Flexible Thread-like Electrical Stimulation Implants Based on Rectification of Epidermically Applied Currents which Perform Charge Balance

Antoni Ivorra and Laura Becerra-Fajardo

Abstract— **Miniaturization of implantable medical electronic devices is currently compromised by the available means for powering them. Most common energy supply techniques for implants – batteries and inductive links – comprise bulky parts which, in most cases, are larger than the circuitry they feed. For overcoming such miniaturization bottleneck in the case of implants for electrical stimulation, we recently proposed and demonstrated a method in which the implants operate as rectifiers of bursts of high frequency current supplied by skin electrodes. In this way, low frequency currents capable of performing stimulation of excitable tissues are generated locally through the implants whereas the auxiliary high frequency currents only cause innocuous heating. The electronics of the prototype we demonstrated previously consisted of a single diode. As a consequence, it caused dc currents through it which made it impractical for clinical applications. Here we present an implantable prototype which performs charge balance for preventing electrochemical damage. It consists of a tubular silicone body with a diameter of 1 mm, two peripheral electrodes and a central electronic circuit made up of a diode, two capacitors and a resistor. We also report that this circuitry works even when water immersed, which may avoid the need for hermetic packaging.**

I. INTRODUCTION

To build interfaces between the electronic domain and the human nervous system is one of the most demanding challenges of nowadays engineering. Fascinating developments have already been performed such as visual cortical implants for the blind and cochlear implants for the deaf. Yet implantation of most electrical stimulation systems requires complex surgeries which hamper their use in diverse clinical scenarios. For instance, that is the case of movement restoration: currently available implantable systems consisting of central stimulation units wired to the stimulation electrodes are not adequate for applications in which a large number of targets must be individually stimulated over large and mobile body parts, thus hindering solutions for patients suffering paralysis due to spinal cord injury or other neurological disorders.

An alternative to centralized stimulation systems could consist in developing a network of addressable single-channel wireless microstimulators which could be implanted with simple procedures such as injection, and which would be activated in coordinated patterns by an external automated controller. In fact, such solution was proposed and tried in the past [1,2]. However, these previously developed microstimulators are stiff and considerably large (diameters > 2 mm) which makes them unsuitable for some applications because of their invasiveness. Further miniaturization was prevented because of the use of inductive coupling and batteries as energy sources.

In [3] we proposed and *in vivo* demonstrated an alternative method for performing electrical stimulation by using electronic implants: the implanted devices rectify bursts of innocuous high frequency currents supplied to the tissue of interest by remote electrodes so that low frequency (LF) currents are generated locally through the implants and these resultant currents are capable of performing stimulation of local excitable tissues without disturbing neighbor tissues. This idea is schematically illustrated in Fig. 1. In comparison to inductive coupling – or to electrochemical batteries – this method offers an unprecedented potential for miniaturization. Note that only two peripheral electrodes are required both for picking-up the high frequency (HF) currents and for performing stimulation. In addition, all necessary electrical components, maybe with the exception of the electrodes, can be integrated in a single integrated circuit or in a tiny hybrid microcircuit.

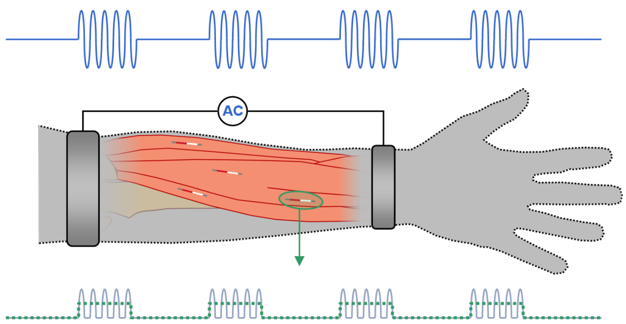

Figure 1: The proposed technology is based on externally applying an inert HF current which is rectified by the implants into LF currents capable of stimulation.

The proposed method requires a minimum voltage drop to operate and this implies that, in most applications, it will be necessary that both electrodes are quite separated (from some millimeters to a very few centimeters). Consequently, we propose elongated implant bodies in which most of their length consists of flexible and stretchable materials whose mechanical properties match those of neighboring living tissues. Hence the implants may look like short pieces of flexible and stretchable thread. Because of such feature, and because of their

L. Becerra-Fajardo and A. Ivorra (corresponding author) are with the Dept. of Information and Communication Technologies of the Universitat Pompeu Fabra, Barcelona, Spain (phone: +34-93-542-1578; fax: +34-93-542-2517; e-mail: antoni.ivorra@upf.edu).

intended functionality, we coined the name “Electronic Axons” (eAXONs) for these implants.

We envision eAXONs with advanced communication, control and sensing capabilities which can be deployed in large numbers thus forming a complex network controlled by an external autonomous unit which delivers innocuous high frequency currents [4]. These systems will be capable of executing complex stimulation patterns such as those that would be required for fine movement restoration in paralysis patients. The advanced eAXONs to be created will require future development of Application Specific Integrated Circuits (ASICs) and specific packaging and interconnection techniques [5]. Meanwhile, we have demonstrated that those advanced eAXONs are feasible by developing non-implantable bulky eAXONs based on discrete electronic components [6] which can be seen performing individual stimulation of segments of an earthworm at https://sites.google.com/site/electronicaxons.

In [3, 5] we demonstrated the method by testing implants consisting of just a diode. We later discovered that such demonstration had already been performed in vertebrates by at least to independent research teams in the 60s [7,8]. However, those studies are barely cited and, in fact, no references to them are found after the 80s. No advanced rectifiers have been proposed until now. In historical perspective it is easy to understand such neglect: at the time microelectronics was at its infancy and, therefore, the coils and batteries were not the miniaturization bottleneck but the electronics.

Simple rectifiers, such as diodes, do not allow the networked neuroprosthetic system that we envision. However, implants consisting of a simple rectifier would be applicable to cases in which a single target must be stimulated in a minimally invasive manner. On the other hand, implants consisting of just a diode are not adequate because they cause dc currents through them. Passage of dc current through an electrode will cause electrochemical reactions that will damage both the electrodes and the tissues [9]. For that reason, charge-balanced waveforms, resulting in a null dc component through the electrodes, are employed in electrical stimulation systems.

Here we present an implantable single-diode prototype which performs charge balance. It consists of a tubular silicone body with a diameter of 1 mm, two peripheral electrodes and a central electronic circuit made up of a diode, two capacitors (acting as a single one) and a resistor.

This prototype may be the basis for minimally invasive systems in which a single target needs to be stimulated (or in which multiple targets are sufficiently separated so that the corresponding implants can be selectively powered from multiple external electrodes). For instance, besides a few applications in the area of Functional Electrical Stimulation, such as peroneal nerve stimulation for the correction of drop foot [10], these systems would be very well suited for applications in the area of peripheral nerve stimulation for treatment of chronic pain [11].

II. PROPOSED SIMPLE CIRCUITRY TO PERFORM CHARGE BALANCE

A. *The circuit and its generic design constraints*

The proposed circuit for performing charge balance is represented in Fig. 2. The implant circuit is drawn in black whereas a simplified circuit corresponding to the rest of the system (i.e. external generator and tissue impedances) is drawn in gray. The nodes A and K represent the electrodes of the implant whose impedances are neglected for the sake of simplicity.

At the beginning of the ac burst, the capacitor is discharged and rectified current flows from K to A through the diode thus progressively charging the capacitor. As the capacitor charges, higher voltage differences between K and A are required in order to obtain conduction through the diode and, as a consequence, rectified current decreases. Once the ac burst finishes, the capacitor discharges through the tissues and the implant resistor.

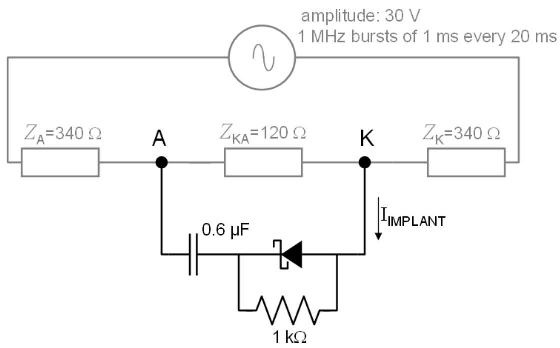

Figure 2: Proposed circuitry to perform charge balance (in black). The indicated numerical values have been chosen for reproducing the experiment performed with the implemented prototype (section III).

A capacitor with a large enough capacitance value must be employed so that rectified current flows for a significant amount of time during the ac burst. In other words, a large capacitance is required in order to allow generation of long enough current pulses capable of stimulation. However, it must be taken into account that the capacitor must fully discharge in between ac bursts and, since the discharge time constant is proportional to the capacitance, such value cannot be extreme. It could be argued that the time constant also depends on the resistance value of the implant resistor, but, it must be noted that such resistance cannot be reduced excessively; otherwise the high frequency voltage to be rectified will be too low because of short-circuiting. In addition, the capacitance value may be constrained due to size limitations. Not many capacitors exist with submillimeter dimensions, capacitances above 1 µF and the capability to withstand some volts or tens of volts as it is required in this application.

Schottky diodes appear preferable to other diodes because of their lower forward voltage drop and their very fast switching capabilities.

B. *SPICE simulation*

Fig. 3 displays some results from a SPICE simulation of the circuit represented in Fig. 2. Specifically, a time transient simulation has been performed and low frequency current and voltage signals have been extracted by means of first order low pass filters (cutoff frequency = 10 kHz). The simulator was LTSpice 4.16 (freely distributed by Linear Technology Corp.) and the SPICE model provided by RHOM Semiconductor for its Schottky diode RB521ZS-30 was employed.

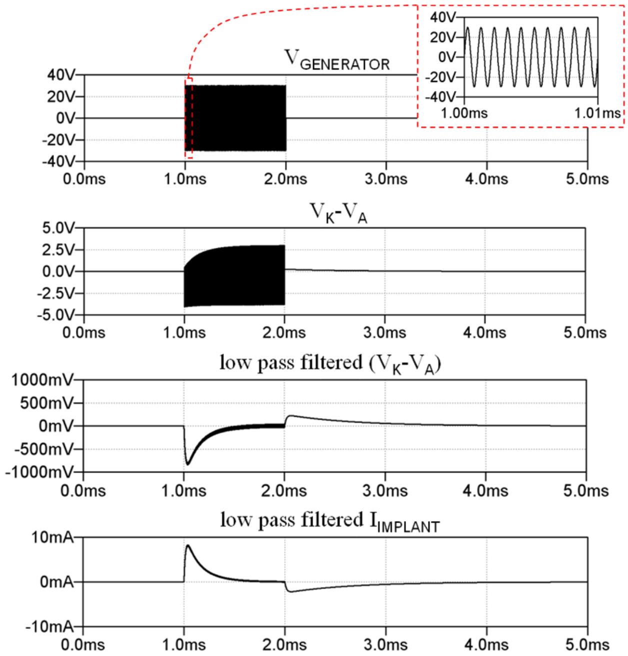

Figure 3: SPICE simulation results for the circuit in Fig. 2.

The simulation shows that a low frequency voltage signal is generated across the implant electrodes which is associated with a low frequency current through the implant (and through the tissue in between the two implant electrodes.) The peak value of the low frequency current transient is about 8 mA and its pulse duration is about 0.15 ms (50% peak crossings) which appears sufficient for electrical stimulation of nerves [12]. Furthermore, note that higher generator voltage amplitudes would be tolerated both by the circuit (the maximum voltage reached at the capacitor is 2.6 V) and by the human body according to safety standards [4], hence even larger currents would be possible. However, the most important piece of information from this simulation is that the average of the current is null which indicates that it is charge balanced.

C. *In vitro demonstration of charge balance and non-critical hermeticity*

The setup illustrated in Fig. 4 was built in order to demonstrate that the proposed circuit performs charge balance and that it will prevent electrochemical damage. The behavior of the proposed architecture (mounted on a PCB) was compared to that of a system consisting of just a diode. Each system was connected to two platinum-iridium wires (76700, A-M Systems, Sequim, WA, USA) which were inserted at a distance of 3 cm (and a depth of about 5 mm) in a 2.5 cm diameter agar cylinder made from a 0.9% NaCl solution. Two aluminum band electrodes were placed on the agar cylinder at a distance of 10 cm and were energized by a 30 V peak sinusoidal signal delivered as 1 ms bursts at a rate of 50 bursts per second. The signal was generated by a function generator (AFG 3022B by Tektronix) followed by a high voltage amplifier (WMA-300 by Falco Systems BV, Amsterdam, The Netherlands).

Low frequency currents through the circuits were obtained by capturing, with a battery powered oscilloscope (TPS2014 by Tektronix), the voltage drop across the parallel combination of a 10 Ω resistor and 1 μF capacitor (RC low pass filter, cutoff frequency =16 kHz). As it can be observed in Fig. 4, the proposed circuit performs charge balance whereas the diode does not.

The high voltage signal was applied for four hours and, after this lapse of time, it was clear the presence of entrapped gas bubbles around the Pt-Ir electrodes connected to the diode whereas no bubbles (or any sort of corrosion indication) were observable on the Pt-Ir electrodes connected to the proposed circuit. Therefore, this experiment confirms that no irreversible electrochemical reactions occur with the proposed circuit (or that they occur at an imperceptible rate compared to that of those that occur with a diode.)

The same setup was employed for another experiment: while the high voltage bursts were being delivered, the proposed circuit was immersed in distilled water and no modification of current waveforms was observable. This result is relevant because it shows that the circuit may be able to operate inside packages which are not hermetic to water in contrast to the case of inductively powered micro-stimulators whose resonant frequency strongly depends on the presence of water [13]. It remains to be tested the long-term tolerance to water.

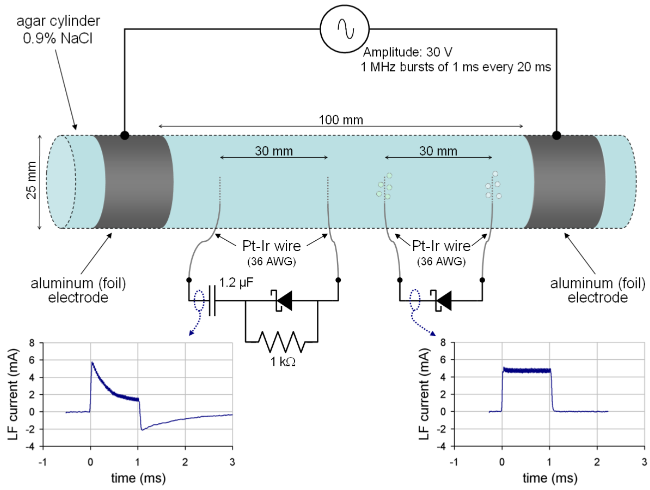

Figure 4: Setup for charge balance demonstration. The proposed circuit is compared to a circuit consisting of just a diode. (References for the components are noted in section III.A)

III. IMPLEMENTED PROTOTYPES

A. *Physical implementation*

The prototype displayed in Fig. 5 was implemented as follows: two SMD capacitors with a measured capacitance of 1.2 μF (02016D225MAT2A by AVX and acquired from Mouser Electronics; supposedly 2.2 μF capacitors), a SMD Schottky diode (RB521ZS-30 by RHOM Semiconductor) and a SMD 1 kΩ resistor (ERJ-XGNJ102Y by Panasonic) were positioned as indicated in Fig. 6 and soldered thus forming the proposed circuit. Two ~2.5 cm long Pt-Ir springs were soldered to the circuit; one to each terminal. (These springs were made by coiling 41 AWG Pt-Ir wire (76700 by A-M Systems) around a 30-gauge needle.) The assembly was gently introduced in a 3 cm long biomedical silicone tube with an outside diameter of 0.94 mm (806400 by A-M Systems). The tube was filled with a biocompatible silicone (MED-6015 by NuSil Technology, Carpinteria, CA, USA) which has a low viscosity when uncured. After curing, the Pt-Ir wire exiting the tube was bent inwards on the tube and another Pt-Ir spring (made with 19-gauge needle) was positioned over it to form an electrode of approximately 4 mm (one at each extreme). Finally, a few drops of silicone were added and cured for securing the electrodes.

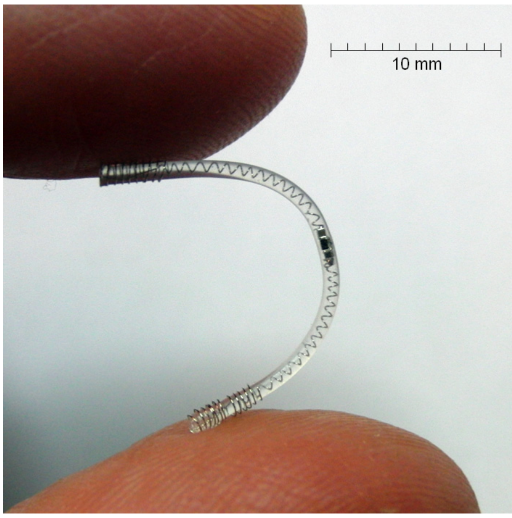

Figure 5: Implemented prototype. The electronic components and the two connections to the electrodes are contained within a silicone body. Both the connections and the electrodes consist of coiled Pt-Ir wires.

As illustrated in Fig. 5 the prototype is highly flexible (bend radius <5 mm). In addition, it can be reversibly stretched for small elongations (1 or 2 mm; ~ 5%). It also survives much larger elongations (50%) but does not recover its length.

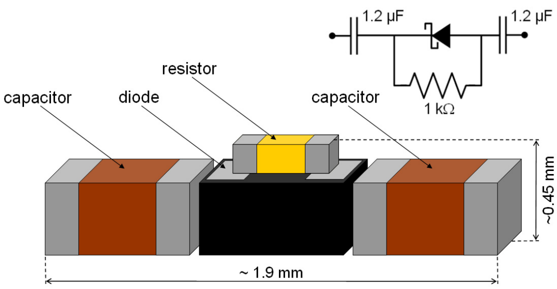

Figure 6: Electronic component placing (and the circuit formed after soldering). Two capacitors are employed in order to double the voltage tolerance (6.3 V + 6.3 V) and for geometrical symmetry.

B. *In vitro demonstration*

The prototype was tested in the setup displayed in Fig. 4. In this case, however, the device was implanted within the agar cylinder and low frequency voltage across electrodes was captured by means of two thin wires (Fig. 7). Neither bubbles nor any sort of corrosion were observable after four hours of continuous operation.

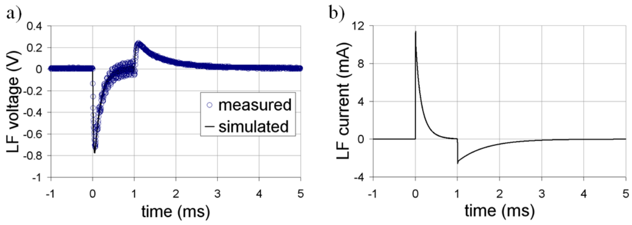

Figure 7: (a) Voltage recorded across the prototype's electrodes and its comparison to simulated voltage. (b) Simulated current for this scenario.

IV. INMEDIATE FUTURE DIRECTIONS

We plan to *in vivo* test these implants during the next months for demonstrating stimulation capabilities and minimal invasiveness. In particular, we are applying for permission from the ethical committee of animal experimentation at our institution for a study with rabbits.

ACKNOWLEDGMENT

AI's research is supported by a Ramón y Cajal fellowship from the Spanish government and a Marie Curie grant (IRG 256376) from the European Commission. LB's research is supported by a scholarship from the UPF.

REFERENCES

[1] M. J. Kane, P. P. Breen, F. Quondamatteo, G. ÓLaighin, "BION microstimulators: A case study in the engineering of an electronic implantable medical device", Med. Eng. Phys., vol. 33, pp. 7-16, 2011.

[2] B. Ziaie, M. D. Nardin, A. R. Coghlan, K. Najafi, "A single-channel implantable microstimulator for functional neuromuscular stimulation", IEEE Trans. Biomed. Eng., vol. 44, pp. 909-920, 1997.

[3] A. Ivorra, "Remote electrical stimulation by means of implanted rectifiers", PLoS ONE, 2011, 6(8): e23456.

[4] A. Ivorra, L. Becerra-Fajardo, "Wireless Microstimulators Based on Electronic Rectification of Epidermically Applied Currents: Safety and Portability Analysis", in Proceedings of the 18th IFESS Annual Conference, ISBN 978-86-7466-462-9, San Sebastián, Spain, June 2013, pp. 213-216.

[5] A. Ivorra, J. Sacristán, A. Baldi, "Injectable Rectifiers as Microdevices for Remote Electrical Stimulation: an Alternative to Inductive Coupling", in World Congress 2012 on Medical Physics and Biomedical Engineering, IFMBE Proceedings, Beijing, China, pp. 1581-1584, May 2012.

[6] L. Becerra-Fajardo, A. Ivorra, "Proof of Concept of a Stimulator Based on AC Current Rectification for Neuroprosthetics", in Libro De Actas XXX CASEIB 2012, San Sebastián, Spain, 2012, pp. p76.

[7] Y. Palti, "Stimulation of muscles and nerves by means of externally applied electrodes", Bull Res Counc Isr Sect E Exp Med., vol. 10, pp. 54-56, 1962.

[8] J. C. Schuder, H. Stoeckle, "The silicon diode as a receiver for electrical stimulation of body organs", Trans. Am. Soc. Artif. Intern. Organs, vol. 10, pp. 366-370, 1964.

[9] S. F. Cogan, "Neural Stimulation and Recording Electrodes", Annu Rev Biomed Eng., vol. 10, pp. 275-309, 2008.

[10] G.M. Lyons, T. Sinkjaer, J.H. Burridge, D.J. Wilcox, "A review of portable FES-based neural orthoses for the correction of drop foot", IEEE Trans Neural Syst Rehabil Eng., vol. 10, pp. 260-279, 2002.

[11] S.Y. Rasskazoff, K.V. Slavin KV, "An update on peripheral nerve stimulation", J Neurosurg Sci., vol. 56, pp.279-285, 2012.

[12] A.R. Sauter et al., "Current threshold for nerve stimulation depends on electrical impedance of the tissue", Anesth Analg., vol. 108, pp. 1338-43, 2009.

[13] P. R. Troyk, "Injectable electronic identification, monitoring, and stimulation systems", Annu Rev Biomed Eng., vol. 1, pp. 177-209, 1999.