Bio-Impedance Characterization Technique with Implantable Neural Stimulator Using Biphasic Current Stimulus

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Abstract—Knowledge of the bio-impedance and its equivalent circuit model at the electrode-electrolyte/tissue interface is important in the application of functional electrical stimulation. Impedance can be used as a merit to evaluate the proximity between electrodes and targeted tissues. Understanding the equivalent circuit parameters of the electrode can further be leveraged to set a safe boundary for stimulus parameters in order not to exceed the water window of electrodes. In this paper, we present an impedance characterization technique and implement a proof-of-concept system using an implantable neural stimulator and an off-the-shelf microcontroller. The proposed technique yields the parameters of the equivalent circuit of an electrode through large signal analysis by injecting a single low-intensity biphasic current stimulus with deliberately inserted inter-pulse delay and by acquiring the transient electrode voltage at three well-specified timings. Using low-intensity stimulus allows the derivation of electrode double layer capacitance since capacitive charge-injection dominates when electrode overpotential is small. Insertion of the inter-pulse delay creates a controlled discharge time to estimate the Faradic resistance. The proposed method has been validated by measuring the impedance of a) an emulated Randles cells made of discrete circuit components and b) a custom-made platinum electrode array in-vitro, and comparing estimated parameters with the results derived from an impedance analyzer. The proposed technique can be integrated into implantable or commercial neural stimulator system at low extra power consumption, low extra-hardware cost, and light computation.

I. INTRODUCTION

Knowing the bio-impedance at the electrode-electrolyte/tissue interface is of paramount importance in biomedical applications [1-4]. Knowledge of the impedance can also be utilized to evaluate the reliability of the electrode and the proximity between electrodes and targeted tissue. For neural stimulator implanted in living tissue, measuring electrode impedance is essential to ensure an effective and safe stimulus is delivered since tissue is chemically reactive to electrode metal [5]. Moreover, charge-balanced current stimulus has been widely used to prevent electrode and tissue damage, but most stimulator systems have less focus on keeping the electrode overpotential within its water window during stimulation. Thus, it is of significant benefit to understand the impedance of

electrode-electrolyte interface that can be schematically represented by an equivalent electrical circuit. If the circuit parameters are known, we can determine the limit of stimulus intensity and pulse width in order not to exceed the water window of the electrode underuse and the compliance voltage of the stimulator.

A simple approach adopted to estimate bio-impedance is based on the injection of a small sinusoidal current with a fixed frequency and the measurement of the evoked voltage at the electrode. However, this only can provide the information of the impedance at a given frequency but the equivalent circuits model is still not available [2]. On the other hand, Electrochemical Impedance Spectroscopy (EIS) has been widely used to derive electrode-electrolyte impedance. EIS is based on the pseudo-linearity characteristic of the electrode and requires a small AC potential (typically 10 mV) to excite the electrochemical cell. Nonetheless, the electrode-electrolyte/tissue impedance is not linear [1]. Doubling the excitation voltage might not necessarily double the current as expected, while stimulation usually evokes a large transient voltage at the electrode. Thus, EIS and other methods based on small signal analysis might not be the best approach for the impedance measurement of stimulation electrode. Economic wise, a high hardware cost and complexity is further required when integrating EIS into a neural stimulator.

Bio-impedance measurement based on voltage/current pulse excitation has been proposed to infer the parameters of a three-element Randles cell [4, 6, 7]. [4] proposed to inject a current stimulus into the electrode and measure the resulting voltage, but only the electrode-tissue resistance can be derived. A sophisticated computation to estimate the impedance is also presented in [6], but complex computation impedes it from being incorporated into implantable stimulators. On the other hand, despite the method used in [7], which is capable of acquiring all parameters of a Randle cell, one of its prerequisites is to deliver an stimulus with infinite pulse width to the electrode. Nonetheless, a stimulus with infinite pulse width is less likely achievable and it would cause electrode overpotential higher than its water window.
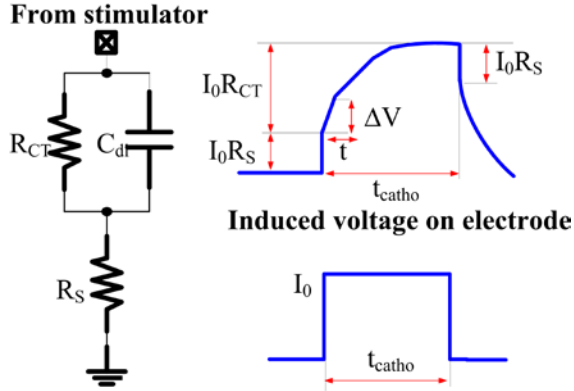
In this paper, we propose an efficient bio-impedance measuring technique based on the excitation using a biphasic current pulse with inter-pulse delay. Leveraging on the electrode characteristic that pure capacitive charge-injection dominates the initial electric charge transfer from the electrode to the tissue when the electrode overpotential is small, and on the deliberately specified period of inter-pulse delay, parameters of a Randles cell electrode model can be determined with simple computation and low hardware cost. A proof-of-concept system is further implemented using a stimulator system-on-chip (SoC) and a microcontroller to

Fig. 2 The proposed biphasic stimulus with inter-pusle delay for impedance measurement and the expected resulting electrode voltage.

validate the proposed method by evaluating the impedance of an emulated Randles cell and a custom-made platinum electrode array.

The remainder of this paper is organized as follows. Section II describes the transient electrode voltage when a current stimulus is injected, while Section III presents the proposed method. Section IV describes the experimental results and discussion. Finally, a summary is given in Section V.

II. VOLTAGE TRANSIENT ON ELECTRODES

Electrical charge is delivered from the electrode through two main mechanisms: capacitive charge-injection and faradic charge injection. A simple three-element Randles cell electrode-electrolyte model consisting of a charge transfer resistance R_{CT}, a double layer capacitance C_{dl}, and a tissue-solution resistance R_S, is herein adopted since both mechanisms are incorporated [8]. Fig. 1 shows the Randels cell electrode model and the waveform of the electrode transient voltage when a step current stimulus with intensity of I_0, pulse width of t_{catho} is injected. Using Laplace transform, impedance of the electrode model and the cathodic stimulus is expressed as $R_{CT}/(1+sR_{CT}C_{dl})$ and I_0/s, respectively. The resulting voltage can be derived by taking inverse Laplace transform of the product of the impedance-stimulus.

$$V_e = (I_0 \times R_S + I_0 \times R_{CT}(1 - e^{\frac{-t}{R_{CT} \times C_{dl}}}))u(t) \quad (1)$$

I_0R_S in (1) is the transient voltage increase when the instantaneous current flowing through R_S. This voltage can be measured immediately after the stimulus is fired for the estimation of R_S. The second term in (1) results from the stimulus current which charges C_{dl}. As pulse-width increases, this voltage drop approaches I_0R_{CT} and reaches a plateau. After the stimulus is finished, charge stored in C_{dl} is discharged through the resistive paths and the resulting voltage on the electrode gradually diminishes. It can be inferred from (1) that a stimulus with sufficiently long pulse-width can drive the subsequent voltage increase of the electrode overpotential to approach I_0R_{CT} and to allow a quick derivation of the R_{CT}. However, this might also drive the electrode overpotential over the range of its water window, causing electrode or tissue damage. Note that once R_{CT} is unavailable, C_{dl} cannot be estimated based on (1).
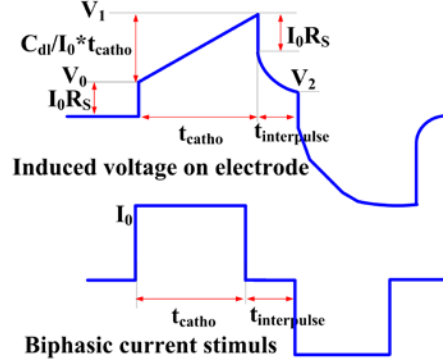
According to the above observation, we are seeking a more deliberate stimulus waveform to excite the electrode in order to yield all the parameters of the Randles cell electrode model with less computation and the prevention of electrode/tissue damage. Herein, a biphasic current stimulus with inter-pulse delay for impedance measurement is proposed and detail of the proposed approach is given in the following section.

III. THE PROPOSED METHOD

By carefully investigating the transient electrode voltage shown in Fig. 1, it can be found that after the initial electrode voltage increment of I_0R_S, there is a short period of time in which the electrode voltage is linearly increasing (ΔV in Fig. 1). This linear voltage increase is due to the pure capacitive current charging C_{dl} and its value depends on the rate of potential change. Based on charge reservation, the voltage increment during this period can be expressed as

$$\Delta V = {I_0 \times t}/{C_{dl}} \quad (2)$$

Once the electrode overportential further increases, Faradic current through R_{CT} starts to conduct a relatively large portion of the injected current from the stimulator, causing a non-linear increment of the electrode overpotential. Based on this electrode characteristic, we proposed to use a low-intensity, short–period biphasic current stimulus with a deliberately inserted inter-pulse delay (Fig. 2). Utilization a small and short stimulus can minimize the fraction of Faradic current, allowing the estimation of C_{dl} performed by simply measuring the resulting electrode voltage at the end of the leading pulse (shown as V_1 in Fig. 2). Subsequently, during inter-pulse delay $t_{interpulse}$, the charge stored in C_{dl} is passively discharged and the resulting electrode potential V_e is

$$V_2 = (V_1 - I_0R_S)(e^{\frac{-t_{interpulse}}{R_{CT} \times C_{dl}}}) \quad (3)$$

R_{CT} can thus be derived as

$$R_{CT} = -t_{interpulse}/(C_{dl} \ln{(V_2/(V_1 - I_0R_S))} \quad (4)$$

Insertion of the inter-pulse delay provides a controlled discharge time and a known timing to sample the electrode potential. Once the electrode voltage is acquired at the end of the inter-pulse period (shown as V_2 in Fig. 2), R_{CT} can be acquired. Finally, a compensating pulse is applied to maintain charge balance. Otherwise, accumulated residual charge might
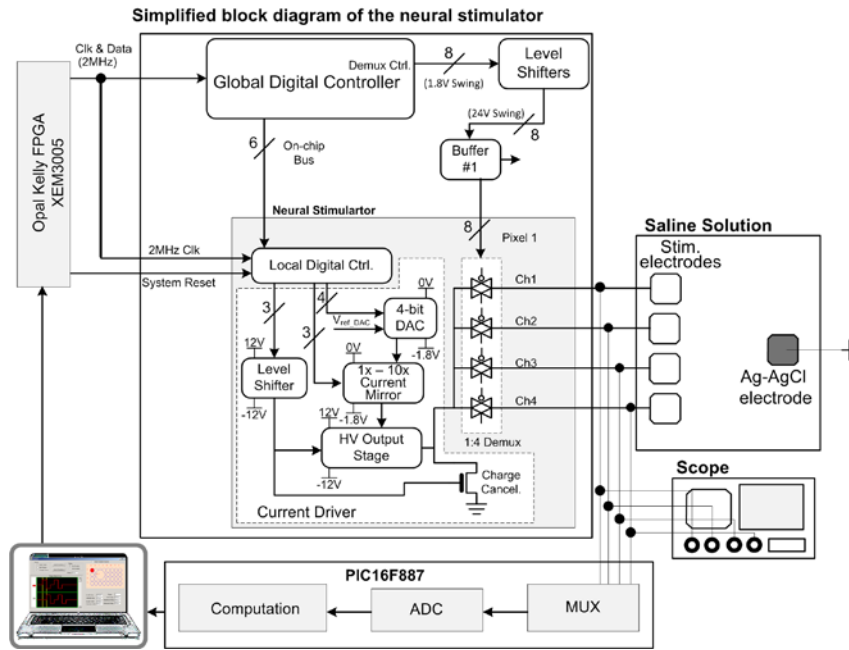
Fig. 3. The block diagrams of the set-up of the bio-impedance measurement. A simplified circuit schematic was modified from our previous work, showing the functional blocks used in this experiment only. Detail of the operation of the SoC can be found in [9].
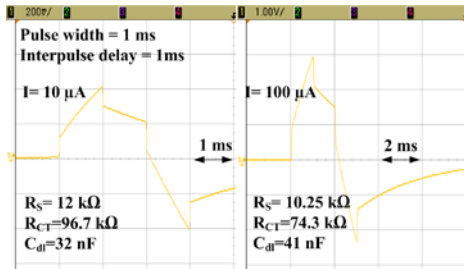

Fig. 4. Measured resulting voltage using lumped-circuit model.

results in a DC offset at the electrode and the DC offset might affect the Faradic process, i.e. affecting R_{CT}, when frequent monitoring of the electrode impedance is performed. Moreover, due to the capability of residual charge removal implemented in our stimulator, a serial capacitor at the stimulator output is not used.

IV. EXPERIMENTAL SET-UP

The proposed bio-impedance characterization technique is targeted at the application of neural stimulators that deliver electric charge to activate the neurons and necessitate the information of impedance at the electrode-electrolyte/tissue interface. Thus, in our experimental setup (Fig. 3), a multi-channel neural stimulator SoC developed in our laboratory [9] was used to generate bi-phasic current stimulus with programmable pulse polarity, intensity, pulse width, and inter-pulse delay. A FPGA (XEM3005 Opal Kelly Inc., OR) was programmed to send stimulation commands to the SoC. Digital control circuits of the SoC subsequently decoded the command and configured the stimulator driver to generate desired current stimulus. A microcontroller (PIF16F887, Microchip Tech. Inc., AR) was adopted to acquire the transient electrode voltage using its built-in 10-bit ADC. The ADC was set to sample only electrode voltages at three points (V_0, V_1, V_2 as shown in Fig. 2). Sampling operation of the

microcontroller was triggered by synchronization signal from the SoC, in which the synchronization signal was implemented using an unused stimulation channel. An oscilloscope was also used to monitor the evoked potential during stimulation.

In order to validate the proposed impedance measurement method, two verification experiments were conducted. In the first experiment, the proposed method was applied onto an emulated Randles cell made of discrete components with known values. In the second experiment, we evaluate the impedance of a custom-made electrode developed in our lab. The stimulation electrodes and an Ag-AgCl reference electrode (P-BMP-1, ALA scientific instruments, NY) were dipped into a phosphate buffered saline (PBS) solution (concentration of 0.9% sodium chloride). Meanwhile, the impedance of the electrode was also measured using the same set-up through an impedance analyzer (HP 4194A) for verification and comparison.

V. EXPERIMENTAL RESULTS AND DISCUSSION

The values of each discrete component of the emulated Randles cell (R_{CT}, R_{CT}, C_{dl}) are 100 kΩ, 10 kΩ, and 30 nF, respectively. We applied biphasic stimuli with intensity of 10 μA and 100 μA, pulse width of 1ms, and inter-pulse delay of 1 ms to this circuit model and measured the demanded resulting voltages. The measured waveform of two respective resulting electrode voltages and the estimated component value is shown in Fig. 4. It can be seen that using small stimulus current results in a more accurate results, while using large stimulus leads to a larger discrepancy compared to the nominal values of R_{CT} and C_{dl} as expected. There is also a slight inconsistency in the estimation of R_S. This is possibly due to the non-linearity of the stimulator driver.
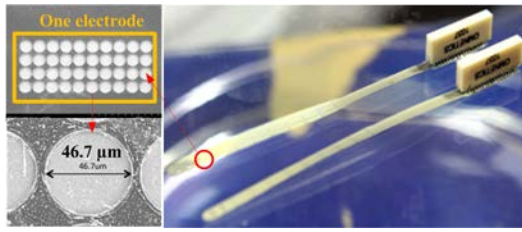
Fig. 5. The pictures of the 3 × 9 platinum/polyimide electrode array.

Fig. 6. Measured parameters of the plantium electrode. Top inset: fixed stimulus intensity of 10 μA and inter-pulse delay of 1 ms; bottom inset: fixed pulse width of 1 ms and inter-pulse delay of 1ms.

We further validated the proposed technique by measuring the impedance of a 3 × 9 platinum electrode array made on a flexible polyimide substrate (Fig. 5). An Omnectics Connector (A79026-001, Omnetics connectors Corp., NM) was used to connect the electrode to the stimulator output. Each single electrode has an area of ~200 μm × 500 μm with 40 exposed circular regions (Fig. 5). Detail of the electrode fabrication can also be found in [10]. R_S, R_{CT}, and C_{dl} of the electrode were first characterized and extrapolated as ~1.8 kΩ, ~15 kΩ, and ~176 nF using HP 4194A. Subsequently, biphasic stimulus was injected into the electrode. Fig. 6 shows the estimated circuit parameters of the electrode based on varied stimulus pulse width and stimulus intensity, respectively. It can be seen that the estimated R_S value is in the range of 1.9~2.0 kΩ, close to the results from HP 4194A. However, as stimulus pulse width and intensity increases, more charge is delivered to the electrode and escalate the electrode overpotential. Therefore, Faradic current gradually increase and it affects the estimation of C_{dl} and R_{CT}, based on (2) and (4). The result and observation imply that using a small stimulus current is preferred in order to more accurately estimate parameters of the equivalent circuits model of the electrode. It should also be noted that there is deviation in our measured R_{CT} and C_{dl}, compared with results from HP 4191A. This can be due to the fact that we are performing large signal analysis, instead of dealing with small signals.

Platinum electrode is known to have a pseudo-capacity. However, for capacitive electrodes, such as titanium nitride, the proposed method can also be applied to estimate C_{dl} and R_S. Also, unlike other impedance measurement approaches used in implantable neural stimulator, the proposed method can yield both C_{dl} and R_{CT}, instead of R_S only. With the knowledge of C_{dl} and R_{CT}, an upper safe bound of the stimulus parameters can be set to ensure the electrode overpotential does not exceed its water window.

VI. CONCLUSION

A novel technique employing biphasic stimulus is proposed to estimate the equivalent circuits parameters of the Randles cell electrode model. A proof-of-concept system made of a stimulator SoC and a microcontroller was implemented to generate the required stimulus and to perform electrode voltage acquisition. Leveraging on the dominating capacitive charging characteristic of the electrode when the electrode overpotential is small, C_{dl} can be determined by injecting a small current and measuring the electrode voltage.
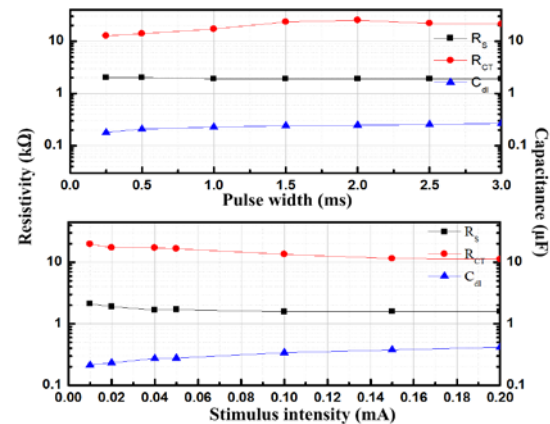
Via the known C_{dl} and sampling the electrode voltage, the R_{CT} can be derived via the insertion of a pre-determined discharge time. The electrode voltage needs to be sampled only at three points and no sophisticated computation and hardware is required, making this approach attractive for implantable and commercial neural stimulators. Moreover, unlike EIS or other methods using small excitation signal in its analysis, the proposed technique is more suitable for characterization of stimulation electrodes in which large electrode overpotential emerges.

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