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Closed-loop control of nervous response

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1. BACKGROUND

Therapies available for pain treatment remain little effective for certain forms of chronic pain (neuropathic, dysfunctional) and are accompanied by numerous undesirable effects. As a consequence, there are growing interests in alternative stimulation techniques, such as transcutaneous electrical neurostimulation (TENS), transcranial magnetic stimulation, or transcranial direct current stimulation. Although these techniques are recognized as effective in the non-pharmacological treatment of pain, there is a need to improve their effectiveness by enhancing them with a self-regulating capacity for personalized and adaptable treatment. The present work introduces a method to maintain the excitability state of a nervous system using information control theory. As a preliminary approach, we used a rat sciatic nerve as biological model, associated with a device that handles the stimulation of the nerve, the acquisition of the nerve response and the control process based on the analysis of the Compound Action Potential (CAP). The efficiency of the regulation process is then assessed by applying an anesthetic droplet on the nerve.

2. METHODS

Nerve preparation: a sciatic nerve was excised from a adult rat and placed in a sealed chamber between a pair of stimulation electrode and a pair of recording electrodes (fig 1.a), and preserved a room temperature above a saline solution layer to prevent drying.

Nerve stimulation: an electrical impulse is applied on one end of the nerve using an extension board for Raspberry (Gertboard), with full control on the amplitude (from 0.2V to 2,048V) and duration (100µs to 600µs).

Electrophysiological response: following the electrical stimulation, the nerve produces the expected Compound Action Potential (CAP), (fig 1.b). CAP is captured using a USB oscilloscope (Bitscope®) and signal is sent to the Raspberry for processing.

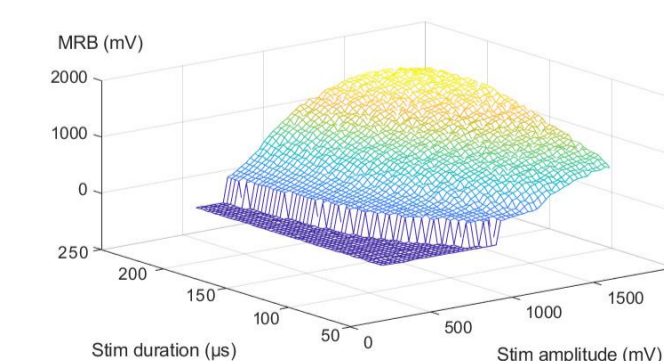
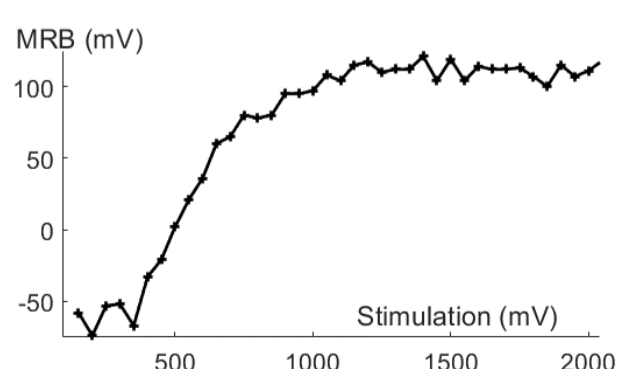
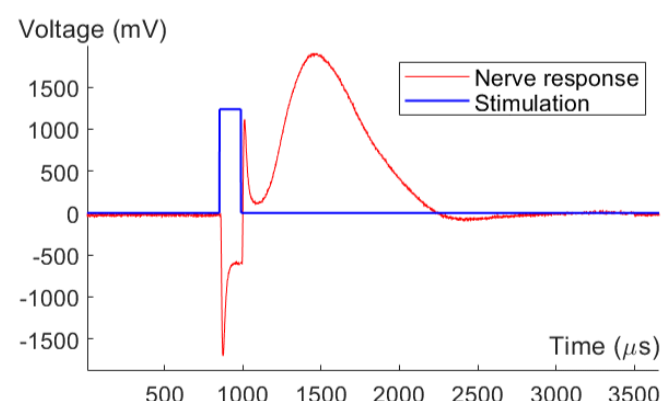
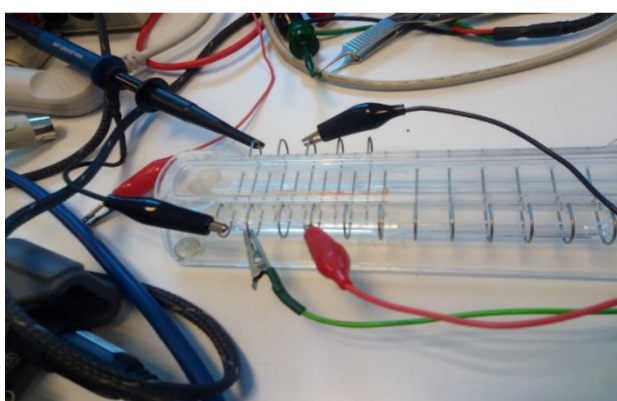


Figure 1: a) a sciatic nerve in the sealed chamber, with stimulation and acquisition electrodes. b) Compound Action Potential (CAP) recorded after electrical stimulation. c) Cap amplitude versus stimulation amplitude. d) Full cartography of CAP amplitude versus stimulation amplitude and duration

CAP processing: maximum response from baseline (MRB) was calculated from the CAP using a raspberry PI 3B+, we verified that the nerve exhibited the expected variation with stimulation amplitude (fig 1.c), and we built a complete cartography of response from stimulation amplitude and duration (fig 1.d).

Control process: following each stimulation, CAP amplitude was compared to setpoint (66% of max amplitude from cartography), and error was corrected using a proportional integral controller to generate the command. Stimulation amplitude was then updated for the next iteration (fig 2). Stimulation was done every 1second (1Hz)

Perturbation: once the nerve exhibited steady CAP, we applied a drop of Lidocaine to initiate progressive fiber shutdown.

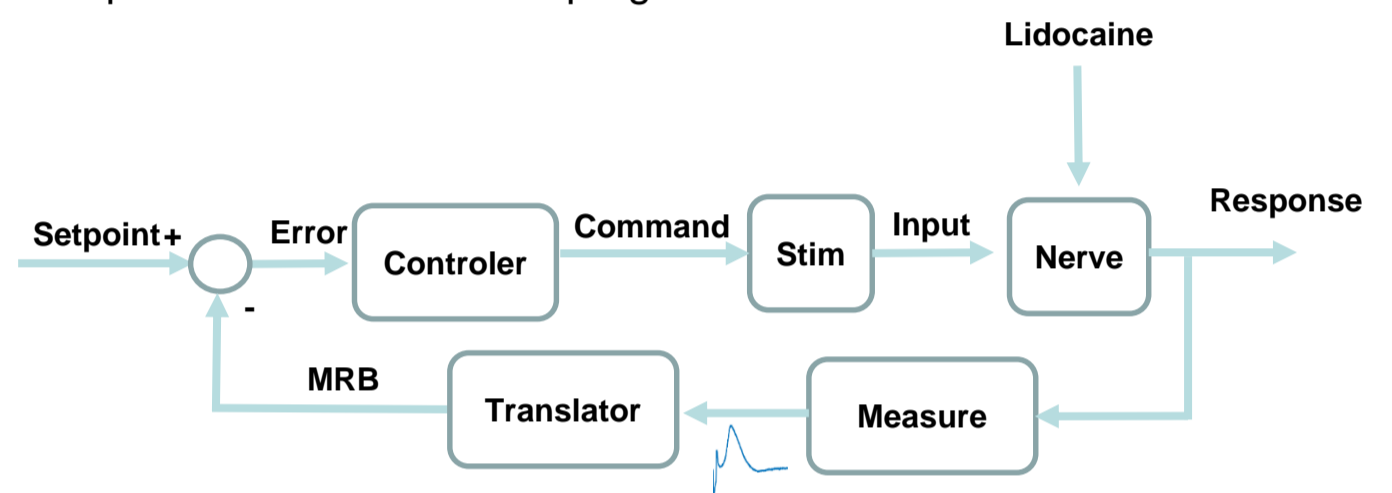


Figure 2: closed loop control process of the nerve response. The loop is done once every stimulation

3. RESULTS

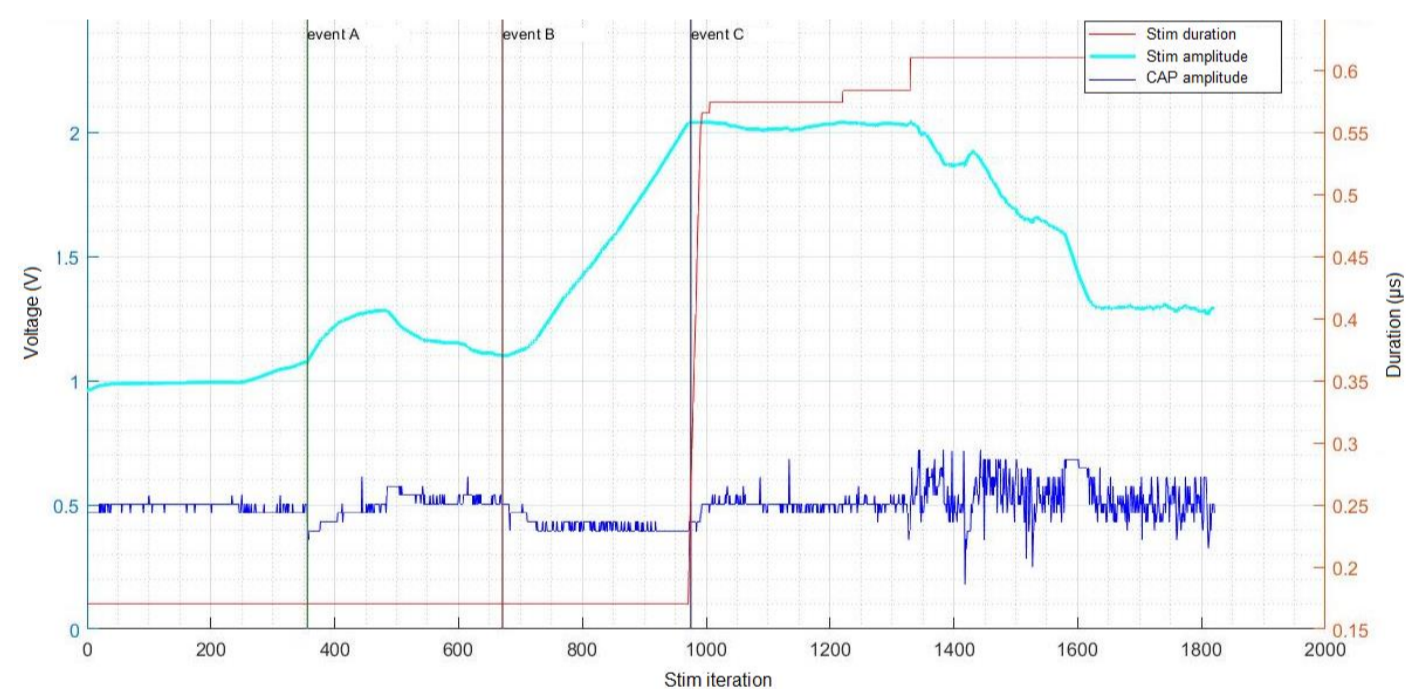


Figure 3: time course of CAP amplitude (dark blue in V), stimulation amplitude (light blue in V), and stimulation duration (red in µs), with lidocaine being applied in event A and event B, and control strategy switching from amplitude to duration in event C when maximum stimulation amplitude was reached

The closed loop successfully recovered CAP amplitude following a small drop after first (fig 3, event A) lidocaine deposit, by increasing stimulation amplitude. After second deposit (fig 3, event B), fibers exhibited massive shutdown, with continuous increase of stimulation amplitude to maintain CAP. Once maximum stimulation amplitude was reached, control switched to duration increase to further recover CAP amplitude (fig 3, event C), until complete shutdown of the nerve.

4. CONCLUSIONS

Our results proved that the excitability state of a nervous system could be closed loop controlled. Future works will enlarge the experimental scale and investigate more complex characterization of CAP using linear algebra.