Proof of Concept of a Stimulator Based on AC Current Rectification for Neuroprosthetics

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Abstract

For several years, researchers have developed techniques to replace and enhance the capabilities of our neural system by means of implantable electrical stimulation technologies. Even though important work has been done in this field, further progress must be accomplished in terms of miniaturization in order to ensure comfort, simpler surgical implantation procedures, and the capability of using multiple wireless smart stimulators for achieving more muscle recruitment. In the past, with the objective of accomplishing an unprecedented level of miniaturization, we have proposed the development of implantable stimulators that would act as rectifiers of AC current supplied by external electrodes. Here it is described the development and evaluation of an addressable stimulator based on discrete component technology as a proof-of-concept of the proposed method. This macroscopic version of the stimulator is capable of generating magnitude controlled bipolar pulses according to commands modulated in the AC current. Multiple evaluations were done to test the device, including DC current testing, in-vitro and in-vivo testing, concluding that the developed system is an effective proof-of-concept of the method proposed, being able to perform controlled electrical stimulation. Electrical current testing showed that anodal and cathodal currents were generated, and in-vivo testing showed the effective electrical stimulation of an anesthetized earthworm. It is concluded that the idea of developing smart rectifiers as implantable stimulators is feasible. This represents a first step towards the design of an implantable device with a miniaturization level without precedents.

1. Introduction

(Note: the present document was mostly built with shortened excerpts from a thesis dissertation written for the Master's Degree in Biomedical Engineering from the *Universitat de Barcelona*.)

For more than fifty years, different engineering techniques have been developed to replace and enhance the capabilities of our neural system by means of implantable electrical stimulation technologies. Still, the development of really small medical devices is critical to ensure simpler surgical implantation procedures, comfort, and the possibility of using multiple wireless smart stimulators to recruit more muscles in a controlled way.

Several electrical stimulators have been developed, allowing the continuous testing and improvement of powering systems, packaging design and electrode materials and configurations. All these aspects are important in order to achieve implantable medical devices that are able to perform properly and safely within the body. To accomplish small sizes, the techniques used for powering up the system have a key role. Important research has been done, and stimulators such as the commercially available BION have successfully demonstrated inductive coupling and batteries as possible techniques of electrically feeding implantable devices. Even though they have accomplished small sizes, in the implantable medical device field they are still considered bulky.

We proposed in [1] a technique that has the potential to achieve less invasive, safer and more reliable implants with a miniaturization level without precedents. The method implies the use of rectifiers of electric current bursts that flow through the tissues. These rectifiers, built as implantable devices, would transform high frequency AC current into low frequency current for localized electrical stimulation.

In short, innocuous AC currents of more than 100 kHz are generated by means of external electrodes, which are rectified by the implant, obtaining low frequency currents (~10 Hz) in a localized way. These low frequency currents are capable of performing electrical stimulation in excitable tissues of the body.

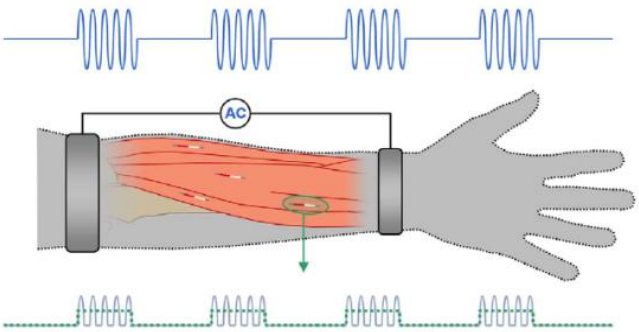

Figure 1. *Illustration of the method proposed in (1) for the use of remote stimulators based on implantable rectifiers. The implanted capsules contain two electrodes (one on each end) and a rectifier. The AC current bursts are applied through external electrodes. Current densities of low frequency capable of stimulating the tissues are generated by the rectifiers.*

In its simplest form, the implanted rectifier consists of a single diode. Such implementation only allows experimental applications, not suitable for clinical practice, due to the fact that there is no control over the stimulation. In addition, neither charge-balanced current waveforms nor enabling/disabling the stimulator would be possible. Therefore, more advanced electronic features are required in order to obtain a smart rectifier that can be used in medical applications.

Here it is described the design of a macroscopic version of an addressable stimulator based on discrete component technology as a proof-of-concept of the proposed method. This design precedes the implementation of an integrated circuit for a miniaturized implantable medical device. A number of electric, *in-vitro* and *in-vivo* tests have been done to determine the behavior of the system while stimulating (e.g. electrode response, stimulation capabilities).

2. Designed System

The developed system consists of three main parts: the circuitry of the implant, the software programmed in the control unit (hereinafter CU) of the implant, and an arbitrary AC signal generator capable of powering the device and create a communication link between the exterior and the interior of the body. In short, these three elements work altogether to accomplish biphasic symmetric charge-balanced current waveforms used for electrical stimulation.

2.1. Implant circuitry

The electronic architecture proposed for the addressable stimulator is based on [2] and is shown in Figure 2. Two internal electrodes are connected to a full wave bridge rectifier (four Schottky diodes model MCL103B-TR by Vishay Semiconductor) and a linear voltage regulator (MCP1802 by Microchip) to power up a microcontroller (ATtiny10 by ATMEL). It enables or disables two current sources made up of NPN transistors (BC817−25LT1 by ON Semiconductor) that modify the amount of low frequency current that flows between the two electrodes. The flow can change its direction depending on the current source enabled. A data signal conditioning subcircuit is included to read, by means of the microcontroller's ADC, the AM modulated information sent in the AC signal; it consists of a RC low-pass filter.

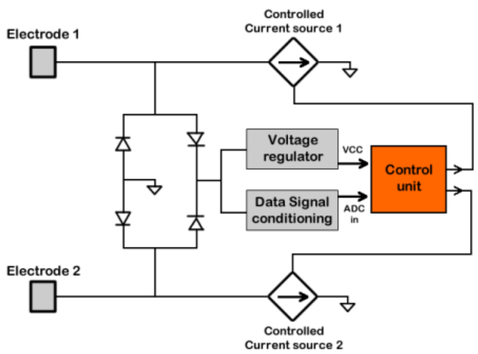

Figure 2. *Electronic architecture proposed for current controlled biphasic symmetric charge-balanced stimulation.*

The implemented circuit consists of SMT components soldered in a single layer PCB. The dimensions of the final version are 4.0 × 4.3 × 0.35 cm. As stated above, this macroscopic SMT version represents a preliminary step towards the development of miniaturized versions suitable for implantation. Figure 3 shows the final appearance of the implemented circuit.

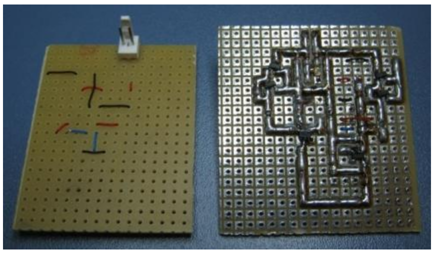

Figure 3. *Pictures of the final version of the circuit. It includes the full wave bridge rectifier, the current sources, the microcontroller and the data signal conditioning subcircuit.*

2.2. External system

As the designed implanted device depends on the input signal generated outside of the body, the external system and the communication protocol are as important as the circuitry and software used for the implant.

The external system is responsible for 1) Providing AC current that flows in the regions where the medical device is implanted, powering up the CU with regulated voltage and supplying high frequency electric current that will be transformed into low frequency current capable of stimulating tissues, and 2) Providing commands that are encoded in the AC current.

The prototype for the external unit consists of a function generator (model AFG3022 by Tektronix) and a voltage amplifier (model WMA-300 by Falco Systems). The system delivers AC currents of 100 kHz as bursts with repetition rates of 20 Hz. The external system is complemented with two electrodes for galvanic coupling with the living tissue.

The communication system used for the device is based on an amplitude modulation scheme. Its purpose is to enable/disable a stimulator when the external system is turned on, accomplishing addressability. A more advanced communication protocol will be used in future versions to ensure more efficiency.

A single burst is composed of two states: high and low amplitudes. The high amplitude is used for the identification and the stimulation phase (which needs the total amount of energy given by the system), while the low amplitude is used for powering the CU and as flag between the identification phase and the stimulation phase. The low amplitudes are set to work in the limit region in which the CU is turned on, but limiting the Joule heating effect in tissues.

During the burst, the high and low amplitude states change to encode information sent from the External System. Four phases are defined: 1) *Start-up time* needed to turn on the CU. 2) *Identification Phase,* which gives information about which stimulator to activate in the stimulation sequence that follows. 3) *Flag* to differentiate between Identification and Stimulation Phases; and 4) *Stimulation Phase*, when the microcontroller enables/disables the current sources in order to generate low frequency current flow between the internal electrodes. This generates local stimulation of tissues. *Figure 4* illustrates this communication protocol.

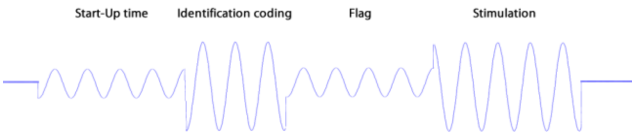

Figure 4. *AC modulated signal used for power and communications. This representation shows a sinusoid waveform. A similarly AM burst is used with square waveform. The timing of the illustration is not represented in scale.*

2.3. Result of the designed system

The use of the galvanic coupling technique in tissue and the high frequency bursts rectification method to power up the CU was effective. The voltage amplifier was able to deliver 48 Vpp to the system, which was distributed in 10 cm of tissue, the distance between the external electrodes when placing them around the tissue. Therefore, the electric field generated was about 4.8 V/cm. The distance between implanted electrodes was approximately 1.23 cm, accomplishing a voltage drop of 5.9 V. The system was able to feed the CU, ensuring the control of the current sources needed for stimulation.

3. Electric testing

3.1. DC current testing

DC current tests were done to analyze the behavior of the circuit, especially if the system had the capability of powering up a CU. This was done using bursts and continuous AC waves. Sine and square waveforms were tested in order to analyze which type of signal would be more efficient for the system due to the fact that square waveforms produce larger averages than sine waveforms.

A sine waveform of 5.9 Vpp, 100 kHz frequency was used. The system was able to generate controlled low frequency anodic and cathodic current flow. The average current obtained when the current sources were disabled is very low, which is understood as the lack of stimulation. When a single current source is enabled, a low frequency current is obtained (either anodal or cathodal). Then the second current mirror is enabled to generate the opposite current direction. This is enough to stimulate tissue.

Using the square waveform, the system was able to stimulate when the current sources were enabled (one after the other). The square waveform had a larger average voltage after rectification, which made it easier to feed the linear regulator used as power source for the CU. Table 1 shows the average currents obtained for each waveform.

Type of waveform	Average Electric current [uA]		
	No stimulation	Anodal current	Cathodal current
Sine waveform	54.4	971.2	-870.3
Square waveform	24.3	726.7	-773.4

Table 1. *Average electric current calculated from the data measured in shunt resistance (5.9 Vpp, 100 kHz). The average was computed after low-pass filtering of the acquired signal.*

3.2. Beta mismatching

As the previous results show differences between anodal and cathodal currents, different computer simulations were run to analyze β mismatching in the current sources. To do so, the NPN transistors' SPICE models were modified, and different simulations were done to see the role of β in the current sources using LTspice IV (LTSpice 4.25I by Linear Technology).

Multiple simulations were made using sine and square waveforms of 5.9 Vpp and 100 kHz. The trials used different combinations of four transistors with β ranging from 140 to 600. When exactly alike transistors were used for the current mirrors with a sine waveform input, anodal and cathodal currents were approximately equal. Differences arose when the input was changed to a square waveform, due to spikes generated in the AC current output when the input signal changes its polarity. These spikes can be diminished from the signal using other types of Schottky diodes, accomplishing a more efficient system, with more similar anodal and cathodal currents, not only for the square waveform, but with the sine waveform.

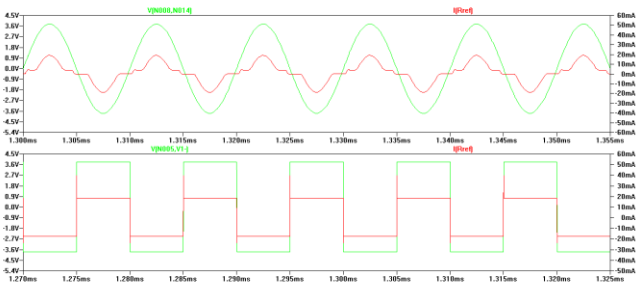

Figure 5. *SPICE simulation of a case of electric current waveform obtained when an anodal stimulation is generated. The sine waveform lacks spikes (upper image), while the square waveform (lower image) includes spikes that affect the low frequency current generated by the current sources.*

For future work it is proposed a microelectronic technique to place the transistors of the current mirrors in the same capsule, preventing the β to differ from one mirror to the other, and accomplishing a more efficient system.

4. *In-vitro* testing

Biological-tissue equivalent phantoms were produced from agar in order to evaluate the effectiveness of the method and the behavior of the implanted electrodes of the proposed system. The phantoms were produced with a mixture of 1.5 grams of agar per 100 mL of a 0.9% solution of NaCl in H_2O.

When a square waveform signal was used as input for the circuit, and the device was enabled for a long period of time (several minutes up to hours), corrosion appeared in one of the electrodes. This is due to the failure to achieve perfect charge-balanced behavior in the system. Nevertheless, it is important to highlight that this defect is not noticed when the device is powered up for a short period of time (e.g. 30 seconds) and that, presumably, will be minimized or cancelled in future versions in which current sources will be better matched.

5. In-vivo testing

Anesthetized earthworms (15 minutes immersion in a 0.2% tap water solution of Chlorobutanol) were used to test the proposed system with simple bursts of AC current. Two types of earthworms were used for the in-vivo testing: Medium and Large Dendrobaena sp. (La Pesca, C/General Castaños 6, Barcelona). The final setup of the in-vivo testing is shown in Figure 6.

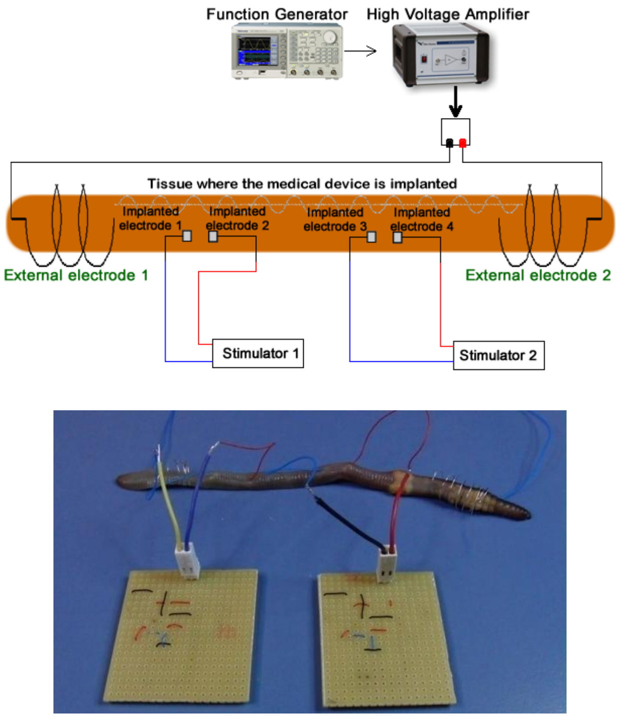

Figure 6. *Final setup for the in-vivo testing using a large dendrobaena earthworm. Illustration of the setup with the architecture proposed for the stimulator (upper image), and the final in-vivo setup (lower image). Two stimulators are used. The external electrodes are separated 10 cm, and the space between the internal electrodes (red and blue wire of each circuit) is 1 cm.*

The distribution of electric field through the tissue agreed to the proposed electric field distribution explained in [1]. Using 48 Vpp in the external electrodes, a 4.8 V voltage drop was measured in the internal electrodes, and this generated 1.8 V to power up the CU and control the current sources responsible for generating low frequency currents for stimulation. A simple burst of high frequency AC current was used to record a video of the stimulation procedure.

No significant change was seen in temperature tests. In addition, when the conditions of the internal electrodes were evaluated, it was noticed that the electrodes could show negative features (e.g. corrosion), only when the process of stimulation had an extremely long duration.

6. Discussion

The macroscopic version of an addressable stimulator is an effective proof-of-concept of the method proposed in [1] which proposes the development of stimulators based on the smart rectification of innocuous high frequency currents flowing through tissues. It has been shown *in-vivo* that the proposed system is able to address two stimulators. The stimulators were capable of generating bipolar currents, and so, minimize electrochemical damage to electrodes and tissues.

The present research is to be continued, improving all the elements of this macroscopic version. Microelectronic techniques will help in the development of more precise current sources and full wave bridge rectifiers and the achievement of miniaturization levels; hardware is to be designed in order to conceive a portable external system, and the communication system must be improved to effectively send information from the exterior of the body to the implant. In addition, the use of flexible and stretchable materials may improve the efficiency of the system, especially for user’s comfort and its use in difficult anatomical applications, such as deep brain stimulation.

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