

RESEARCH

Development of Spinal Cord Stimulator for Chronic Pain Treatment

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Abstract

This paper presents the development of a Spinal Cord Stimulator (SCS) prototype targeted to the treatment of chronic pain. A SCS system is usually comprised of a telemetric transmitter and a implantable stimulation circuit, also referred as implantable pulse generator (IPG). The transmitter acts as an external programmer, sending stimulation parameters such as signal amplitude, frequency, pulse-width and type of waveform to a modulator circuit. The stimulation circuit then applies pulses according to the specified parameters directly into the epidural space of the spinal cord with the help of electrode leads surgically implanted in the mentioned region. We first present a theoretical background on the subject of spinal cord stimulation. Then we present the methods behind our architecture and hardware selection, with a detailed view on each section. Experimental procedures done in our laboratory are also presented as well as our methods of analysis. Finally we analyze the accuracy of our prototype in comparison to commercially available SCS systems and discuss about future hardware and system architecture changes.

Keywords: Chronic Pain; Spinal Cord Stimulation; amplitude; frequency; pulse-width

Introduction

Chronic pain is a persistent type of pain that can negatively affects one's well-being, level of function and quality of life [1]. Although it is hard to define the level of persistence, this type of pathology is often referred as pain lasting greater to 3 from 6 months [2] and it can be provoked by injuries and general damage to the nerves, among other causes [1]. According to [3] approximately 100 million U.S. adults suffer from this disease.

Spinal Cord Stimulation (SCS) is one of the available treatments for neuropathy. The first reported use of SCS happened in the late 1960s, when Dr. Shealy first conducted dorsal column stimulation in a patient suffering from terminal cancer [4]. Its use has increased since then with near 14000 SCS implantations occurring annually world-wide [5]. The stimulation procedure is usually done by placing electrical leads into the midline epidural space of the spinal cord to send mild electrical pulses. As a result the feeling of pain is actually replaced by a better tolerated tingling sensation, also known as paresthesia [6]. These pulses can usually vary according to basic parameters which correspond to the signal's amplitude, pulse-width and frequency

with the last normally ranging from 40 Hz to 125 Hz (50 Hz being the most commonly used) [6].

Compared to conventional medical management (CMM) alone, which is normally the administration of analgesic drugs [7], SCS improves pain relief, quality of life, functional capacity and patient satisfaction in selected patients with neuropathic pain. However, as SCS stimulators are invasive implanted devices, surgical infections and other complications can happen [7].

Recently, SCS has become increasingly successful in the long term due to refined patient selection criteria, greater accuracy in electrode placement, and improvements in multipolar and multichannel systems [4].

In our studies we found little references with respect to the impedance of the region where SCS devices stimulates. Author [8] states this value can significantly change with respect to the electrode lead position in the dorsoventral region. The impedance of the stimulated region greatly affects the stimulator battery but, according to the same author, it has not been extensively studied. Great impedance variations can also reduce the quantity of current coming out from the electrode leads, therefore reducing the levels of *paresthesia* in the patient [9]. Hence we seek to develop a SCS system which can measure impedance values while stimulating. This feature will give a specialized doctor the information about how adequately the electrode is inserted and if there is any malfunction on the lead or the pulse generator. Also, we propose a fairly simple way to modulate bipolar quadratic pulses with adjustable frequency, pulse-width and amplitude, which is the main purpose of a implantable pulse generator.

Theoretical Background

Spinal cord stimulation technique is based on the gate control theory of pain, first presented by Melzack and Wall in 1965 [10]. Also based of Melzack and Wall's gate theory, small nervous fibers are responsible for transmitting pain signals into the nervous system by opening the *gate* in the dorsal column of the spinal cord. Stimulation of larger nervous fibers, on the other hand, can actually close the gate on small fibers, and thus blocking pain signals. In other words, the SCS principle is basically to stimulate a region with larger fibers (the epidural space of the dorsal column) in order to stop the pain signal transmission arriving from the smaller fibers [10].

Even by knowing the working principle of SCS, there are still much to be defined about the stimulation itself, such as the place and type of lead to be used, signal amplitude, frequency, pulse-width and waveform and even components of a SCS system and its biocompatibility with the human body. These topics are discussed here in a brief manner we can provide reader with a detailed view on the aspects behind the spinal cord stimulation field.

Physiology behind Spinal Cord Stimulation

The two main parts of the nervous system are central nervous system(CNS) and the peripheral nervous system(PNS). CNS is responsible for the functions of the body and mind as intelligence, memory, learning and emotion. Thus PNS deliveries sensory information to the CNS and is responsible to carry motor commands to peripheral tissues [11].

The spinal belongs to CNS and is surrounded by 30 bone *rings*. These rings are called vertebra and the bones compose the spinal column. Each vertebra is named according to the region of the spinal cord they lie [11].

To understand SCS is very important to comprehend the anatomy of the spinal cord. Dealing with a superficial way, the cervical vertebra are located in the region of the neck and are represented as C-1 to C-8. The vertebra below cervical vertebra are the thoracic vertebra, they lie at the high of the chest, where the ribs are connected and are called T-1 to T-12. Down from thoracic vertebra and above the pelvis are the lumbar vertebra, represented by L-1 to L-5 and lastly stands the sacral vertebra, from the pelvis to the end of the spinal column, that is represented by S-1 to S-5 [11].

During the last three decades Spinal cord stimulation has become indispensable for treating certain chronic pain cases. This stimulation arose from the gate-control theory, used in segmental pain suppression [10]. The idea behind SCS is to apply electric stimulation to the dorsal columns of the spinal cord, because of the large diameter afferent fibers [12]. Linderoth also applied then the electrodes epidurally to the dorsal aspect of the cord [12], as showed in Figure 1.

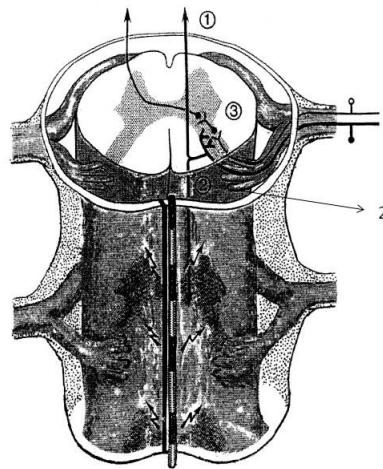


Figure 1: The Classical Theory for pain inhibition by SCS [12].

With the help of figure 1, [12] explains the SCS used for pain inhibition. From the dorsal columns spreads current that is applied onto the dorsal dura. This current activates fibers in dorsal with two types of transmission of impulses: orthodromic, showed in Figure 1 as (1), and antidromic, showed as (2) in Figure 1. The responsible for paraesthesia felt by the patient is the orthodromic activity. The antidromic impulses are transmitted via dorsal column fiber collaterals to the dorsal hippocampus below the cathode(s). At this point, they excite neurons activating the gate mechanism, showed as (3), and then they inhibit the transmission in the small diameter fiber systems subserving pain [12].

By gate control theory, it is possible to assert that the activation of the coarse fiber systems interrupt or inhibit transmission of nociceptive information and predict all types of pain would be suppressed [12].

Types of Spinal Cord Stimulation

There are several biomedical companies that commercialize implantable spinal cord stimulation devices [13]. While some can differ on minor details like frequency, pulse-width and waveform, most of these devices can perform voltage and current stimulation under different *stimulation programs*. These program will vary the modulation aspects previously cited.

Voltage and Current Driven SCS

Electrical modulated signals can be supplied to the patient's spinal cord by a constant voltage or current power source. Despite the fact that most SCS devices can stimulate by voltage and by current, there are studies made with patients who use SCS implantable devices in order to determine which one is more effective. Studies made by [14] and [15] tested constant-voltage (CV) and constant-current (CC) stimulation on patients with implantable SCS devices, alternating groups which initially started their treatment with CV to CC and vice-versa. The results from these three researches concluded that more than 70% of these patients preferred CC stimulation for reasons such as coverage of the painful area, achievement of lower-levels of pain and even increase in the quality of life.

Signal Amplitude, Frequency and Pulse-Width and Waveform

To achieve the most beneficial pain relief for an individual patient, spinal cord stimulation parameters like the configuration of active electrodes, the stimulation frequency, pulse width and pulse amplitude of the signal can be adjusted to the patient's needs. The electrical stimulation of the large-diameter fibers in the dorsal column elicits tingling sensations (paresthesia) in most patients [16].

According to [17], the most often used frequencies of SCS in the clinic are around 50 Hz, but in general they can vary between 30 and 120 Hz. There are also new types of stimulation paradigms for SCS that use high frequency stimulation up to 10 kHz [17], but here will be treated the traditional SCS. Tests made by [17] used a pulse width of 1ms and amplitude was set at 90 % of the paresthesia threshold. They obtained an average reduction of 37% of pain in a Visual Analogue Scale score, that is a method to measure levels of pain. When a increase at the stimulation amplitude is applied, then mostly the intensity of the perceived paresthesia increases and the covered body area enlarges, because an increased number of dorsal column fibers is recruited [17].

In neurostimulation the pulse amplitude and width relate directly to the depolarization of the cell membrane and are therefore critical parameters for determining the locus of excited tissue [18].

To determine the best pulse width and amplitude for each subject [19] made a study based in select a pulse width range with eleven values of width: 50, 100, 200, 300, 400, 500, 600, 700, 800, 900, and 1000 μ s. They randomized pulse width testing order for each subject to minimize potential sequence bias. They held constant both anode-catode combination and stimulation frequency for each subject

throughout the experiment. For each pulse width configuration, they used the following protocol: stimulation was turned off and the pulse width was programmed at zero amplitude. To obtain an accurate measure of perception threshold, they used a modified ‘method of limits’ technique: They increased the amplitude slowly from zero mA until the subject reported first perception of paresthesia and then they recorded this amplitude. Stimulation amplitude was decreased slowly until the subject reported a complete loss of paresthesia and they recorded this value. The amplitude was then increased until first perception and that was also recorded. Then, they asked the subject to paint all areas of paresthesia on the human figure with the stylus on the tablet PC. Stimulation amplitude was then increased from perception threshold until the subject reported discomfort and that amplitude was recorded as the discomfort threshold (M). Immediately, the amplitude was decreased until the subject reported that it was at a maximum comfortable level (M-). At M- the subject was given the tablet to draw the extent of paresthesia on the human figure on the tablet PC. The amplitude was returned to zero and the next pulse width was programmed. They paused the stimulation for approximately 1 minute between pulse width settings. After the subjects tested all the pulse width, they could choose a favorite pulse width value between the tested values to be used in their stimulator. They found also a maximum comfortable stimulation amplitude, that was fixed at 90% of the usage range for all subjects. Across all subjects, the favorite pulse width was set from $350\mu\text{s}$ (240–470) to $400\mu\text{s}$ (240–525). Still, subjects who chose a new pulse width obtained an increase in paresthesia pain overlap of 56% (14 – 89%), from 27% (23 – 60%) to 48% (41 – 81%). The median amplitude found was 2.5mA (1.3–3.3 mA) [19].

Pulse generators are most typically used to stimulate active tissues electrically. Normally, pulse waveforms are used. This is because they are easily generated and substantially efficient at depolarizing nerves and muscles [19]. But usually in SCS, pulse amplitude is more relevant for the stimulation control [19]. [20] have shown that quadratic pulses are the most commonly waveform used in SCS.

Evaluating Load Parameters

As it was already discussed, SCS systems do stimulate, whether by voltage or current, specific regions into the epidural space in the spinal cord. Knowing the impedance between the placed electrodes is crucial to assure the efficiency of both stimulation as the amount the amount of current and voltage (for CV and CC, respectively) vary with the change of the impedance. This principle is actually based on Ohm’s Law, where the voltage between electrodes is equal to the product between the current which flows from one pole to the other and the electrical path impedance. One other way to state Ohm’s law is to say that the current which flows from one pole to the other is equal to the voltage between them multiplied by its impedance. Both Equations are shown in (1) and (2):

$$V(I) = Z \cdot I \quad (1)$$

$$I(V) = \frac{V}{Z} \quad (2)$$

Knowing the load impedance in a circuit is very important for power consumption efficiency. According to Thevenin's Maximum power transfer, the load impedance for maximum power transfer has to be of same value as the Thevenin's equivalent circuit impedance Z_{th} (is impedances are considered pure resistive). For this reason the need of impedance matching is considered for the development of any circuit connected to a load. However, most studies which actually measure spinal cord impedance range do it for refractory angina stimulation, which is made more towards the cervical region than the lower-thoracic one, this being more targeted for chronic pain treatment [21].

Authors [8], in their study on impedance variations in the spinal cord for both cervical and low-thoracic areas, explicit that the load impedance greatly affects the modulator battery life and that this impedance (spinal cord impedance) varies mostly with respect to the position of electrode arrays. According to their trial tests measuring the impedance on patients stimulated by common quadripole array electrodes, the lowest levels of impedance can be encountered when stimulating the cervical regions of the spinal cord (C3-C7) and highest values are from the lower-thoracic stimulation (T7-T12).Also, according to the same authors, there is a negative correlation between the load impedance and the number of days since the surgical placement of the stimulator. The measured values for the lower-thoracic were of $547 \pm 151 \Omega$ found by [8].

Biocompatibility and Electrical Insulation

There are many design features that must be considered in SCS and a important one is biocompatibility of the implanted device and electrodes. The durability of the implant is also a fundamental parameter to be determined [22].From a clinical point of view is not easy to get access to autologous donor material and the immunological problems associated with allograft rejection have led to a search for artificial biomaterials [11].

Since its discovery as biomaterials, membranes natural rubber, has been the subject from several studies, and its physical properties, microarchitectural and biocompatibility initially determined models animals, lying currently undergoing use in humans [23]. Such materials proved to be the foundation for an innovative biomaterial with excellent results in the healing of chronic ulcers of the esophagus, and in reconstitution and drilled tympani, observing neovascularization evident around the prosthesis and diabetes foot, showing the possibility of tissue neoformation, and the biocompatibility of the natural latex (*Hevea Brasiliensis*) in the form of esophageal prosthesis was investigated and observed, with no signs of allergic manifestation [24].

The use of synthetic materials for replacement or increase of biological tissues, has always been a concern in the medical and dental areas. To this end, various devices are manufactured from metals, ceramics, polymers and more recently composites. In fact, new materials are not always in the strict meaning of the word, are materials of which use new properties obtained by different chemical compositions and fabrication processes. The success of a material used as a biomaterial in medical devices, beyond the biocompatibility and other characteristics cited above, is related to to the facility and capacity of the material to be molded into tricky

formats. Usually the requirements of biomaterials can be grouped into four main categories: biocompatibility, ability to be sterilized, functionality and reliability.

The use of materials and implant bioengineers is the third generation of biomaterials. This field, there are few examples in the market because many are under development. Illustrate this step the tissue implants to regenerate tissue, and not simply replace it, as artificial skin (Integra® Life Science), cartilage regeneration of joints (Carticel®, Genzyme Co.), the reabsorbíveis bone cements, the genetically modified biological components (such as cells or bone morphogenetic protein - BMP2) associated with ceramic calcium phosphate, collagen or hydrogels, titanium surfaces with nanometric coverings of calcium phosphate ceramics and three-dimensional structures phosphate ceramics cell associated calcium.

With regard to the material designed to provide biocompatibility to the proposed system, we defined some essential features: presenting biocompatible physical and chemical characteristics, have low antigenicity and impermeable and flexible. Thus, it is chosen as the raw material extracted from natural latex rubber *Hevea brasiliensis*.

Studies indicate that a great problem about obtaining stable intracortical recordings is the tissue reaction of the CNS against implanted electrodes [25].

Cells of CNS react to implanted materials, also called foreign body. The main cell related to brain tissue is the neuron. The location and processes of the neuro soma are determinant to the quality of the electrical signal [25].

As reported by [25], there is very little consensus about the optimal manner to implant recording electrodes. The approaches differ on the speed, method and depth of electrode insertion. [25] also noted that many studies have associated biologically induced electrode failure to the initial trauma of implantation, thus experimenters implanted electrodes with different speeds. They report that groups have found that a high velocity approach (8.3 m/s) minimizes tissue damage [25].

[26] recommend covering homogeneously electronic modules and transitions to the cables and electrodes with parylene C in a plasma-deposition polymerization process. Hence, should be ensured the electrical insulation, high chemical resistance with respect to biostability, and biocompatibility.

Hardware Description

Based on developed devices from [27],[28] and [29], a Spinal Cord Stimulation System is basically composed of:

1 Neuromodulators or Stimulators

From a bottom-up perspective the neuromodulator is the device responsible for stimulating the patient's spinal cord. According to [9] who describes general stimulators architectures, neuromodulators are comprised of:

- (a) Power Management: Responsible for delivering power to the entire neuromodulator circuit and even controlling its consumption.
- (b) Transceiver: Wireless communication device responsible for capturing stimulation parameters such as current amplitude, frequency and pulse-width from the external programmer.
- (c) Digital Controller: This device acts as the stimulator coordinator, receiving data from the transceiver and power from the power management block and controlling the stimulating through the stimulation front-end.

- (d) Stimulation Front-End: It is the interface between the Digital Controller and the electrode leads. Usually responsible from converting voltage signals into their current equivalent and vice-versa.

2 Electrodes

As previously mentioned, SCS electrodes (commonly referred as leads) are surgically implanted in the epidural space of the spinal cord. The best contact position for the electrode is usually selected through empirical tests, as stated by [20]. The author affirms that the same empirical approach has led to the design of multi-contact electrodes. This statement is reinforced by the Internal Neuromodulation Society, which asserts that even two, three or four electrode leads can be inserted in the epidural space, one may having up to 16 electrical contacts [30].

SCS electrodes also vary with respect to their polarity. According to [13] an active electrode can be a positive *anode* or a negative *cathode*. Electrical current flows from the cathode to the anode and its direction varies according to the number of anodes [30]. Monopolar stimulation is omnidirectional and less spatially efficient, but it can stimulate a specific spot with greater amount of current when compared to multi polar types of stimulations. These last (bipolar, tripolar and quadpolar), however, can stimulate a highly specific volume of tissue and are able to spread potential current gradient to other regions where there is no physical connection to the electrode [13].

Electrode polarity and geometric position on the epidural space also affects the threshold voltage for paresthesia. Author [20] developed an extensive study on these regards using a SCS computer model from the University of Twente. The model simulates not only a three-dimensional volume conductor model of the spinal cord, but also models of myelinated nerve fibers. Results from the author showed that bipolar and tripolar stimulation by a single electrode, symmetrically placed over the dorsal columns, give the widest paresthesia level.

Electrode displacement and internal breakage can be undesired issues, common problem in many early SCS randomized controlled trials and case series [30]. Electrode migration can result in the change of impedance between electrode contacts, causing greater power consumption from the SCS device and even current saturation [9]. Electrodes can also distance themselves from their contact region with the spinal cord, which also would inflict in a significant increase in the impedance between electrodes [8].

A very important consideration about electrodes for Spinal Cord Stimulation is the electrode-electrolyte interface. Author [31] states that when a metal (in this case the electric contact of an electrode lead) is immersed in an electrolyte a potential is set up between both. This phenomenon is commonly referred as a *double-layer*. As reported by [9], two types of reaction can take place in the electrode-electrolyte interface: *faradaic* and *non-faradaic* reactions. *Faradaic* reactions are the ones wherein there is actual across the interface, while *non-faradaic* reactions are the kind where there is no electrode-electrolyte charge-transfer due to a capacitive effect on the electrode. According to the author, unlike *non-faradaic*, which are solely capacitive, *faradaic* reactions can in some

cases be considered as irreversible reaction, resulting a net change of the environment chemistry that can alter the electrolyte pH and therefore damage the surrounding tissues. Another requirement from electrode stimulation is that all the charge injected from an electrode be recovered afterwards, known as *charge balancing*.

3 External Programmers

These devices are responsible for sending stimulation parameters (amplitude, frequency, pulse-width) to the neuromodulator circuit. They can also charge this circuit if the SCS device is rechargeable, such as in [27]. It is very common for commercial devices to have two types of external programmers, one designed for patient's use and one specifically made for the use of a specialized doctor.

Methods

The Spinal Cord Stimulation device to be build here, if seen from a top-down perspective, is comprised of two main devices: an external programmer (EP) and a stimulation circuit (SC). The external programmer, like previously mentioned, is the device where the user can configure stimulation parameters such as waveform, frequency, pulse-width and others. The stimulation circuit, on the other hand, is an implantable device which receives these data through wireless communication and stimulates the targeted region of the spinal cord with the use of electrode leads.

External Programmer

Our external programmer prototype has a software interface that requires the following parameters from the user:

- 1 Type: Choices are between Constant Voltage (CV) or Constant Current (CC) stimulation
- 2 Signal Amplitude: The amplitude of the voltage or current signal waveform.
- 3 Frequency: The frequency of the modulated pulse.
- 4 Pulse-Width (also referred as Duty-cycle): The signal pulse-width, which is the time period wherein the signal remains active when in it period.
- 5 Total time of stimulation: It can be for specific periods or non-stop.

Once these parameters are defined, the user has to press an initiate button so these data can be wirelessly sent to the stimulation circuit. Also, voltage and current parameters from the front-end of stimulation circuit back to external programmer. The values are shown onto a Display, so the user can see the value and respective variation of the load impedance as stimulations goes on.

Regarding its components, the external programmer is basically comprised of a microprocessor integrated with a wireless transceiver and a LCD display. It also features a very basic functions keyboard for stimulation configuring.

Stimulation Circuit

The stimulation circuit (SC) receives data coming from the external programmer (this circuit also has a wireless transceiver). Once signal amplitude, frequency and pulse-width parameters are received, the stimulation begins. Whether by voltage or current, these signals will be sent to the stimulation front-end, where they will be then delivered to the electrodes.

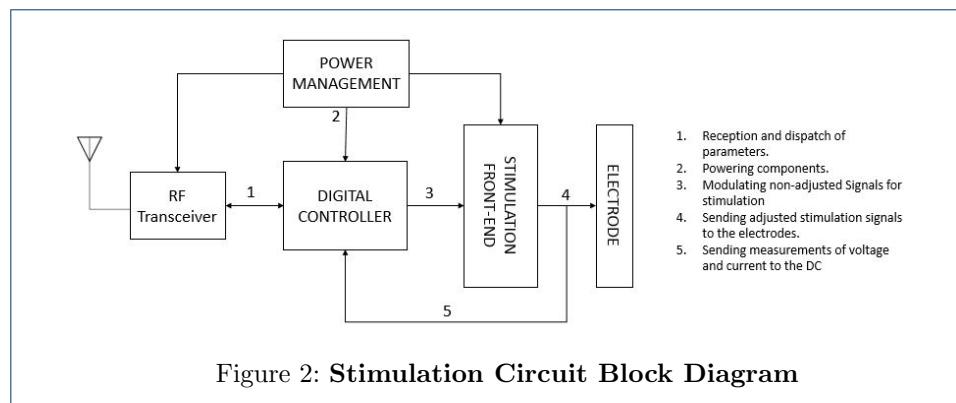


Figure 2: **Stimulation Circuit Block Diagram**

Power Management

The stimulation circuit is composed of devices with different voltage supplies and power consumption. Hence the power management delivers power to all these devices in different voltages and current specifications, respectively. Among others, the power management features a battery, DC-DC converters and voltage regulators.

DC-DC converters are responsible for converting higher voltages into lower and vice-versa. In this particular case, the voltage supplied by the battery (V_{batt}) will be converted into the lower-voltage levels and then supplied to the previously mentioned devices in the power management block.

Supplying and maintaining an highly accurate voltage is quite crucial for this system as it can potentially avoid systematic errors that discrepancies between the desired stimulation current or voltage and the actual one that is delivered to the electrodes.

Transceiver

The communication between the external programmer and the stimulation circuit is bidirectional. In one way the external programmer sends the formerly cited stimulation parameters to the SC whereas the SC sends back parameters such as voltage and current being applied to the spinal cord tissue and the amount of power being consumed by the SC circuit. For such tasks, a wireless transceiver is used. Its main purpose is to establish this two-way communication between the EP and the SC.

Digital Controller (DC)

The digital controller of this SC will be executed by microprocessor. It will be responsible for modulating the signal pulses, controlling the total time of stimulation and registering the values of voltage and current on the stimulation front-end output. Additionally, the microprocessor software disposes of a specific Interrupt Service Routine just in case of new stimulation parameters arrival. In this case, the SC stops the stimulation for very brief period of time in which new stimulations are being passed on from the external programmer. The stimulation ranges for signal amplitude are:

Parameters	CV	CC
Amplitude	0 to $10.5\text{ V} \pm 0.05\text{ V}$	0 to $25.5\text{ mA} \pm 0.1\text{ mA}$
Frequency	10 to $250\text{ Hz} \pm 5\text{ Hz}$	30 to $250\text{ Hz} \pm 5\text{ Hz}$
Pulse-Width	60 to $450\text{ }\mu\text{s} \pm 10\text{ }\mu\text{s}$	60 to $450\text{ }\mu\text{s} \pm 10\text{ }\mu\text{s}$

Table 1: Stimulation Ranges

We chose these values in order to implement a system that can work under similar parameter values as commercialy available SCS devices [32].

In order to keep track of the stimulation circuit power consumption, the digital controller is integrated with the power management section. Thus it can gather power consumption data and the quantity of battery still left to be used.

Stimulation Front-End

The stimulation front-end is the interface between the digital controller and the electrodes. It is responsible for adjust the stimulation signal which comes from

the DC so it can properly stimulate the spinal cord tissue when directed to the electrodes.

The stimulation front-end comprises two types of stimulation: Constant Voltage and Constant Current. For each one of them there is an specific circuit topology. A demultiplexer is used to direct the signal coming out from the digital controller to its right path, whether it is the CV adaption circuit or the CC one.

Even though the digital controller is able to modulate pulses in terms of frequency and pulse-width (duty-cycle), it is not able to change the signal's in an analogue level. Hence a Digital-to-Analog (DAC) converter is used. The DAC receives from the microprocessor the desired digital signal amplitude and outputs the equivalent analogue value. This value is then filtered by a Low-pass filter so high-frequency noise is reduced. After this procedure the signal is in its right amplitude, frequency and pulse width and ready to be directed to the CV or CC circuit.

As the signal which comes out from the low-pass filter is in voltage form and also is the CV stimulation, little needs to be done. Thus, the CV adaptation circuit is mostly comprised of a current-limiting switch (for safety reasons) which will not only limit the amount of current that goes throughout the electrode but also to prevent current flowing in the opposite direction. To amplify the signal amplitude, a Voltage-Controlled Voltage Source is the used as the final component of the CV circuit. This type of circuit can increase the input voltage V by a gain A_v , yielding the output voltage V_o as shown in equation (3). A simplified model of a VCVS circuit can be seen in Figure 3. Also, negative feedback may be used to adapt the output terminals impedance as desired.

$$V_o = A_v \cdot V \quad (3)$$

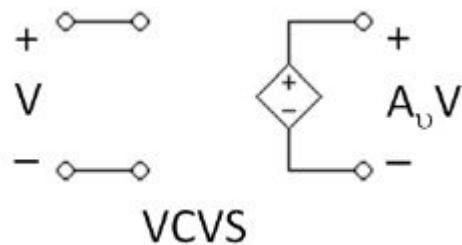


Figure 3: Voltage-Controlled Voltage Source

However, stimulating with CC requires a more complex component, a Voltage-Controlled Current Source (VCCS) or transconductance amplifier. It receives the voltage signal V at input, which also comes out from the low-pass filter, and reproduces the equivalent current signal at the output increased by a gain A_g (see equation (4)). The output impedance of the VCCS circuit can also vary using negative feedback. Figure 4 is the equivalent model for the VCCS topology)

$$I_o = A_g \cdot V \quad (4)$$

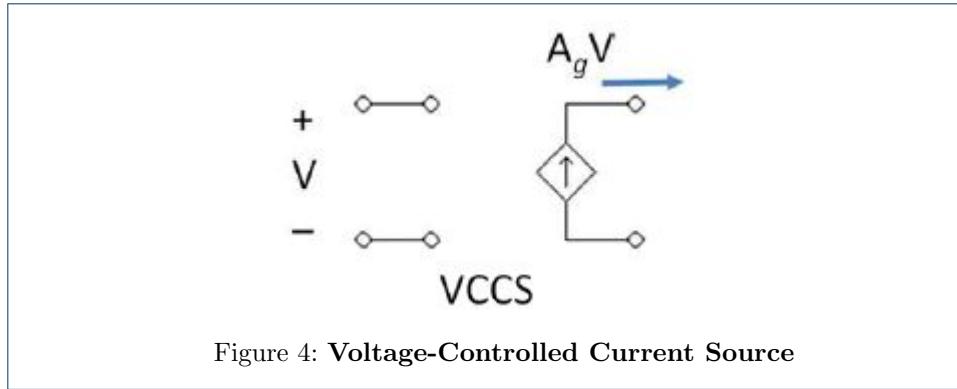


Figure 4: Voltage-Controlled Current Source

The last element of the stimulation front-end intercalates pulses between the electrode cathode and anode contacts. This way a bipolar stimulation can be done. To perform this signal transition between the electrode poles, a switching circuit was implemented. This way the signals on the electrodes poles will always have a 180 degrees phase difference between each other.

Electrodes

The electrodes have not yet been implemented in this system. Instead, all stimulation tests will be made with similar resistance value resistors. Hence, 5% accuracy resistors are being used to evaluate the stimulation signal response with respect to impedance changes. Similarly to the procedure used in [17], we will use a resistor to simulate the lead used for transmitting the pulses from the stimulation circuit to the electrodes. This lead resistor will be in series other resistors simulating the electrode and epidural contact impedances. Although not ideal, this type of simulation will assure our system reliability and will allow us to verify its accuracy.

Development so far

We decided to implement the system gradually, first focusing on choosing devices that could simulate the external programmer and the stimulation circuit. For that we elected the EZ430-RF2500 development kit as the ideal for building the system (See Figure 5). The kit contains two USB-programmable target boards with the microprocessor MSP430F2274 and the wireless RF transceiver CC2500, not mentioning 12 General purpose Inputs/Outputs (GPIOs) and highly integrated and ultra low-power architecture [33].

We used one of the target boards to simulate the working principle of an external programmer. Then, using a terminal emulator in a personal computer and plugging the target board onto the PC, we were able to send the stimulation signal amplitude, frequency and duty-cycle parameters to the other target board, in which the stimulator circuit prototype was implemented. We reckon that commercial devices use pulse-width in time units instead but we used the duty-cycle parameter instead just to ease the evaluation of our results.

The other target board from the EZ430 kit was programmed to receive those three stimulation parameters. The signal amplitude directed to a Digital-to-Analog converters. A code was implemented for the microprocessor to modulate quadratic pulses with the frequency and duty-cycle values received from the external programmer. This signal is proper in terms of frequency and duty-cycle but it is not

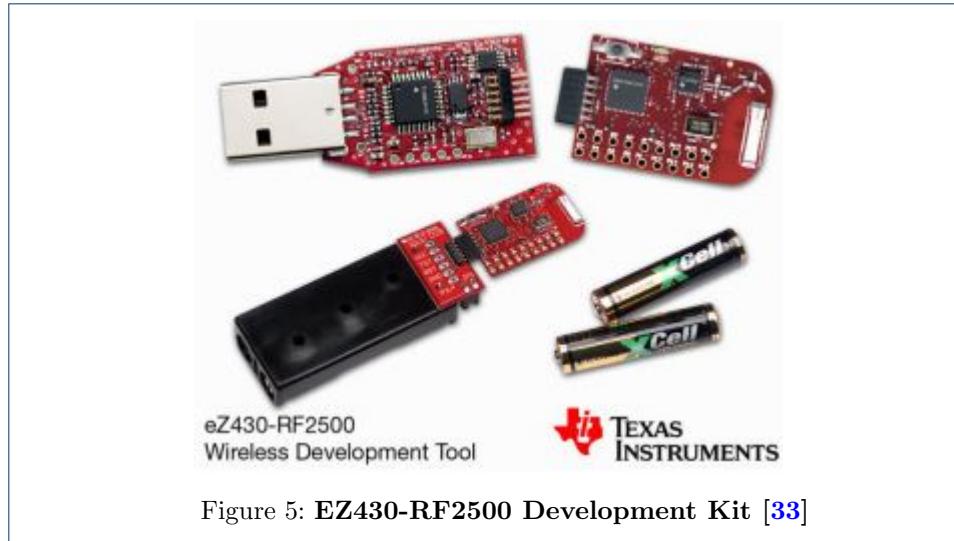


Figure 5: **EZ430-RF2500 Development Kit** [33]

necessarily in the right amplitude. To adequate the signal to its right amplitude, we used a BJT NPN transistor in switching mode to act as an amplitude modulator for this signal. Figure 6 illustrates the working principle of this amplitude modulation circuit. When the modulating signal is at its high value (3.6V for the MSP430F2274), there is current flowing into the transistor base and hence there is also current flowing from V_{dac} to the ground, meaning that V_{out} is at its lower level (almost 0 volts). When the pulse is at its low-level (almost 0 volts as well) there is no base-base current in the transistor and consequently no collector-current. As there is no current flowing to the collector terminal in the transistor the output voltage V_{out} will have the same value as V_{dac} . Thus this configuration acts as an amplitude modulation for the modulating signal which comes from the microprocessor.

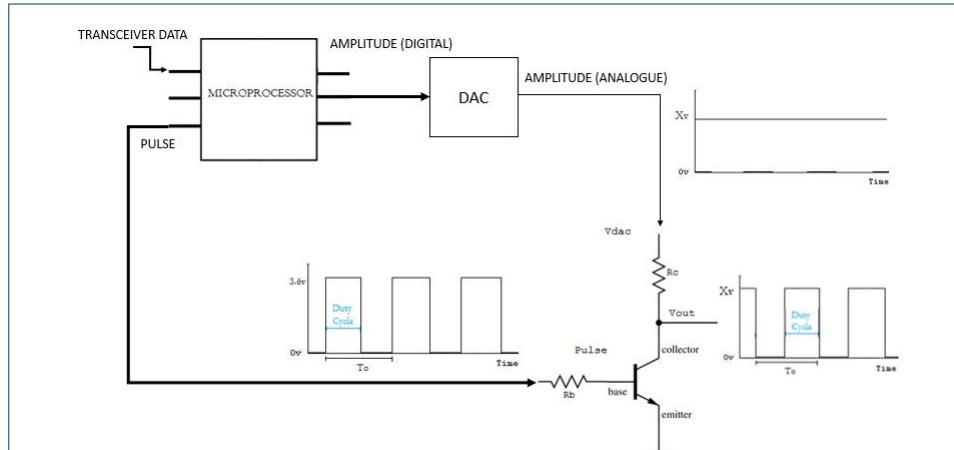


Figure 6: **Working principle of the Amplitude Modulating Transistor**

There are several additions to be made to this prototype but summarily this system we developed has an external programmer which can successfully receive all information required and transmit it to a stimulation circuit. Even though our

stimulation circuit is still far from what we desire, it can modulate quadratic voltage pulses with adjustable amplitude, frequency and duty-cycle.

We will continue to develop the system maintaining its original main scopes but with some few alterations. The first one is to add different stimulation signal waveforms for both increasing the device robustness and for the potential study of patient's reaction to new waveforms in SCS devices. We will also port all the developed software made for the MSP430 to an *ATMEGA 168/V* family one. Furthermore we will also use the RF Module NRF24L01+ instead of the CC2500. It is an RF modulating device with carrier frequency of 2,4 GHz as well but with lower-power and it features an auto package-retransmission model, apart from the fact that it can be used with the *Atmega* model and it allow us to use a stand-alone version (no development kit, just the microprocessor and peripheral circuits).

Experimental procedures

To simulate our stimulator circuit we used Multisim 12.0. The simulated circuit is showed in figure 7. We utilized a function generator (XFG1) to simulate the pulses we needed, that in the neurostimulator will be given by the microprocessor. The pulses amplitude stands between 0V and 3.6V, which is the voltage provided by the microprocessor. We used a switch (S2) to represent the digital voltage output desired, that will be also given by the microprocessor. Therefore, the voltage value given by S2 will also vary between 0V and 3.6V. The digital output is then connected to a digital-analog converter(U1), that uses a positive reference voltage of 3.6V and a negative reference voltage of 0V. By using an oscilloscope, represented by XSC1 in the simulation, we measured the voltage value obtained at the Collector terminal of the transistor (V_o) and the pulse amplitude of XFG1. The transistor (Q2) have a function of switching. The resistance value of R2 was the greatest value available we had.

To assemble and test the circuit, we used the pulses generated by the microprocessor to control V_o , and measured that with an oscilloscope.

We can find the error, or discrepancy, between the DAC voltage and output voltage by using equation(5).

$$Error(\%) = \frac{|VDAC - V_o|}{VDAC} 100\% \quad (5)$$

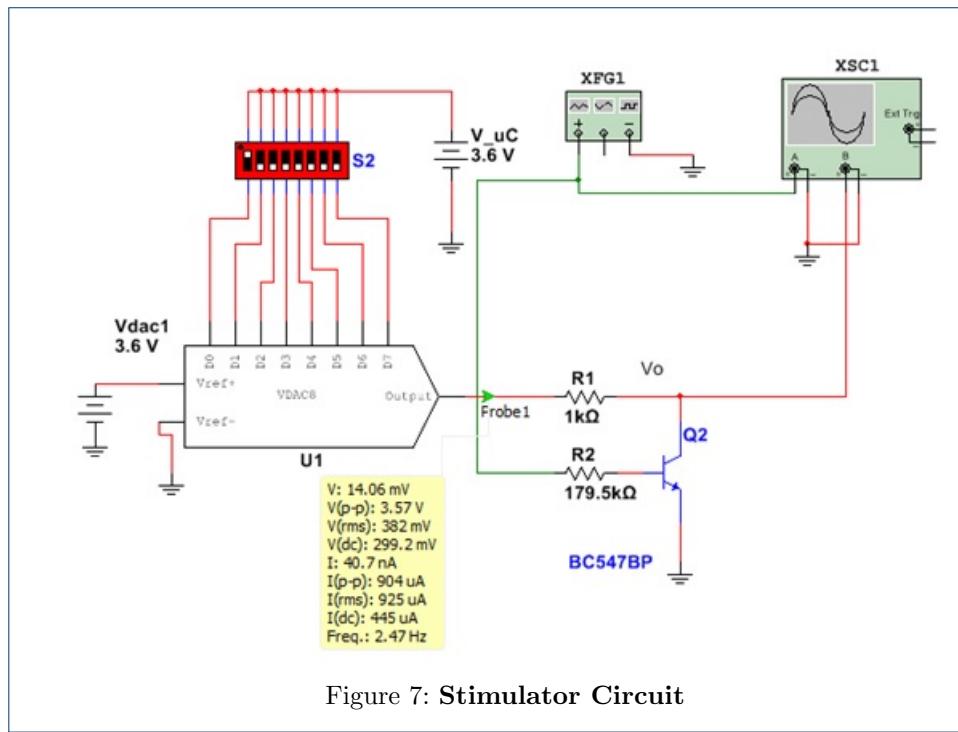


Figure 7: Stimulator Circuit

Preliminary Results and Discussion

As previously said, our initial development was to use two EZ430-RF2500 target boards and make one send stimulation parameters so the other could modulate quadratic pulses accordingly. Hence developing a communication software was our first endeavor. Using the communication protocol implemented by Texas Instruments known as SimpliciTI and using the terminal emulator *RealTerm* we designed a program for external programmer target board that requires amplitude (in Volts), frequency (Hz) and duty-cycle (%) and sends the data to the other target board, which modulates the pulses. The result of this software implementation can be observed in figure 8, in which two terminal emulators are shown, one interfaced with the external programmer and the other with the modulator. In one terminal we insert some example data for amplitude, frequency and duty-cycle. When entered, these values can almost instantaneously be seen in the other terminal, meaning that the stimulator target board has successfully received the parameters.

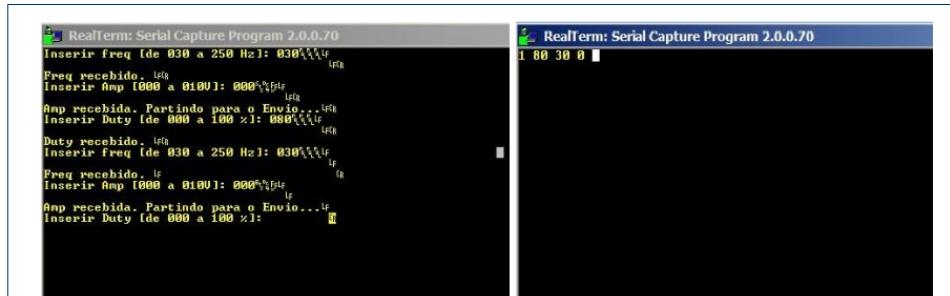


Figure 8: Images from both targets terminals

To modulate the quadratic pulses we also implemented a code for the stimulation target board that receives the parameters of frequency and duty-cycle and modulate theses pulse as desired. Unfortunately the amplitude was not used due to malfunction in the digital-to-analog converter, which is soon to be corrected.

The voltage value given by the DAC and the output voltage we reached in simulation are showed in the table 2 as Vdac and Vo, respectively. This table shows also the error value between both the measures, that we found by using equation(5) and represents the discrepancy between the measured values.

Vdac (Volts)	Vo (Volts)	Error (%)
3,586	3,586	0,000
1,786	1,786	0,000
0,886	0,886	0,000
0,436	0,436	0,000
0,211	0,211	0,000
0,098	0,099	0,102
0,042	0,042	0,000
0,014	0,015	2,837

Table 2: Obtained Values of Vdac, Vo and Error

It is important to reach a minimal value for the error, to guarantee a system with accuracy, mainly because this system will be implanted and must maintain patient safety.

Conclusion

With defined parameters of stimulation, SCS has been used efficiently to treat chronic pain [4].

This paper presents a study of concepts related literature encompassing the design theme, such as biomaterials, chronic pain, devices for treating chronic pain, electrodes. The main focus of this study was to characterize the device that we are proposing as an alternative to currently available systems.

The device we proposed will be used in order to satisfy the need of pain relief, with stimulation parameters as frequency, pulse-width and pulse amplitude well defined liable to changes according to the needs and pain levels. The parameters run with good precision and accuracy.

For future works, we would like to implement the entire stimulation circuit using stand-alone microprocessor, voltage converters and amplifiers, hence making it more robust and accurate. By using a feedback approach and replacing BJT transistors with CMOS components we also expect to improve the system's precision, impedance matching and consequently power consumption. The best of way of simulating impedance variations will be evaluated in order to test our stimulator circuit under a more realistic scenario.

Conducting a study that develops a neurostimulator is a challenging task, and previous research has showed that contributions have been added to this study. However, spinal cord stimulation still is a complex study as it is a field of study composed by both medical and engineering areas, merged for the sake of achieving patients pain relief. In a more general perspective, we believe that it is an endeavor of anyone who is entering the field of biomedical engineering to extensively study concepts regarding both mentioned areas as they are critical for successfully developing for one's studies.

Competing interests

The authors declare that they have no competing interests.

Author's contributions

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