Parallel electrochemical measurements of implanted neural recording microelectrodes

Zhe Hu, Philip Troyk, Glenn DeMichele

***Abstract*— An electrochemical instrument capable of parallel measurement of 16 microelectrodes was used, for the first time, for evaluating 32 implanted microelectrodes i*n-vivo*. The result reveals the inadequacy of traditional single-frequency impedance measurements as an assessment of microelectrodes. The combinational measurements of cyclic voltammetry (CV) and electrochemical impedance spectroscopy (EIS) provide more comprehensive information of the "health" of implanted microelectrodes. Parallel measurements allow investigators to gather this information for a large number of electrodes at much faster speed than have been traditionally available.**

I. Introduction

Microelectrodes arrays (MEA) with large counts of individual electrodes (e.g. FMAs by MicroProbes for Life Science, MD) have been widely used for neuroscience research during neural stimulation and/or recording experiments. Extensive research and manufacturing refinements have been focused on new biocompatible materials/coatings for the microelectrodes to lower recording electrode impedances, and increase stimulation charge delivery capacity [1][2]. There are numerous technical difficulties related to the production of electrode arrays, which in totality, complete with its cabling and connector, is actually a complex transducer system. The array typically goes through a high precision manufacturing process which include electrode etching, coating, activation, and delicate cable/connector assembly. Prior to implantation, the array must survive multi-step procedures such as user preparation, sterilization, and finally the animal surgery. After surgery, animal movements that break wires, connectors unreliability, electrode shaft insulation deterioration, or even improperly applied voltages during neural stimulation can notably limit the implanted lifetimes of these systems. .

Currently there is no simple method to check the "health" of the whole MEA system, especially after it has been implanted. For example, the impedance at 1kHz of electrodes measured in a beaker at the manufacturer's site is often the only data available for an implanted array. Knowing that most electrodes behave differently *in vitro* than *in vivo* [3], and that changes typically occur over time at the electrode/neural tissue interface, a single-point impedance measurement provides limited insight into the expected lifetime of the implanted electrodes. There exist a rich set of electrochemical methods, such as cyclic voltammetry (CV), Electrochemical Impedance Spectroscopy (EIS) and constant current pulsing voltage transient responses, that are powerful diagnostic and research tools for studying progression of the electrode/tissue interface, and the reliability of the implant electrode array system. CV is a large signal measurement that provides a plethora of information about the nature of the electrochemical reactions at the electrode/neural tissue interface, and can reveal possible leakage or insulation deterioration along the electrode shaft. EIS measures impedance at multiple frequencies to provide magnitude and phase signature patterns for comparing electrodes on a small-signal basis.

Unfortunately, CV and EIS are usually performed with bulky bench-top potentiostat instruments that are difficult, or in some case even dangerous to use for *in-vivo* measurements. Furthermore, it typically takes at least 5 minutes to complete one set of measurements (50mV/s CV and 1Hz to 10kHz EIS) on a single electrode, when using a single-channel potentiostat instrument. That amounts to 80 minutes for an array of 16 electrodes. These obstacles make it impractical for researchers to gather information from MEA *in-vivo*.

Here, we report the first time use of a specialized 16-channel MicroElectrode Tester (MET16) for parallel electrochemical measurements [4] *in-vivo*. MET16 has been designed to simultaneously measure 16 microelectrodes, both *in-vitro* and *in-vivo*. It is capable of CV, EIS and current pulsing measurements that can be used to evaluate the condition of implanted neural stimulating/recording electrodes in large MEA systems. Because of the time efficiency afforded by the parallel measurement, it shortens the experiment time by 16 times, and makes frequent and periodic *in-vivo* measurements feasible.

II. Material and Methods

In accordance with an approved animal protocol at Northwestern University, and immediately following implantation surgery into the motor cortex of an anesthetized monkey, a 32-microelectrode array (manufactured by MicroProbe for Life Science, MD) was measured with a MET16.

Two weeks after implantation surgery, the same measurements were repeated on the same array while the animal was under sedation.

At the onset of the measurements, the MEA counter and reference electrodes were independently measured, using the MET16, with respect to the metal connector housing mounted on the animal's skull. This was done to evaluate connectivity of these electrodes, thus assuring the safety of the subsequent microelectrode measurements, since these measurements are potentiostatic in nature and require counter and reference electrodes in order to control the magnitude of the applied potentials. Subsequently each of the 32 electrodes were measured in two "banks" by manually switching the MET16 connector.

A typically-used slow-rate CV at 50mV/s (-0.6V - +0.8V wrt to PtIr reference) was chosen to investigate the electrochemical responses at the neural/electrode tip interface. EIS spanning from 1Hz to 10kHz was also measured, in contrast to traditional 1kHz single-point impedance.

In both sessions, the animal wasn't housed in any faradaic cage, but was kept sedated to avoid CV motion artifacts. Because the MET16 is electrically well-isolated from its power supply and computer connections, it can float to the same voltage level which is that of the metal pedestal on the skull of the monkey, and this minimizes ambient noise currents and movement artifacts. That allowed the

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measurement of currents in the sub-nA range. Fig 1 shows a block diagram of the MET16 system.

Within 10 minutes, all CV and EIS measurements were completed on all 32 electrodes.

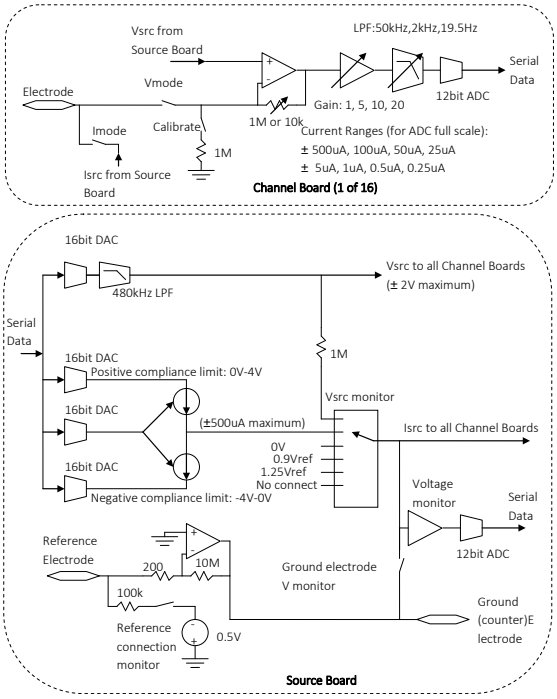

Figure 1. MET16 GUI window viewing CV results in a web browser

III. Results

As a web-based scientific instrument, the data collected by MET16 are saved in open format (CSV and JSON) files, and are automatically uploaded to a central server, such that they can be shared among multiple researchers or made public over the internet. The electrode experiment data (CV, EIS and current pulsing) can be viewed on any device that supports a modern web browser. Space does not permit presentation of the EIS data here.

Fig. 2 shows CV data of all 32 electrodes in 32 plots taken immediately after the surgery. Because these electrodes were intended for neural recording, the CV currents are, as expected, in the low-nA range.

It is evident that even though the specified physical configurations are the same for all electrodes (exposed surface area), no two electrodes display exactly the same signature patterns resulting from the CV. Some of these differences could be due to manufacture variation in terms of the shape of the electrodes, or possibly wear and tear during surgery (insertion) and handling, thus causing changes in electrochemical properties of the electrodes. The CV measurements clearly identifies 4 open connections at connector terminals E1, E2, E7 and E32, as demonstrated by the flat CV curves.

Fig. 3 shows the same type of CV measurements two weeks after implantation. The original four open connections remain unchanged (as expected). In addition, there are significant changes in the CV curves of three additional electrodes E6, E22, and E24, which all show a steep anodic current turn-on at about +0.4 volts, which is atypical of the Pt tips of these electrode.

Fig. 4. shows the overlay view of several electrodes: E1, E14, E18 and E22 in one plot. One can easily identify from features of the CV measurement open circuit, a typical small electrode, a larger electrode, and abnormal electrode. Table 1 shows their single-frequency 1kHz EIS impedance magnitudes taken by the manufacturer, *in-vitro*, and the 1kHz impedance magnitude taken from the EIS scan of the MET16.

IV. Discussion

Looking at the CV data in Figs 1,2, notable variations exist between all 32 electrodes that were intended to be identical, especially for electrodes E8, E14, E18, E20, E29, which indicate larger surface areas than all others. The flat CV curves for electrodes E1, E2, E17, E32 reveal open circuits. The change in the CV curves for electrodes E6, E22, and E24, suggest fluid leakage at the site of the connector, or within the interconnection area of the array. This conclusion stems from the rapid onset of current at ~+0.4V, which is uncharacteristic of Pt, thus suggesting fluid exposure of a different metal type, as is used within the interconnection system.

V. Conclusion

The post-surgery evaluation of the implanted microelectrode array by the MET16 produced significant information. Parallel CV and EIS measurement were essential to quickly collect data *in vivo* over a large number of electrodes, and the fast measurement execution time reduced animal stress and motion artifacts in the collected data. This collected data will serve as our baseline for this animal, and as more data is collected, we will be able to observe the long-term drift of electrode characteristics in a chronic implant. This data will hopefully lead to the discovery of root-cause failure mechanisms and illuminate ways to improve the reliability of these implanted systems.

Electrode ID	***1kHz impedance (MOhm) measured by manufacturer***	***1kHz impedance (MOhm) measured in-vivo***	***notes***
E1	0.7	43	open circuit
E14	0.5	1.24	small electrode
E18	0.7	105e-3	large electrode
E22	0.5	1.12	abnormal electrode

TABLE I. Traditional 1kHz impedance of 4 different microelectrodes

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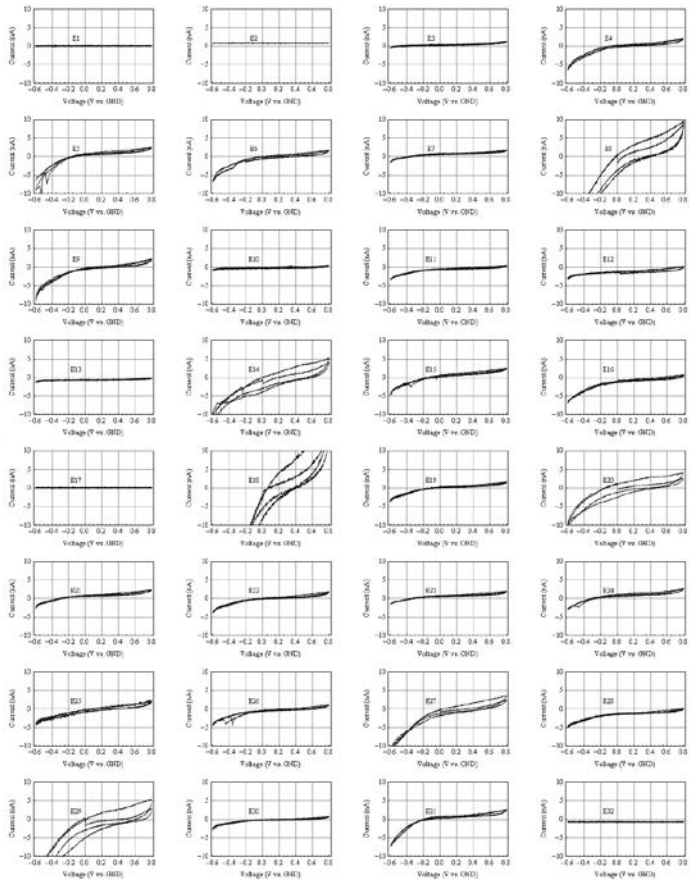

Figure 2. CV data for all 32 microelectrodes measured *in-vivo* immediately following implantation

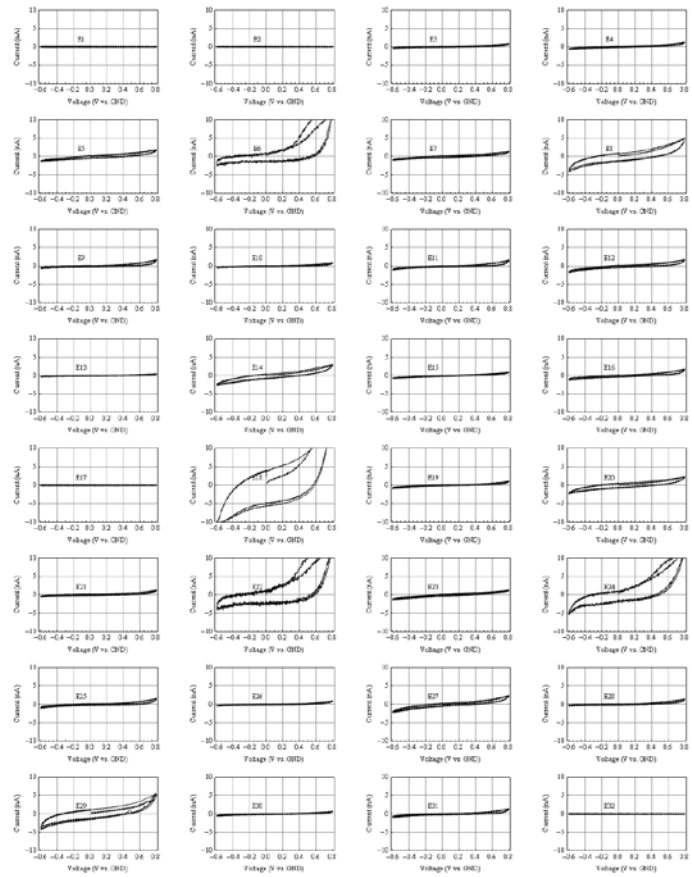

Figure 3. CV data for all 32 microelectrodes measured *in-vivo* two weeks following implantation

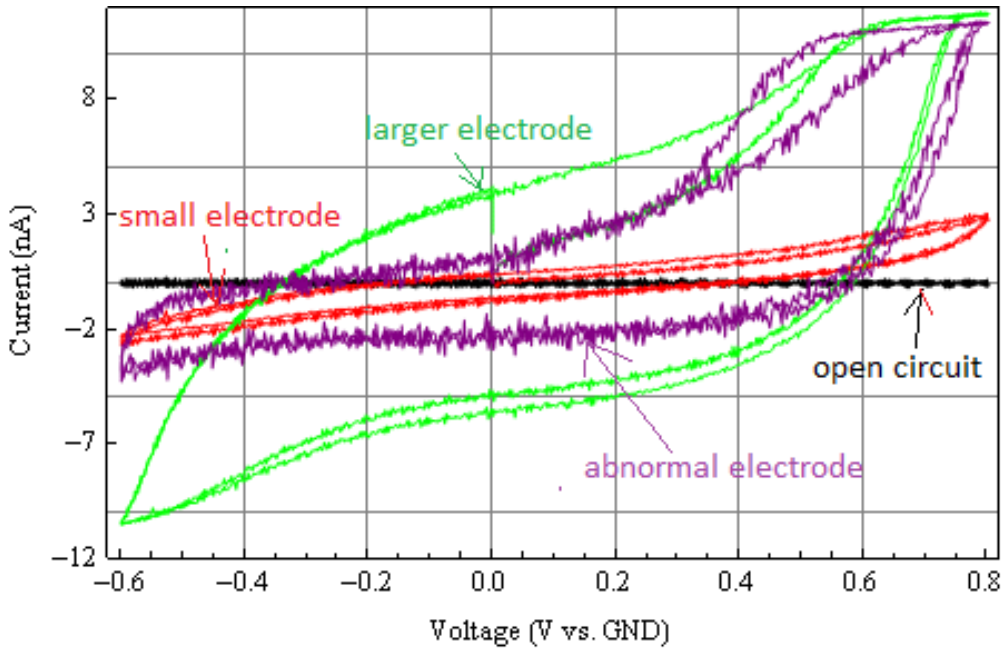

Figure 4. CV data for four electrodes showing distinct characterisics.