THE BRAIN CLOSED-LOOP STIMULATION METHOD WITH THE BIOPOTENTIAL MEDIATION OF THE SUBTHALAMIC NUCLEUS FOR THE PARKINSON'S DISEASE THERAPY

Radu BĂZĂVAN[1]

Closed-loop stimulation is an advanced method compared to current version of deep brain stimulation therapy utilized for the patient's suppression of the neurological motor deficiencies. The new method approach in this paper eliminates the encountered difficulties by using the current medicine open-loop procedure. Hence, closed-loop stimulation method, operates independent and auto-adaptive.

Keywords: close-loop stimulation, deep brain stimulation, electric stimulation, biopotential

1. Introduction

The scientific aim of the paper establishes a different approach of the Deep Brain Stimulation (DBS) characterized as an open-loop function, used in clinical practice. The current purpose of the DBS procedure has an efficient therapeutic reduction of the motor deficiencies triggered by Parkinson's disease and/or Essential Tremor [1-3]. The lack of a cure of the Parkinson's disease has psychic effects on a patient. Nevertheless, its disease symptoms are initially alleviated by a drug therapy. The recommended drug therapy and procedural law allocated to the motor disabilities is initially effective [4-6], but consistently applied in time becomes less effective.

For the patients identified with an advanced stage of Parkinson's disease and a different medical reaction from the expected one during the prescribed drug therapy, the neurosurgical intervention is applied after establishing patient’s neuronal profile.

The therapeutic electrical DBS tehnique is similar to the one of implantable cardiac pacemaker. Hence, DBS defines a conceptual need of an assigned excitatory signal transmission up to the neural tissue appointed throughout patient’s anamnesis. The electrical stimulation signal is applied by a single implanted macroelectrode or an array of microelectrodes implanted in the designated cerebral target point [7-9] named Subthalamic Nucleus (STN) or Globus Pallidus Interna (GPI). The electrical connection of the signal generator to

[1]PhD student, Medical Engineering Researcher, Bucharest, Romania, e-mail: radu.bzv@gmail.com

the electrodes is made using an electrical wire extension. The wire extension path [10] is set from the patient's STN/GPI tissue to his subclavian area (e.g. the subclavian zone is the place of the stimulatory signal generator).

2. Outcome of open loop DBS

The DBS devices are produced by a single international producer. The open-loop operational system, depicted in Fig. 1, represents a limitation of the DBS method. .

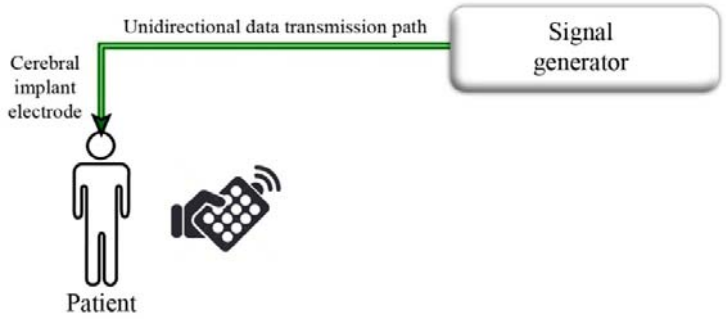


Fig. 1. Functional diagram of the open loop stimulator.

The current medical system used for the open-loop cerebral stimulation consists of [11-13]:

- A set of cerebral implantable bipolar or quadripolar electrodes:
  - one bipolar or quadripolar electrode for the unilateral stimulation;
  - two bipolar or quadripolar electrodes for bilateral stimulation;
- Signal generator:
  - default signal with the characteristics ranges pre-established by the electrophysiology physician;
  - possibility of changing the signal parameters by the patient on the set range;
- Remote control used by the patient in order to change the stimulation signal parameters.

Because of the many physical and behavioral changes in status of the patient during 24 hours, the DBS open-loop device activity along it's motor disease symptoms suppression, score a provisional and descending rank during the therapy. That is because changes of the patient's physical body content (e.g. water content, minerals, proteins, etc.), behaviors (e.g. active, calm, etc.), and the psychic state (e.g. quiet, agitated, anxious, etc.) modifies the motor deficiencies symptoms. Thus, the Parkinson's disease symptoms exhibit either a pregnant or a

temperate event. Therefore, the actual open-loop DBS system used in the medical therapies is marked with an inconsistency of the motor deficiencies suppression during the day [14-16].

The open-loop DBS supplies a constantly and permanently recognizable pattern that can produce:

- electrical stimulation with a high amplitude voltage when the patient has reduced symptoms up to a total absence;
- electrical stimulation applied with a low voltage signal characteristics to the high motor deficiencies symptomatic events;
- electrical stimulation of the cerebral target point with a very high amplitude voltage, thus producing a neural tissue trauma.

The open-loop DBSmethod, offers the possibility of adjusting the electric parameters of the stimulation signal (e.g. voltage, pattern), using a remote control that radio-communicates with the signal generator. Nevertheless, the patient's control over the implanted device is limited, and allowed only if the neurophysician preliminary accepts this possibility. Moreover, the manufacturer must include this remote control option into the product capabilities. Therefore, the patient have the option to change the parameters of the stimulation signal, but only by the physician prescribed recommendations which are furthermore set to the device's functional ranges. Consequently, the patient is forced to interact with the implanted system's control interface in order to improve the quality of life, thus the DBS functional procedure during the therapy becomes complex.

3. Proposed Method

In the Closed-Loop Stimulation (CLS) system the subthalamic nucleus is monitored as a response of the previous stimulation. Therefore, the CLS concept requires multiple activities necessary to be simultaneously performed, Fig. 2.

An a priori cerebral signal recording after electrical stimulation facilitates the adaptation of the future electrical stimulation signal parameters. Thus, post-stimulation medical therapeutic activities can constantly and continuously eliminate the neuronal motor deficiencies by a real-time operation [14-16].

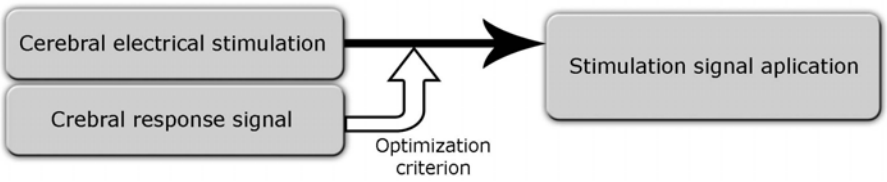


Fig. 2. STN signal recording .

The adaptive stimulation signal generation by the received brain response totally suppresses the neuromotor deficiencies symptoms of the patient. Therefore the optimized values of the electrical signal sent to brain by the implant electrodes are permanently adjusted by patient's neurodynamic status. Compared to the open-loop method, the proposed method provides the following benefits [14-16]:

- an increased efficiency to the motor signals neuromodulation and a stable operation, adjusting stimulation parameters correlated to cerebral signal response;
- an increased protection to cerebral tissue anti-trauma during stimulation;
- elimination of the patient interaction with implanted stimulator system;
- a reduced power consumption of the stimulation system, thus an extended battery power autonomy.

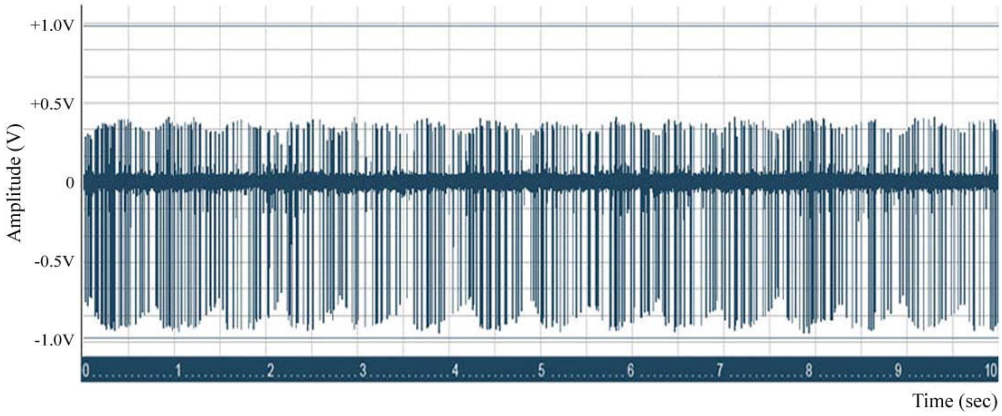


Fig. 3. STN signal recorded with a 2000 amplification factor.

The collected waveform, Fig. 3, exhibits an original 50 ... 500 μV, 1 ÷ 1500 Hz frequency of the carrier signal and its amplitude modulated with the 3 ÷ 7 Hz oscillation associated with the parkinsonian tremor.

The recorded response is transmitted to the generator through an adaptive signal parameters named *signal transformer*. The purpose of the signal transformer is to average the STN biopotential. Thus, precisely quantifies the energy over the alternating signal flexions in order to optimize the motor deficiencies suppression. The adapted parameters of the signal transformer are the voltage, frequency and amplitude modulation of the generated stimulation signal. The CLS principle is depicted in Fig. 4 [14-16].

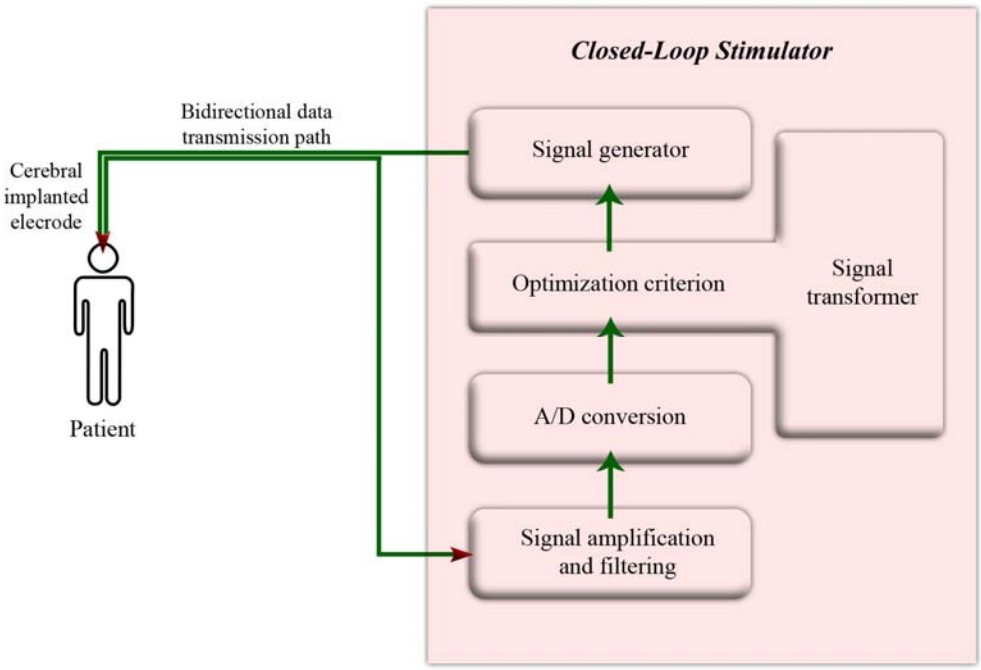


Fig. 4. Block diagram of the closed-loop stimulator.

Compared to conventional DBS open-loop process, the signal generator of the proposed CLS system operates along an adaptive process, using the following values of the parameters, obtained via experimental tests on patients:[14-16]:

- Square pulse signal type;
- Voltage, U = 0 ÷ 10V (0,5 ÷ 1,5V usual process values);
- square pulse duration, d = 60 ÷ 450 μs;

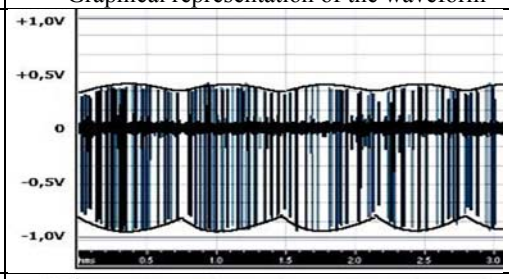
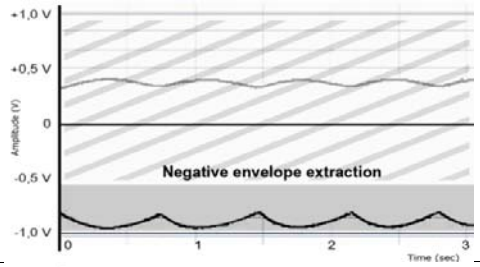
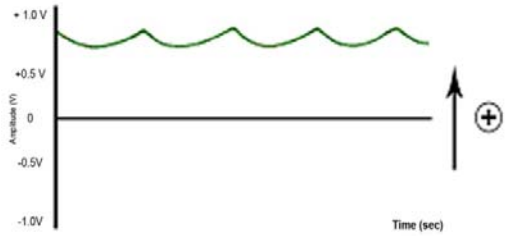
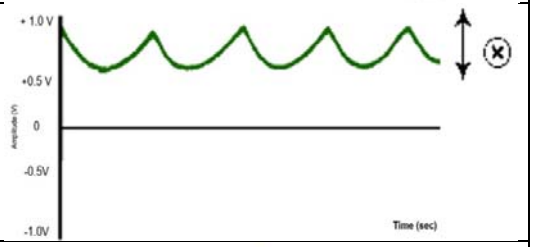
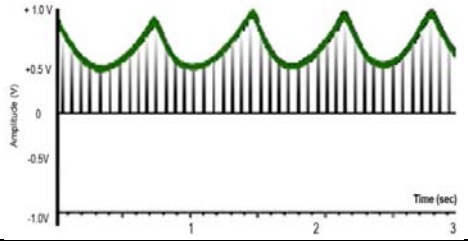
  (60 ÷ 120 μs are the usual process values); (1)
- Square pulse frequency, f = 30 ÷ 225 Hz

  (130 ÷ 160 Hz are the usual process values);
- Antiphase amplitude modulation of the square signal, with the negative envelope phase of the recorded signal.

The optimization criterion forces the readjustment of the new stimulating signal according to data collected by brain response signal [14-16], Table 1.

Table 1

Operating principle of the optimization criterion

No.	Transformation activity	Graphical representation of the waveform
1	STN signal collected from a patient who has motor deficiencies: • sinusoidal carrier signal: 1 - 1500 Hz; • amplitude modulation with 3 - 7 Hz sinusoidal signal.	
2	Envelope detection of the STN gathered signal.	
3	Voltage augmentation of the row no. 2 waveform, by a voltage constant addition (i.e. additional voltage factor).	
4	Vertical extent of the sinusoidal waveform by multiplying its voltage values with a constant.	
5	Amplitude modulation with the table row no. 4 waveform toward the square pulse generated signal with (1) characteristics.	

4. Results of the Novel Method

Closed-loop electrical stimulation applied to the neurocerebral tissue through an equivalent electronic scheme [17-25] of STN area, Fig. 5, transfers a square signal to the device output along the following features:

- Square pulse frequency 133 Hz
- Square pulse duration 120 μs (2)
- Additional voltage factor 0.67 V
- Voltage amplitude limit max 2 V
- Generated square signal is real-time amplitude modulated by the negative envelope of the gathered response signal.

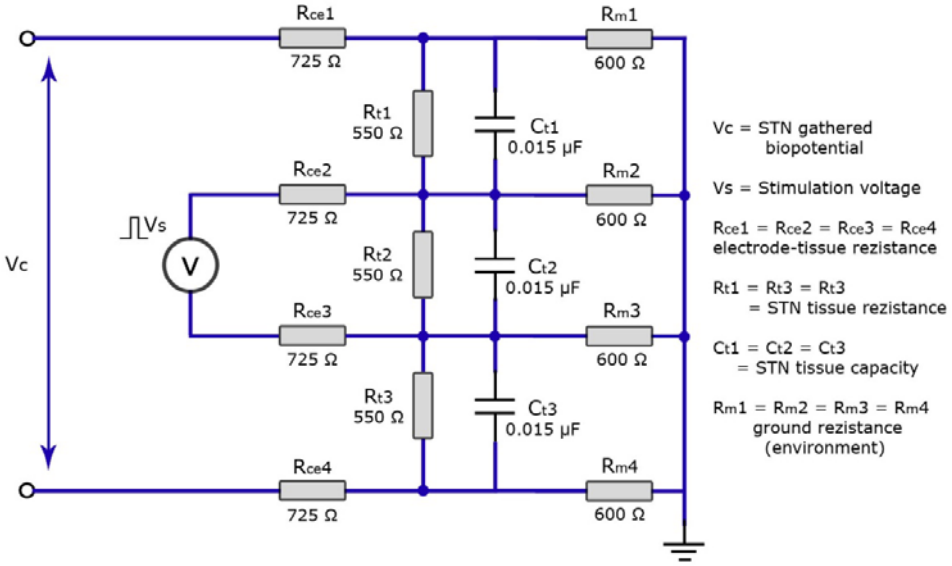


Fig. 5. Equivalent electronic circuit of STN tissue with its implanted macroelectrodes

The approach of this paper regarding the proposed CLS method is depicted in Fig. 6 and Fig. 7 the advantage of a stimulator signal auto-adaptation, and the low voltage of 1,5 V reached after a 15 seconds period of activity.

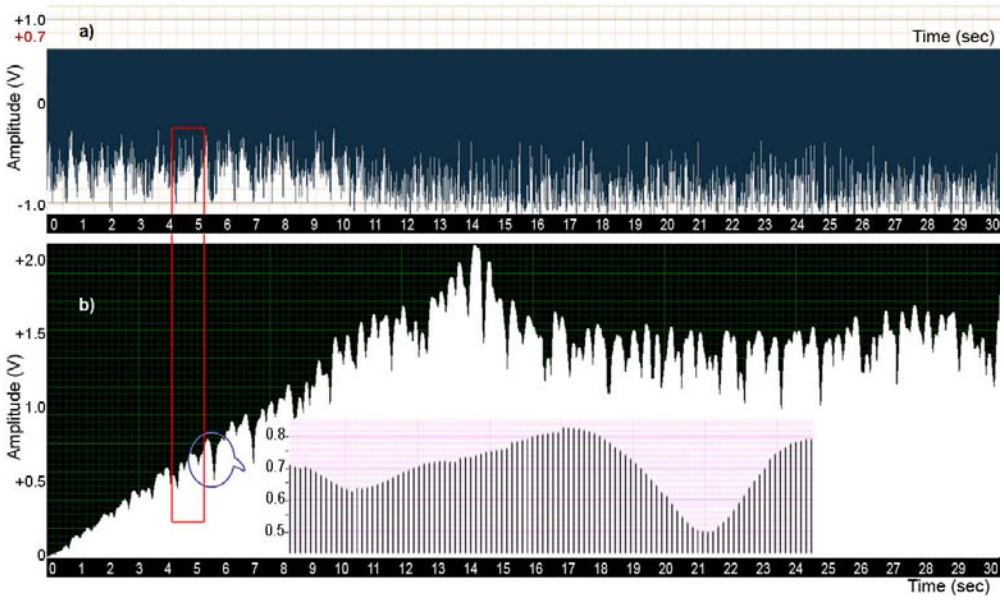


Fig. 6. STN target location:
a) signal recorded as a response to subthalamic stimulation.
b) stimulating pulse signal.

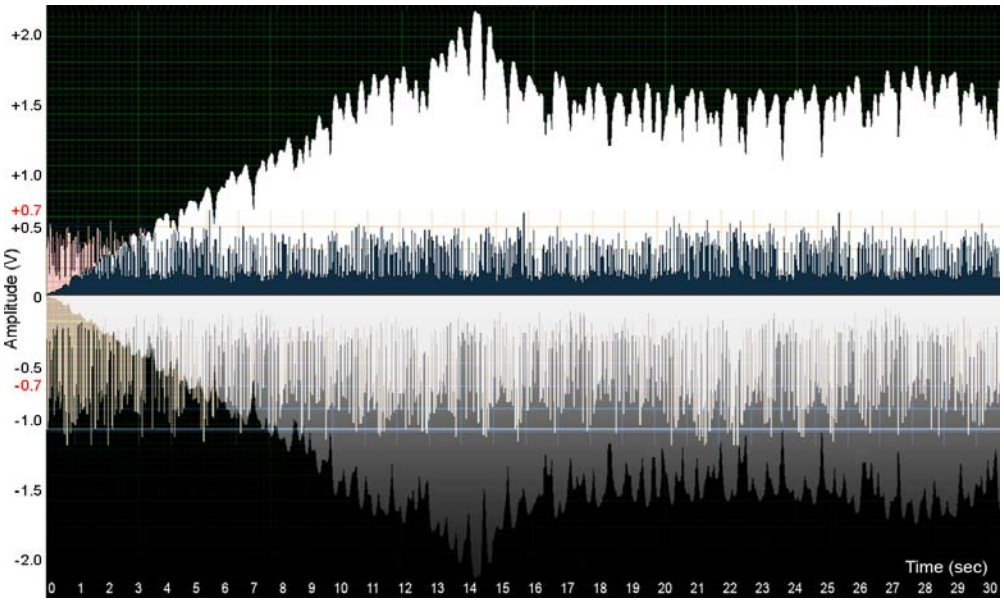


Fig. 7. STN target location: STN recorded signal without a stimulation, overlapped to the generated square signal.

Fig. 7 exposes two different signals overlapped, representing a graphical interpretation of the practical CLS system activity. The upper signal represents the STN recorded signal, and the lower waveform represents the mirrored stimulator signal.

The therapy performed with a CLS method is made with an equivalent electronic scheme of the STN tissue is depicted in Fig. 5. The CLS simulation indicates a much smaller need of an admissive energy to the tissue, and a permanent suitable waveform tilled in Fig. 8a that follows the proposed CLS method.

As a comparison to proposed CLS method, the contemporary DBS method is depicted in Fig. 8b a signal characterized by a constant voltage amplitude and instantaneous power[2].

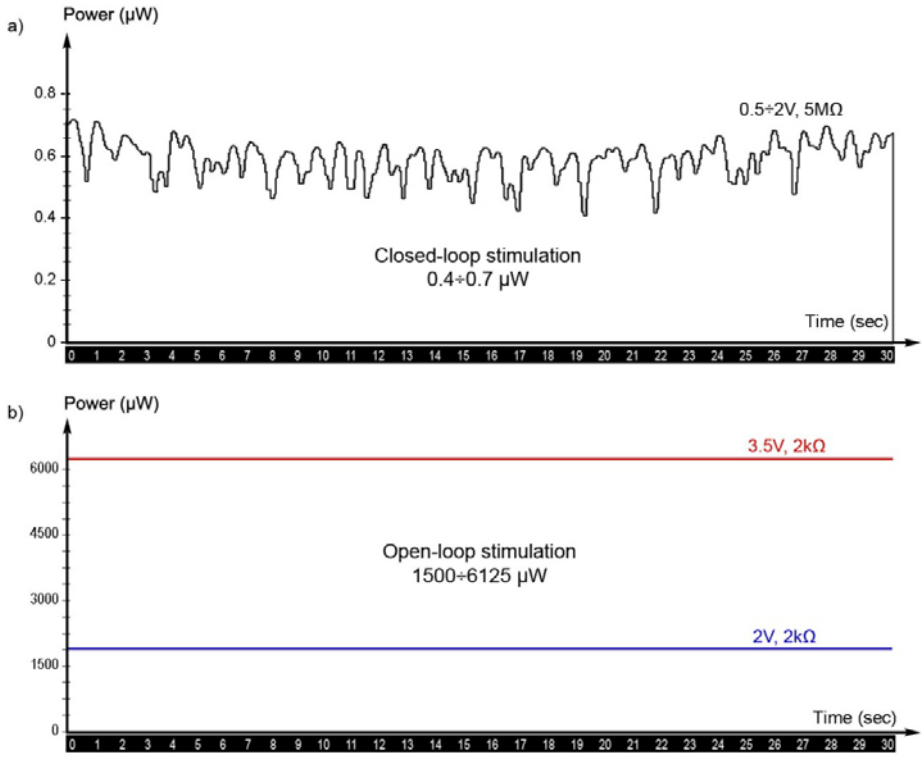


Fig. 8. STN target location:
a) Instantaneous power energy applied by CLS method in a stable period of cerebral stimulation.
b) Constant instantaneous power energy applied by the classical DBS method.

[2] DBS characteristic set is listed by the system manufacturer in its device operation manual.

5. Conclusions

Eliminate the patient's need for interaction with the implanted device – The adaptive functioning of CLS to subthalamic tissue eliminates the patient need to adjust manualy the system parameters.

Low and stable signal energy emission – The applied signal to the subthalamic tissue has at least half low voltage amplitude against the contemporary method used. Furthermore, this low voltage signal applied to the subthalamic area protects the neuronal tissue subjected to electrical stimulation.

A reduced sensitivity of the recorded signel against the stimulation artifacts – The CLS method makes the CLS process maximum tolerable to stimulation artifacts due the strictly positive voltage stimulation supply against a negative voltage responce signal intake.

Extended battery power autonomy – The electrical power supply of the CLS system upholds a low voltage signal generation in order to mediate the STN tissue biopotential. Thus, the functional autonomy of the proposed device is extended up to 3 times compared to open-loop devices used in current medicine.

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