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Design and Testing of a Closed-Loop Neurochemical Modulator

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***Abstract*— Here we show the initial design of a USB-powered, low-cost device for closed-loop neurochemical modulation (CLNM). The device monitors neurochemical levels and can activate delivery of external stimuli. With the goal of designing a long-term in vivo neuromodulation device, CLNM can acquire fast scan cyclic voltammetry, as well as conduct electrochemical impedance spectroscopy to monitor electrode state.**

***Clinical Relevance*— The specificity and efficacy of neuromodulation systems can improve by closed-loop devices using neurotransmitters to inform therapeutic intervention.**

I. INTRODUCTION

Neurotransmission controls brain function and disease, but traditional neuromodulation platforms can only interact with the brain electrically. Novel closed-loop (CL) systems seek to monitor neurotransmitter (NT) concentration and use it as a biomarker to inform intervention [1]. Fast-scan cyclic voltammetry (FSCV) with carbon fiber microelectrodes (CFMEs) can monitor NTs *in vivo* and in real time, but increases in CFME impedance due to biofouling can degrade FSCV accuracy [2]. Even so, many state-of-art CL neurochemical platforms do not have electrochemical impedance spectroscopy (EIS) capability to determine the electrode stability. Hence, CLNM, a closed-loop device for real-time NT monitoring via FCSV equipped with EIS measurement capabilities.

II. METHODS

The basic architecture of CLNM consists of a microcontroller unit, ADucM355, and an operational amplifier, OPA4192 (Fig. 1A). The AduCM355 has a high-speed DAC (HSDAC) to set the working electrode (WE) potential for FSCV and EIS, and a low-power DAC (LPDAC) to provide stimulation in a CL system. CLNM has a maximum scan rate of 500 V/s and a frequency sweep of 1–10^5 Hz. The OPA4192 amplified the HSDAC output with a gain of 2 and achieved a scanning window of –0.5 ~ +1.9 V, suitable for providing excitation waveforms for dopamine (DA), serotonin, and other NTs. The ADuCM355 features a programmable transimpedance amplifier (TIA) for nA current sensitivity. The current measurement is digitized onboard by a high-speed ADC and transmitted via USB. CLNM is controlled through a Phyton GUI (Fig. 1B) [3]. In the GUI the user can set FSCV/EIS parameters, visualize data in real-time data visualization, and export it to a CSV file.

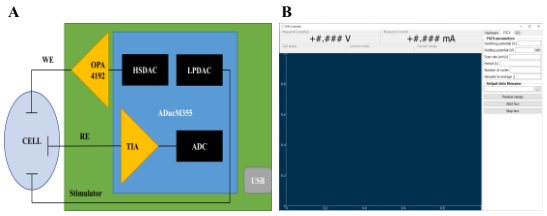

Figure 1. CLNM design. (A) Basic architecture. (B) GUI.

EIS was performed with CFME (n=3) as WEs and an Ag/AgCl reference in 1X PBS, with a 10 mV sinusoidal input and 10^1–10^4 Hz frequency sweep. Similarly, EIS was conducted on the Gamry Reference 600 (Fig. 2A). FSCV was subsequently acquired with a CFME at 400 V/s, from –0.4 ~ +1.3 V *vs.* Ag/AgCl, in 0.7 mM DA solutions (Fig. 2B).

III. RESULTS

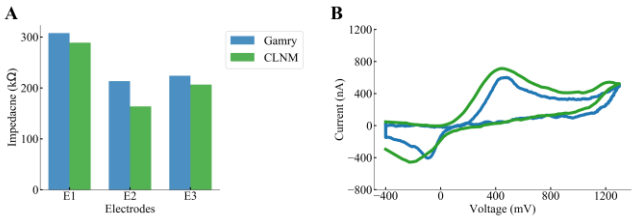

Figure 2. (A) Comparison of 1 kHz impedance collected with the CLNM and a Gamry potentiostat on 3 representative CFME. (B) Background-subtracted voltammograms of 0.7 mM DA collected with the CLNM and the Gamry potentiostat.

IV. DISCUSSION & CONCLUSION

The results show good agreement between FSCV and EIS data collected with CLNM and Gamry. We plan to conduct additional tests *in vitro* and *in vivo*, develop a thresholding logic based on DA concentration, and implement our full CLNM platform using NTs as biomarkers.

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