimulator

7.2.1 Design of the Bench-top Stimulator (Stim'ND)

Stim'ND is based on two main parts, a digital part and an analog one. The analog part of Stim'ND is dedicated to stimulus generation and the digital part, corresponding to the stimulation controller, embeds the functionalities required for the stimulation execution and its remote programming and control. This Stim'ND, whose global architecture is schematically represented in Figure 7.1, relies on the FES distributed architecture paradigm consisting in decentralizing stimulation control close to the electrodes (Andreu et al., 2009).

7.2.1.1 From specifications to design of the stimulator

Globally, the stimulator must allow the generation of multichannel current pulse stimulus patterns, with the possibility to modify waveform, amplitude, pulse duration, pulse rate, number of pulses, number, and timing of active

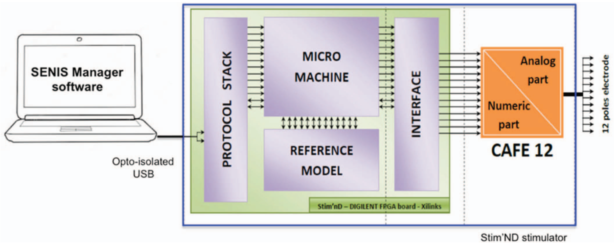

Figure 7.1 Schematic representation of Stim'ND architecture.

Table 7.1 Stimulator specifications

Stimulation Parameter	Range	Step Size
Pulse waveform	Fully programmable	1 μs step
Pulse amplitude	5 mA	1.3 μA (using 1/15 ratio) 20 μA without ratio programming
Pulse duration	Fully programmable	1 μs
Time between two stimulation sequences	Fully programmable	1 μs
# Pulses in a pulse train	Fully programmable	Application software dependent
Frequency of pulses in a pulse train	Fully programmable	Single pulse mode, 10–500 Hz
# Sites activated in full synchrony	Up to 12	Individually as anode and cathode but at least one of each type, total simultaneous current limited to 5 mA

channels. Moreover, the modification of the pattern's amplitude and duration, must be allowed "on-line," i.e., while the stimulation is running. This functionality is called real-time modulation and is performed using an experimenter-dedicated computer.

From a technical point of view, its specifications are given in Table 7.1. Since the stimulator must be able to execute different kinds of stimulation waveforms on different electrode configurations, we thus designed it according to two main concepts: 3D electrodes and microprograms (MPs).

3D electrode: The stimulator drives the thin-film intrafascicular multichannel electrode array (TIME-3H) with a maximum number of simultaneous poles to be driven set to 12. Since active channels can correspond to any TIME-3H configuration, the stimulus generator must be fully configurable, both in terms of poles' electrical configuration (active poles and their polarity) and in terms of accurate current repartition between active poles. Such a configuration is called “3D electrode” (VE). A VE is thus an entity that can be specified through the software environment and executed, from an analog device configuration point of view, by the stimulator. The possibility to specify different VEs is of importance since for an electrode placed within the same nerve a number of possible combinations of active sites are supposed to induce different sensations. This feature is based on the hypothesis that a somatotopy exists within the targeted peripheral nerve.

Microprogram: Since several waveforms can be tested, from a simple pulse to a pulse train and even other waveforms than pulses, the stimulator must offer a simple way to program pulses, ramps, and any combination of them to define more complex waveforms like trapezoidal waveforms or approximated exponential ones. Moreover, the polarity of the waveform is easily defined to provide charge-balanced waveforms. The stimulator being remotely programmable, a stimulus (i.e., a sequence of waveforms) is described by means of a MP.

Thus the stimulator, via its embedded specific processor (cf. Section 7.2.1.3), must offer a set of instructions that eases the description of a stimulation profile. Since some parameters of the waveform must be modulated in real-time during experiments, to find sensation and pain thresholds, parameters of the stimulus – duration, amplitude, time between pulses, and time between two stimulus (stimulation frequency) – must be externally modifiable parameters. That means that these parameters will have an initial value specified by the corresponding instruction of the MP and an effective value modified by remote control, at any time while stimulation is running.

Since some parameters of the waveform can be modulated in “real-time” during experiments, the security must be ensured on both sides:

– First, a security module embedded in the stimulator must ensure that a specified set of constraints will always be respected. If not, this module must immediately stop the stimulation and notify the detected violation to the operator. Specified constraints will concern, for instance, the maximum charge quantities that can be applied; these constraints will be defined prior to the use of the stimulator, i.e., parameters cannot be modified once the stimulation is running.
– Second, from the control environment in order to limit the range of amplitude and duration values that can be applied; this feature aims at ensuring comfortable and painless sensations.

Since different stimulus (MP) and multisite stimulations (VE) can be achieved for sensation comparison purposes, the stimulator should allow quick swapping between two multisite stimulations to ease experiments.

So, the stimulator offers the possibility to remotely execute and switch between two MP/VE (one at a time). Finally, since the stimulator must be remotely controlled, it embeds a communication module.

7.2.1.2 The Stimulus Generator

Concerning the analog front-end, the basic idea consists in providing synchronous current sources for each pole. The new idea we introduced (Guiraud, 2011) is based on the decoupling of the ratio and the global current control. To do so, a unique digital to analog current converter (DACC) is used followed by a programmable current divider. In this case the current is controlled in a completely different manner.

The most interesting benefits of such structure are that it allows:

- A constant step size of the global current amplitude *Iref* and a constant maximum amplitude *255*Iref*, whatever the ratios are if their sum is constrained to 16.
- An independent control of ratios and global amplitude.

However, equivalent structures between both solutions may be found but the cost is high. In a solution with 12 DACC, if we want to guarantee the specifications in the worst case, we have to provide for DACC with 12-bit resolution that leads to 144 bits word length. Moreover, DACC are much more power supply demanding than dividers. An ASIC for a 12-pole structure has been developed (Figure 7.1). This structure is able to provide sinking or sourcing currents in order to allow each pole to be configured either as a cathode or an anode (Figure 7.2). The programmed current divider at each output stages, allows to map the VE concept to the hardware directly.

Indeed, this advanced output stage allows for a higher level of software abstraction. In fact, on a functional point of view, both features mean different things. The ratios configuration determines on which zone of the nerve the current lines that induce action potentials are focused, whereas the global amplitude is linked to the extent of this area around the focus point. Our structure further optimized software design and data-flow.

7.2.1.3 The stimulation controller

The stimulation controller is the digital part of the stimulator. Its architecture relies on a set of interconnected modules; each one corresponding to previously mentioned functionalities.

The **execution module**, called “micromachine,” can be seen as a specific and very small processor, similar to an application-specific instruction-set processor (ASIP) that runs MPs written in a FES-dedicated, reduced 32-bit

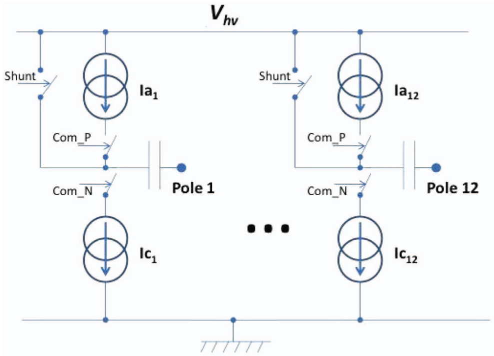

Figure 7.2 Principle of the output stage. Each channel can be configured as shunt (anode) for passive discharge, anode controlled current or cathode controlled current. One current source is used and spread over the 12 poles through ratios (Ia_i, Ic_i).

instruction set (summarized in Table 7.2). Doing so, it set the output configuration (VE) and drives the analog subsystem by calibrating the current pulse (waveform, amplitude, duration) to be applied to the multipolar electrode (Figure 7.3).

The instruction set is limited to four basic instructions:

- *SIT*. This instruction generates a positive or a negative pulse with a given intensity *I* during a given time *T*. A *RT_SIT* instruction is a *SIT* where *T* and *I* can be remotely modulated (during execution). In Figure 7.4, the seventh instruction is a *SIT* generating a positive pulse of 5 mA amplitude and 300 µs width.
- *RP_SIT*. This instruction generates a positive or negative ramp with a given step magnitude *I*, a given step duration *T*, during a number of steps *N*. It can also indicate that the starting intensity is dependent on the preceding instruction. A *RT_RP_SIT* instruction is a *RP_SIT* instruction where *T* and *I* can be remotely modulated. In Figure 7.4, the third instruction is a *RP_SIT* generating a train of 21 positive pulses (steps) with a 200 µA variation of amplitude and a 10 µs pulse width.
- *NST*. This instruction sets the high impedance state or generates a limited passive discharge on active anodes and cathodes during a given time *T*. A *RT_NST* instruction is a *NST* where *T* can be remotely modulated. In Figure 7.4, the ninth instruction is a *NST* enabling a passive discharge during 20 ms.
- *Loop*. A *Loop* instruction is interpreted as a termination marker for the MP. At termination it generates a limited passive discharge followed by a

Table 7.2 Instruction set of the Stim'ND micromachine

Name	Description	Possibilities	Parameters
NST	Discharge instruction	Passive discharge or Inter stimulation	Time (0–16 777 215 μs)
SIT	Basic stimulation instruction		Intensity (0–255 μA) Time (0–511 μs)
LOOP	Loop instruction	Finite or infinite Passive discharge or Inter stimulation	1–32 768 loop
Conf_P	Pole configuration	Anode, cathode, shunt (anode), high-impedance	
Conf_R	Ratio configuration	Ratios $K/16$	K (1–16)
RT_NST	Real-time discharge instruction	Passive discharge or interstimulation	Time (0–16 777 215 μs)
RT_SIT	Real-time stimulation instruction	Modulation of I and T	Intensity (0–255 μA) Time (0–511 μs)
RP_SIT	Ramp stimulation instruction	Current intensity dependence with previous instruction	Initial intensity (0–255 μA) Initial time (0–255 μs) Step number (0–255) Intensity step (0–255 μA) Time step (0–255 μs)
RT_RP_SIT	Real-time ramp stimulation instruction	Current intensity dependence with previous instruction Modulation of I and T	Initial intensity (0–255 μA) First step duration (0–255 μs) Number of steps (0–255) Intensity step (0–255 μA) Time step (0–255 μs)

global passive discharge for all poles or puts the poles in high impedance state. It also embeds a jump operation addressing a previous instruction in the sequence, to generate a loop in the MP. This back jump can be repeated many times or infinitely until program explicit stop, as it is the case of the last instruction of the MP given Figure 7.4.

Two other instructions are used to configure the analog output stage, since this configuration is separated from the stimulation profile itself:

– *CONF_P* is the instruction used to configure active poles. For each pole to be used, it defines whether a pole is a cathode, an anode, a shunt (not controllable anode) or is in high impedance state. The unique *CONF_P* in Figure 7.4 specifies that poles 1 and 3 are cathodes and pole 2 is an anode.

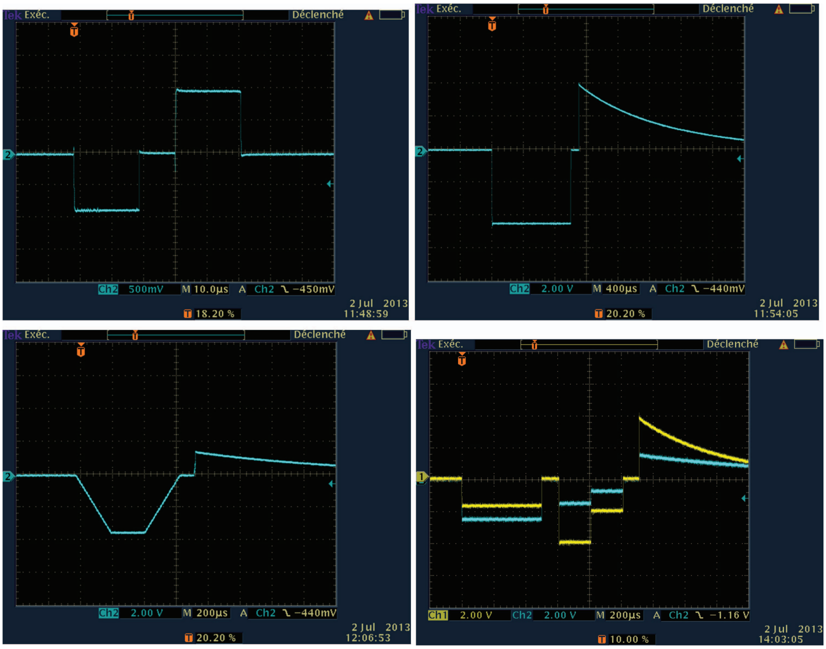

Figure 7.3 Four different stimulation waveforms generated by the miniaturized stimulator in bipolar mode (left-up). Rectangular biphasic charge balanced waveform (20 µs, 1 mA) with interstim (right-up) biphasic with passive discharge (1 ms, 4 mA) (left-down) biphasic trapezoïdal pulse with passive discharge. Train of pulses on a tripolar configuration with different current ratios, followed by a passive discharge (right-down). The signal is generated on a 1 kΩ resistor.

Inst.		*I*	*T*	*Steps*	*Note*
CONF_P	Cathodes : 1, 3, anode : 2				
CONF_R	K1 : 75 %, K3 : 25 %, A2 : 100 %				
RP_SIT	+	200 µA	10 µs	21	
NST			20 µs		interstim
RP_SIT	-	200 µA	10 µs	21	
NST			100 µs		discharge
SIT	+	5 mA	300 µs		
NST			20 µs		interstim
SIT	-	5 mA	50 µs		
NST			100 µs		interstim
NST			20 ms		discharge
LOOP					endless

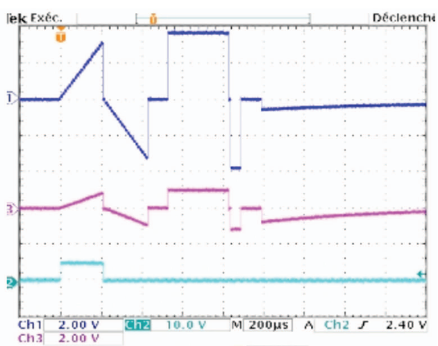

Figure 7.4 Example of 48-byte MP (left). Resulting stimulus with ch1 being cathode 1, ch3 cathode 3, and ch2 a trigger (right).

- *CONF_R* is the instruction used to configure ratios of current between active poles (controlled anodes and cathodes). In Figure 7.4, the unique *CONF_R* specifies that 75% of the current will be generated by cathode 1 and 25% by cathode 3.
- If *CONF_P* and *CONF_R* instructions must be used at the beginning of MPs, they may also be inserted anywhere else in the sequence of instructions to dynamically reconfigure poles and ratios, in order to apply different waveforms to the selected poles.

The **interface module** supports the interface with the stimulus generator. It ensures the effective electrical configuration of the analog device corresponding to the VE on which the stimulation has to be applied. It also maps control signals used by the micromachine with input signals of the analog device.

The **monitoring module** is based on a reference model in charge of monitoring in respect of neurophysiological constraints. These constraints are described Table 7.3; for instance, *Qmax* is set to 120 nC which is the safe limit of charge injection that the TIME-3H electrode can support. The monitoring of these constraints is based on simultaneous application of the stimulation to the nerve (via the stimulus generator) and to the reference model. Each time the micromachine sends a command to the stimulus generator, it sends the same command to the reference model. If any constraint is violated, the reference model forces the micromachine to immediately stop the stimulation and commute to a safe state. Thus, any error detection puts the stimulator into a safe mode regarding the physiological system under control (putting the output stage into a discharge mode). The micromachine then must be remotely rearmed by the experimenter in order for the stimulation to be once again authorized.

The stimulator does not perform any embedded diagnostic; it only indicates the type of error that has been detected. Note that any error due to the MP itself (e.g., coding error) is directly detected and managed within the execution module.

The **communication module** contains a three-layer protocol stack structured according to the reduced OSI-model with application, MAC (medium access control) and physical layers. The MAC layer provides logical addressing (and thus packet filtering) and deterministic medium access control mechanisms, based on a master/slave model (Godary et al., 2013). The application layer decodes the incoming packets, executes

Table 7.3 Parameters of the monitoring module

Name	Description	Parameters
QMax	Maximum quantity of electrical charges injected by "stimulation" (SIT $>$ 0), or by "active discharge" (SIT $<$ 0)	Electrical charges limit (0–6.5535 μC) with a 100 pC step
QThreshold	Maximum accepted residual quantity of electrical charges after passive discharge (after the end of a microprogram)	Electrical charges limit (0–6.5535 μC) with a 100 pC step
Min LPD duration	Minimum passive discharge time (after the end of a microprogram)	Duration limit (0–65 535 μs)

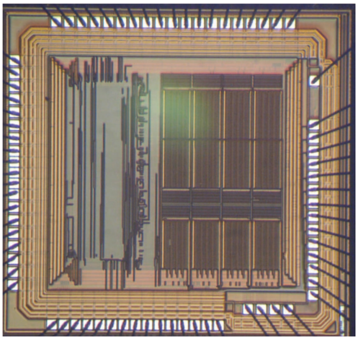

Figure 7.5 12-pole ASIC that can be seen in the center, about $4\ \mathrm{mm} \times 4\ \mathrm{mm}, 0.35$ μ HV technology.

the request by controlling the micromachine and the reference model, and it also encodes responses. From an application point of view, the application layer supports all the communication with the experimenter-dedicated computer (cf. Section 7.3.1): download/upload of MP and VE, start/stop/commute/rearm of MP, notification of error detection, monitoring parameters' initialization, and remote modulation of stimulation parameters.

7.2.2 Prototyping of the Stimulator

The prototype of bench-top stimulator Stim'ND is essentially based on the assembly of two chips, a digital chip and an analog one. The analog chip is an ASIC (Figure 7.5) and the digital one is an FPGA, both being detailed afterward.

7.2.2.1 Prototyping of the stimulus generator

This is the heart of the device. It is connected to the patient via the charge balancing capacitors and the electrodes. It consists in analog stages only, and mainly a digitally driven current sources and digitally configurable switches. The current sources are based on a patented method (Guiraud et al., 2010) that allows performing synchronous multipolar stimulation with fixed ratios whatever the total current is. The global current source is based on a 10-bits resolution DACC, and the ratios can be programmed with a 4-bit resolution. As the DACC is controlled by the micromachine with a resolution of 8 bits, we used the 2 remaining bits to further improve the accuracy of the stimulator. We thus divided the relative error over the whole scale by a factor of 3 leading this error below 5% (Figure 7.6). It is able to source and sink up to 5 mA under a 16 V DC voltage, on capacitive load. The pulse width is externally controlled; the ASIC is able to manage pulse widths as short as 500 ns, but a step of 1 μs is first proposed according to the needs.

7.2.2.2 Prototyping of the stimulation controller

Four modules constitute the stimulation controller, described in Figure 7.1. Modules are specified by means of Petri nets (PNs) based components and analyzed. Their implementation on programmable electronic device (FPGA) is done using HILECOP tool[1] (Leroux et al., 2015). For illustration, the PN model of the monitoring module is shown in Figure 7.7 (the PN models of the other modules being too complex to be shown).

Once modules have been composed and this composition analyzed, the full digital architecture is automatically translated in VHDL [c1][2] using HILECOP; the global PN, resulting from the assembly of the PNs of the modules, contains about 700 places and 800 transitions. This digital architecture constitutes a GALS system (globally asynchronous locally synchronous) since its components have their own clock and are interconnected by means of asynchronous signals. Two memories, directly described in VHDL (i.e., not generated by HILECOP), are used: the first memory is used to store the MPs, and the second one is used to store stimulation parameters that are on-line modified (remote stimulation modulation). Then this digital architecture is validated by simulation at RTL [c2][3] level using industrial tools,

[1]High-level hardware component programming tool, ensuring automatically the model transformation from PN-components to VHDL, language from which a FPGA can be programmed.

[2]Very high speed integrated circuit hardware description language.

[3]Register transfer level.

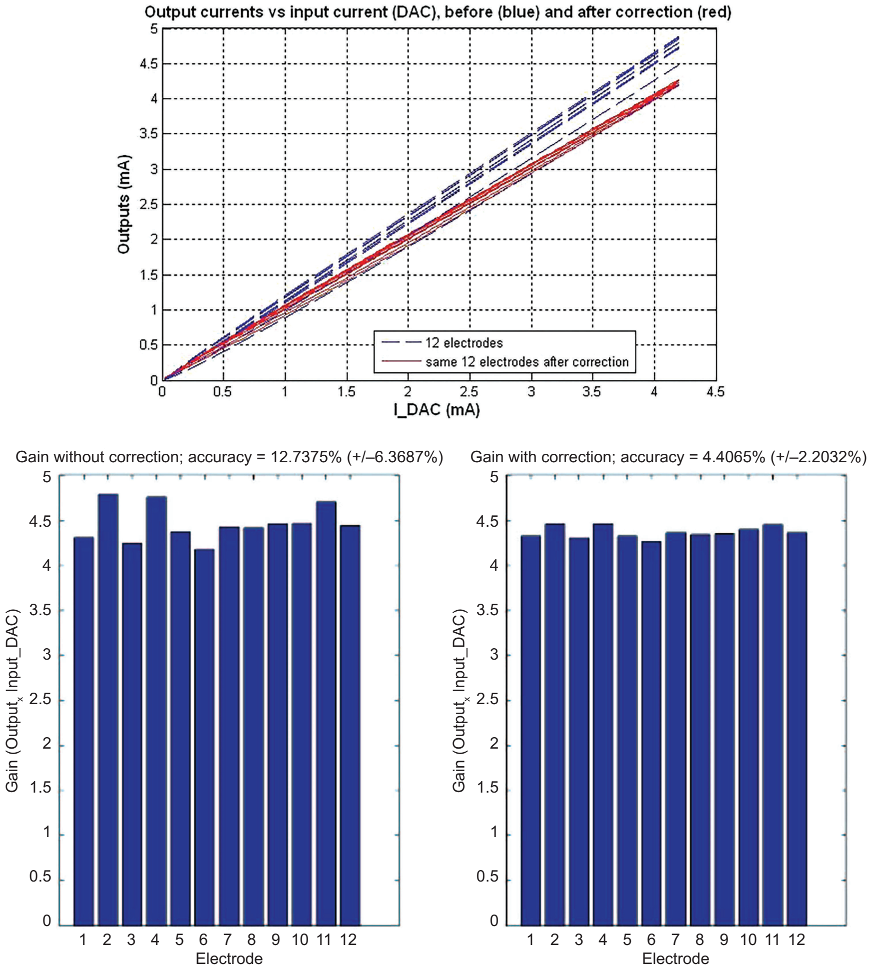

Figure 7.6 As the DACC is on 12 bits but only 8 bits are finally coded, the 4 lower bits are used to compensate the current error following an affine linear law. It cuts down the error from about 20% to less than 5% error over the full scale.

directly implemented on a programmable electronic component (FPGA) and functionally validated according to a set of validation-dedicated scenarios.

The stimulator controller embeds two memory zones to store two MPs (the configuration of the VE being included in the MP). The stimulator reacts to the following commands: *Start* (starting the stimulation according to the selected MP, i.e., *start_z0* or *start_z1*), *Stop* (stopping the ongoing

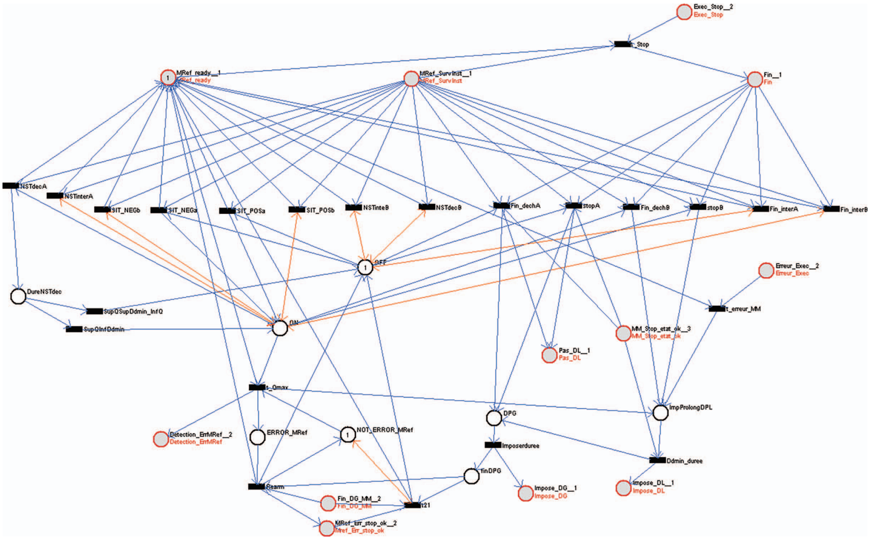

Figure 7.7 PN model of the monitoring module (reference model).

stimulation), *Rearm* (rearming the stimulation after an error detection), and *Commute* (changing the active MP). It also reacts to commands used to change values of stimulation instructions (intensity, duration, etc.).

7.2.2.3 Prototypes of stim'ND

First of all, the bench-top stimulator (Figure 7.8, left) integrates safety aspects in terms of power supply and connectivity. The power supply of Stim'ND is based on batteries whose recharge system ensures that no stimulation can be performed while batteries are recharging. It terms of connectivity, Stim'ND is based on an optically insulated USB link. Moreover, to avoid any DC component all output channels (to electrode contacts) are capacitively coupled. Last, Stim'ND embeds a safety device allowing, if required, isolating the

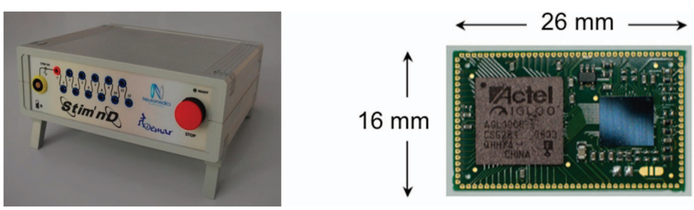

Figure 7.8 Stim'ND prototypes (left) the benchtop version (right) the miniaturized version.

patient and the stimulator outputs; this full emergency insulation of the patient from the stimulator relies on a global switch that opens all the circuits between electrodes and the stimulator, and makes a short circuit between all the electrodes to ensure no floating differential voltages. Besides, at all the software levels from the embedded digital controller (the reference models) to the remote configuration and control application, safety is considered to ensure robust and redundant checking.

7.3 Software Suite

Several software tools have been developed during the project. The first software is SENIS Manager: it allows configuring, programming, and controlling all stimulators that are connected to the controller-like computer. The second software, based on SENIS Manager API, has been developed for impedance measurement purpose in order to verify the condition of the electrode and the quality of the contact between the electrode and the neural tissue. The third software is the psychoplatform described Chapter 9. These three software applications remotely control the stimulator thanks to the embedded protocol stack that makes any stimulator a communicating unit.

To allow for such remote control of the stimulators from any of those software, the architecture has been designed and developed according to a multitier architecture. It exploits a "runtime module" that acts as a middleware in charge of communicating with stimulators (Figure 7.9); an application programming interface is provided to connect the different software to this runtime module.

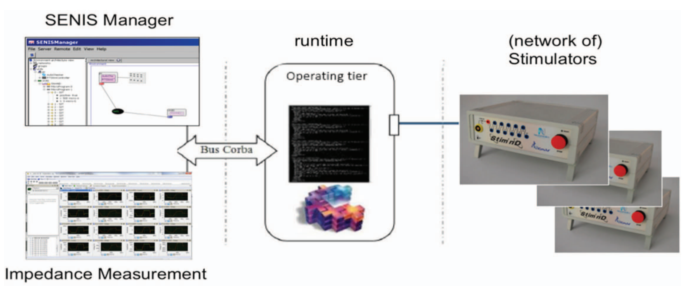

Figure 7.9 N-tier architecture allowing remote control of the stimulators.

7.3.1 SENIS Manager

SENIS Manager (Passama et al., 2011) is a software environment allowing for FES architecture configuration. It consists in configuring each stimulator that is connected to the dedicated network mastered by this controller-like computer (i.e., that running SENIS Manager). The network can be a bus or serial link. Discovering connected stimulators is based on a dedicated service that checks if any stimulator is present (64 possible nodes).

Figure 7.10 (left) shows a simple architecture composed of the PC with its associated control-box and one stimulator connected to the computer through an isolated USB link in this case.

- Functionalities associated these entities are given in Figure 7.10 (right): On the PC node the *AutoChecker* is used to periodically check (at runtime) that each unit is still connected and the *RTStimController* is used to control the stimulation process at runtime. On the stimulator node, the *Stim'ND* functionality corresponds to stimulation facilities of this kind of stimulator.
- Stimulation profile editing (Figure 7.11). It permits a graphical specification of the stimulation profile, from which it generates the corresponding MP. Depending on the instruction used some parameters of the profile can be modulated.
- Electrode configurations (Figure 7.12, left). It allows describing configuration of the 12 channels (poles), setting active poles, their polarity and ratios of current repartition between active poles knowing that the sum of current ratios for cathodes must be 100% (as for anodes).
- Stimulators programming consists in downloading MPs in its memory areas as well as setting the parameters of its reference model (safety

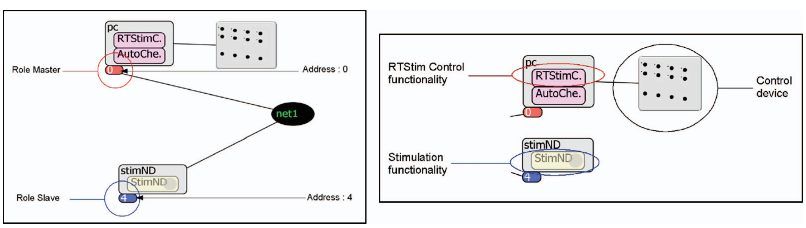

Figure 7.10 Example of simple architecture (left). Functionalities associated to entities (right).

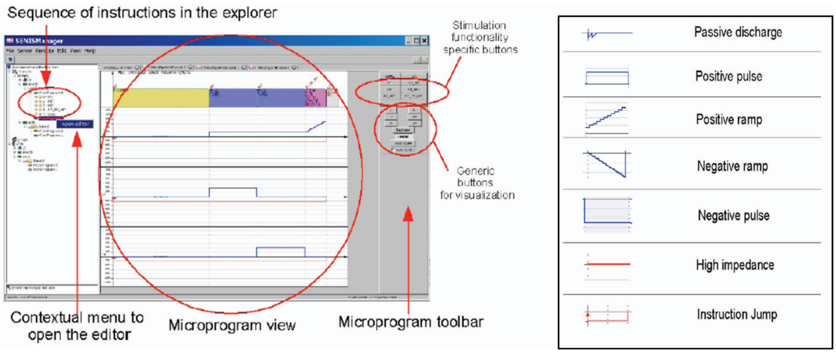

Figure 7.11 Stimulation profile editing (left). Correspondence between icons and instructions (right).

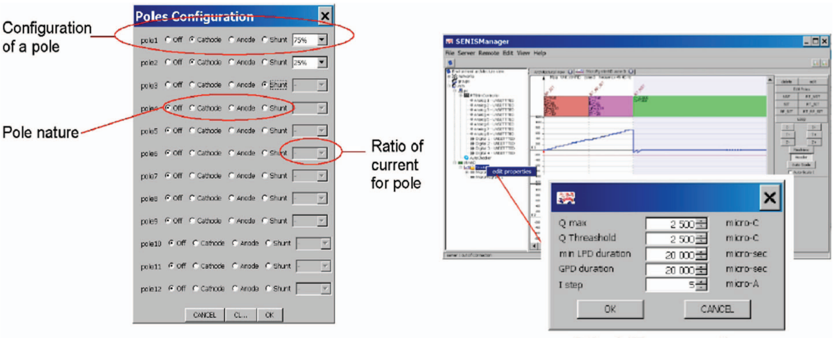

Figure 7.12 Electrode configuration (left). Configuring reference model parameters (right).

module), as, for instance, the maximum quantity of injected charge (Figure 7.12, right).

- Once configured and programmed, any stimulator can be remotely controlled. Stimulation control relies on two main facilities that are commands and stimulation modulations through online modification of the stimulation parameters. This can be done through the HMI as well as from a dedicated control-box (Figure 7.13) with four push-buttons and eight rotary ones; association of push-buttons to *RT commands* (start, stop, commute, rearm) and rotary ones to *RT updates* of parameters (*I*, *PW*) is simply done through the software. For each rotary button, the user has to associate: the concerned entity (i.e., stimulator), the concerned MP, the RT instruction and the parameter to be modulated, as well as min and max values for the given parameter (i.e., min and

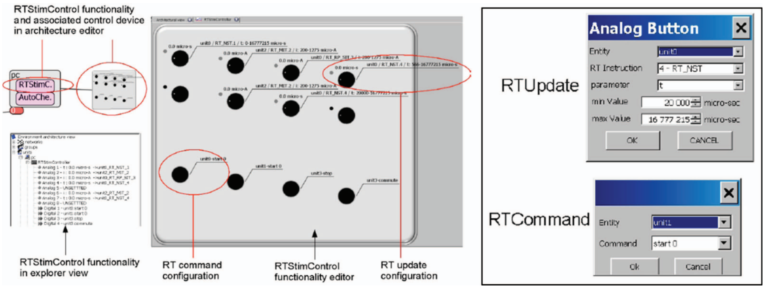

Figure 7.13 Configuring the control-box (left). Configuration of buttons (right).

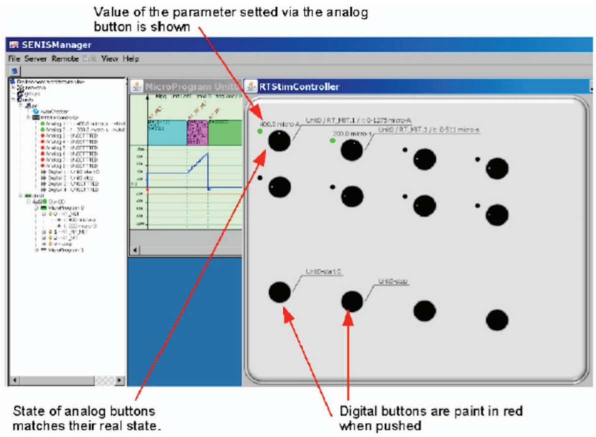

Figure 7.14 Following of the stimulator and control-box states.

max values of the button). Using a control-box allows the practitioner to keep attention on the stimulated target when controlling the stimulation rather than on the screen.

Once started, the stimulator state and control-box parameters are continuously monitored as shown Figure 7.14 where the stimulation is running and parameters are modulated, and Figure 7.15 where a constraint violation has been detected by the stimulator that immediately went to a safe state, waiting to be rearmed.

Different stimulations can be specified playing with the MPs' internal repetition and computer-driven sequencing of MP execution (Figure 7.16).

SENIS Manager can deal with individual entities (unicast addressing) and groups of entities (multicast addressing), belonging to the same network. Thus it allows for synchronized remote control of stimulators (RT commands only) for multisite coordinated stimulation.

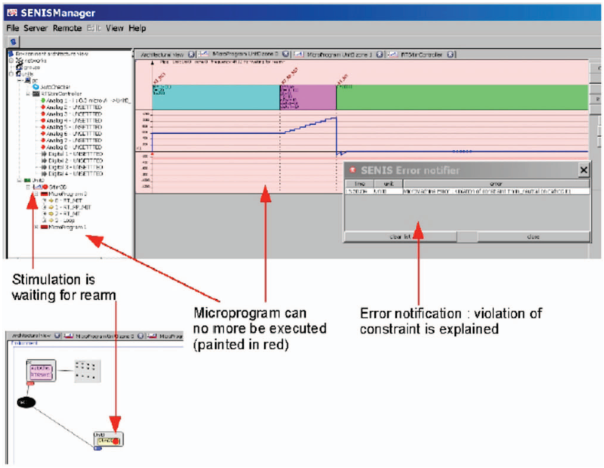

Figure 7.15 Notification of a constraint violation to the control environment.

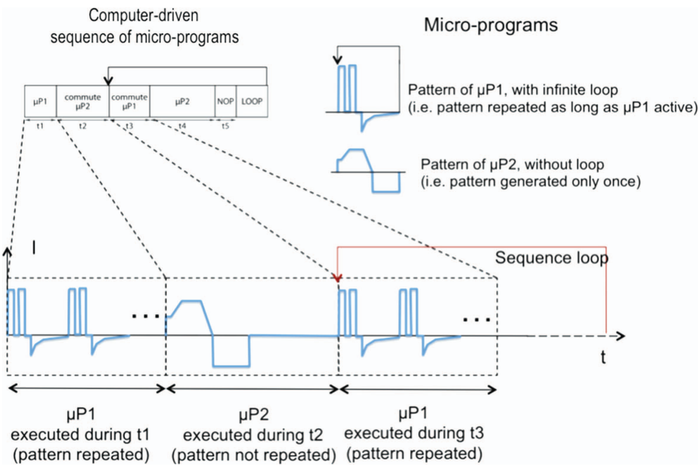

Figure 7.16 Example of microprogram sequence.

7.3.2 Impedance Follow-up Software

In order to verify the condition of the electrode and the quality of the contact between the electrode and the neural tissue, during the implantation of the TIME electrode and at few time instants after the implantation, the impedance of each site of the four implanted TIME electrodes has been measured using indirect method. For that purpose a small controlled-current stimuli (biphasic rectangular pulses of 40 μA, 300 μs duration of each phase) were generated using each of the TIME electrode stimulation sites as a cathode and the reference (GND) site of each electrode as the anode. While the stimuli were generated the voltage drop between the cathode and the reference site as well as the voltage drop on the 1 kΩ resistor inserted in series with the TIME electrode have been measured. Based on those two measurements it was possible to determine the impedance of each electrode site versus each of the two reference sites (left and right) of the same electrode as well as between the two reference sites of each electrode.

In order to facilitate those measurements and to ensure that the measurements during follow-ups are performed in the same way, two applications have been developed. The first one has been developed using the Microsoft Visual Basic Express programing language (Figure 7.1) and allowed to generate a sequence of stimuli for various sites of the TIME electrode using the Stim'ND stimulator. It also allowed pausing stimulation after generation of stimuli for the particular site, leaving the time for the experimenter to evaluate the results. The second application was developed using the National Instruments LabVIEW Signal Express programing language and allowed to record the voltage drops in the moment of stimulation and also to immediately display results of the measurements for up to eight different stimulation sites combinations (Figure 7.17 – example of the results obtained right after the surgery for the TIME electrode implanted into the median nerve, results

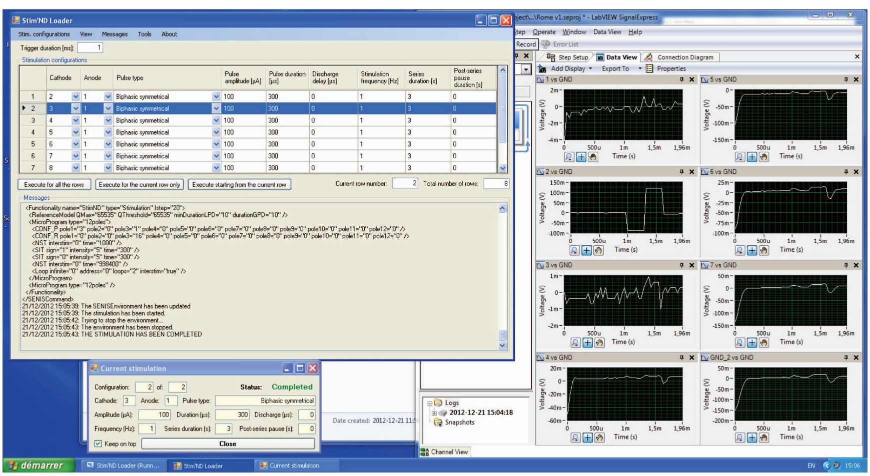

Figure 7.17 The screenshot shows the control of the stimulator on the left and the resulting current-voltage curves from which the estimation is performed (ratio of U and I at the end of the active phase).

obtained for the stimulating sites on the right side of the electrode versus the right reference site).

Each of the implanted TIME electrodes had 16 contacts: seven on the left side, seven on the right side, and two reference sites (one on the left side – LGND and one on the right side – RGND). Therefore, for each TIME electrode four measurement series were performed:

- Seven contacts on the left site and the right reference site versus the left reference site
- Seven contacts on the left site and the left reference site versus the right reference site
- Seven contacts on the right site and the left reference site versus the right reference site
- Seven contacts on the right site and the right reference site versus the left reference site

The measurements for each site has been performed versus each of the reference sites in order to determine the reference site with lower impedance and to be able to estimate impedance of all the stimulating sites even if one of the reference sites was broken.

The developed application allowed performing each measurement series (i.e., measurements for eight combinations of stimulating sites) in less than

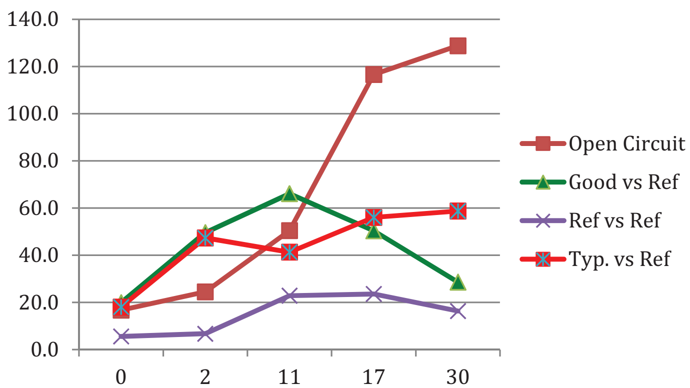

Figure 7.18 The four graphs represent the rough estimation of impedances (kohms) of all the 56 contacts. Two different profiles of impedances were found (green increase then decline, red constant increase). The references are much bigger so the impedance is much lower. Finally, open circuits have a clear and strong increase of the impedance from day 17.

1 min. Because for each of the four TIME electrodes four measurement series were performed (4 measurement series $\times$ 4 TIME electrodes), using those applications it was possible to perform the measurement of impedance for all the stimulating sites of the four TIME electrodes in less than 15 min.

The impedance measurements have been performed during the implantation of the electrodes, in order to verify the correct position of the electrode and to provide feedback to the surgeon, and also right after the surgery as well as 2, 11, 17, and 30 days after the implantation in order to track the changes of the impedance during the course of the experiment. The results of the measurements are presented in Figure 7.18. It may be observed that at the last day of measurement (i.e., 30 days after the implantation) only seven sites had higher impedance than expected (i.e., above 80 $k\Omega$).

7.4 Discussion

The stimulator Stim'ND has shown its suitability to achieve selective multipolar stimulations. However, the different control modalities of the stimulator, through different software and operators, have also revealed some necessary improvements. Modulating the stimulation profile simultaneously playing with several parameters of several instructions still is a cumbersome and inefficient procedure. A new processor, more particularly a new set of instructions, must be designed to allow the modulation of all or part of the stimulation profile with notably preservation of charge-balanced stimulation.

As stimulation often relies on executing different kinds of stimulation waveforms on different electrode configurations, we designed the stimulator according to 3D electrode (VE) and MP concepts. Nevertheless at this stage the description of a 3D electrode is inserted into a MP, thus limiting the possible reuse of each of these entities. The stimulator should be able to be programmed via these two entities, namely the tuple {VE, MP}, constituting so key elements of a high-level programming language.

Finally, SEF applications may require the sequencing of different stimuli (i.e., different tuples {VE, MP} executed in sequence). Remotely controlling this sequencing poses a performance problem in the sequence of stimulations, the remote control necessarily inducing a latency of communication and decoding. One of the solutions would be to decentralize this functionality, i.e., to embed it directly into a stimulation unit, at the expense of complexity, surface, and consumption.

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