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A laboratory instrument for characterizing multiple microelectrodes

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Abstract— **The task of chronic monitoring and characterizing a large number of microelectrodes can be tedious and error prone, especially if needed to be done *in vivo*. This paper presents a lab instrument that automates the measurement and data processing, allowing for large numbers of electrodes to be characterized within a short time period. A version 1.0 of the Electrode Analyser System (EAS 1.0) has already been used in various neural engineering laboratories, as well by one electrode array manufacturer. The goal of the current work is to implement the EAS 2.0 system that provides improved performance beyond that of the 1.0 system, as well as reducing size and cost.**

I. INTRODUCTION

With the advent of implantable multi-electrode array (MEA) containing a large number of microelectrodes [1], [2], researchers can perform neural stimulation/recording experiments of increasing complexity. At the same time, sustaining and verifying the functionality and integrity of the electrodes becomes an essential part of chronic experiments. When faced with changing or variable results, including reduced amplitude or loss of neural signals, the researcher is often faced with not knowing whether the neural network, or the electrode array itself is responsible for the changes. While systems comprised of expensive and complex impedance, electrochemical, and stimulator analysis equipment can be assembled, what is most needed is a cost-effective self-contained instrument to characterize implanted microelectrodes on a regular basis.

From our extensive testings of existing MEA systems, a number of problems can adversely affect neural recording or stimulation experiments. These include electrode array manufacturing defects such as encapsulation leakage, or cross coupling between electrodes. On the user side, problems at the time of implantation including electrode damage due to handling, other problems that may emerge during chronic use of the electrodes such as corrosion of the electrode connectors, cable connection failure, or deterioration of the electrode material itself, all cause frustrating and compromises of expensive and time-consuming animal experiments. When comparing results between researchers, it would be extremely valuable to have a common basis of comparision for the quality of the electrodes used for the recordings or stimulations. Otherwise failure of the electrodes themselves might be inadvertently misinterpreted as changes to a neural network, shifts in stimulation thresholds, or neural tissue damage.

Some of these electrode problems can be easily diagnosed with very simple instrumentation, while others require careful electrochemical measurements such as cyclic voltammetry (CV) and electrochemical impedance spectroscopy (EIS). In any case, manually testing each electrodes within a large (as high as 96), or even a smaller (16) group of implanted electrodes can be tedious and error prone, not to mention the difficulty in subsequently cateloging and processing the data. (e.g. before/after implantation) to see the trends and changes.

In this paper, we describe research for the development of a lab instrument, Electrode Analyzer System (EAS) that can quickly and automatically measure an array of 16 electrodes while storing and visualizing the collected data via web technology. A first version of this system, EAS 1.0, is capable of cyclic voltammetry (CV), electrochemical impedance spectroscopy (EIS), and stiumulus pulsing. The standard electrochemical measurements, CV and EIS, can capture valuable information about the integrity of microelectrodes. EAS 1.0 also uses constant current pulsing to characterize stimulating microelectrodes, since their charge injection capabilities are known to differ greatly between *in vitro* and *in vivo* environments [3].

EAS 1.0 was built around several discrete external instruments (e.g. a Gamry potentiostat, a neural stimulator, a Tektronix scope and a reed relay switching array), using various software modules that tie them together. The present development is to integrate the functionality of that external hardware into a single EAS 2.0, so as to miniaturize the instrument and thus reduce the hardware complexity, cost, as well as facilitating software development.

The goal is to make complex electrode characterization easily accessible to a standard neural physiology laboratory, without the cost and learning associated with the assemblage of a complex collection of off-the-shelf instruments. In addition, by adopting web-based technology, each EAS can upload data to a central server where a large amount of electrode measurement data can be shared among researchers.

II. EAS SYSTEM

A. EAS 1.0 Hardware

The center of the current EAS 1.0 system (Fig. 1) is an array of reed relay switches depicted in Fig. 2. They connect any individual electrode either to the Gamry potentiostat (a single channel system) for CV and EIS measurements, or to a constant current stimulator that can measure electrode voltage and current waveforms during a neural stimulation

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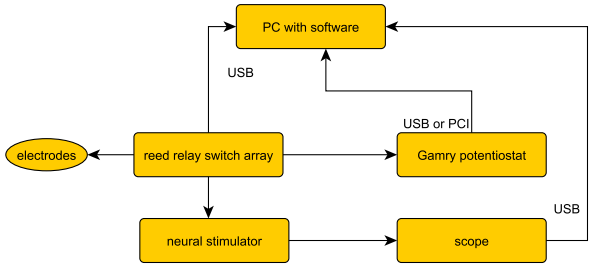


Fig. 1: EAS 1.0 System Diagram

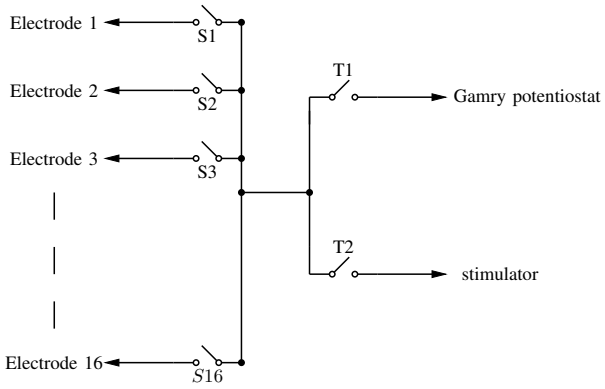


Fig. 2: Diagram of EAS 1.0 Reed Relay Switch Array

pulse. Reed relay switches are chosen to minimize the leakage current, which is essential for accurate CV and EIS measurements.

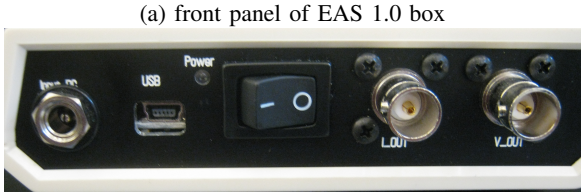
All the reed switches are digitally controlled. Delay circuitry is built-in to ensure proper sequencing so that in a typical 3-electrode-configuration, the working electrode is switched before the reference and the counter electrodes, to minimize the transient damage to the electrodes, or the neural tissue.

Currently the EAS 1.0 system uses an Arduino MCU as the control unit. The MCU also commands a stimulator chip (custom V6 stimulator chip, by Sigenics) to generate neural stimulation pulses. The stimulator chip is also capable of iridium electrode activation, by growing AIROF. The front and back panel of the hardware is shown in Fig. 3. The box communicates with the PC via the USB port.

The scope (e.g. picoscope or Tektronix scope) that captures the electrode voltage and current waveforms also has a USB interface. The Gamry potentiostat can be USB or PCI card based, which comes with Gamry's own running environment.

For safety, the whole front-end circuitry needs to be electrically isolated from the PC side during animal testing. Therefore voltage sensing safety circuitry is included to promptly disconnect the working electrode in the event of over-voltage faults. Such faults can occur if the electrical connection to the reference electrode were to fail during a potentiostat measurement, during which the potentiostat would force its output voltage up to its compliance limit which is usually on the order of ± 50V—an unfortunate

(a) front panel of EAS 1.0 box



(b) back panel of EAS 1.0 box

Fig. 3: Picture of EAS Hardware

characteristics of the commercially available Gamry system.

B. EAS 1.0 Software

A typical electrode testing session involves measuring CV, EIS and current pulsing sequentially on each electrode within an array. The software coordinates and performs the measurements after the user chooses the settings in a GUI (Fig. 4).

In the current 1.0 system, all but one external hardware devices (Gamry potentiostat) provides some kind of programming interface.

The Gamry potentiostat system provides a scripting language (called Explain) inside its running environment called Gamry Framework. Both CV and EIS measurements can be scripted within the Framework for a single electrode. The difficulty is to inform the switch array to switch to the next electrode once the measurement has completed.

To circumvent the limitation that the Gamry Framework has no open API, we use its scripting language to send the "message" outside in two different ways:

- Gamry Explain scripts can write digital signals to its auxiliary DIO card. The MCU in EAS can listen to the digital signal on the 4 DIO lines of the Gamry system.
- Gamry Explain scripts can write text messages to the status bar of the Gamry Framework software window. With the help of AutoIt software, these messages can be grabbed externally.

Once the user has chosen all the experiment parameters and clicked the "start" button, the GUI software generates a Gamry Explain script from a template file and then executes it through the Gamry Framework. The GUI program then waits for the messages from the Framework, signaling the CV and EIS measurements completion, to switch the reed relays, so as to begin a new batch of measurements on the next electrode automatically. The GUI also controls the scope and the stimulator for the subsequent measurements.

All the measurement data are transformed into JSON format files that can be stored and queried in a MongoDB database remotely. A light-weight NodeJS web server program retrieves the data from the database and forks "child" programs to analyze the data. The results are sent back

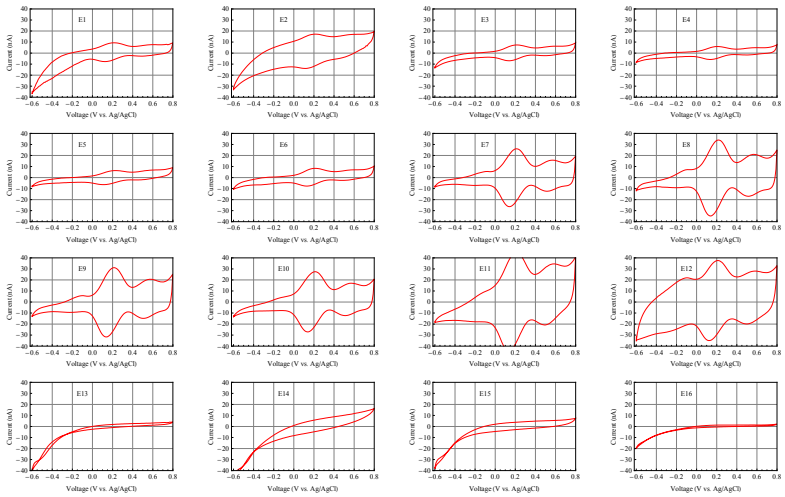


Fig. 5: CV (50mV/s) of AIROF microelectrodes in PBS

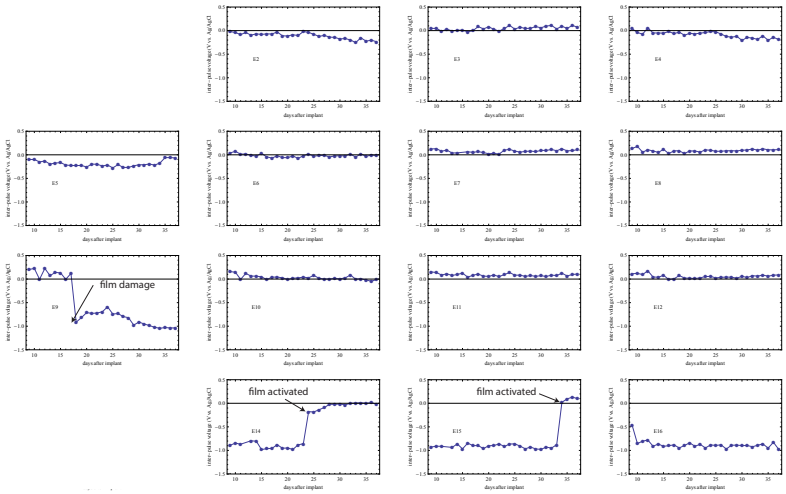


Fig. 6: Inter-pulse voltage of AIROF microelectrodes *in vivo*

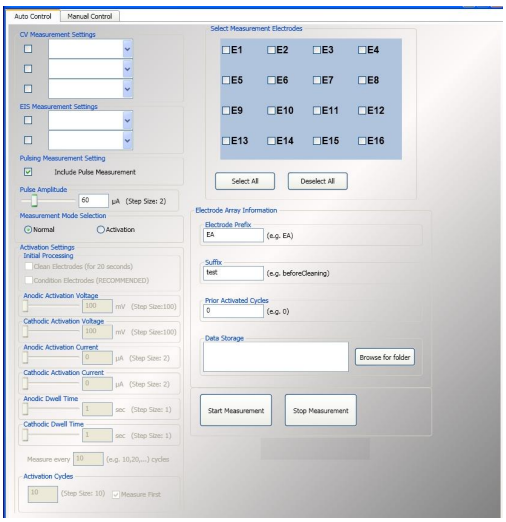
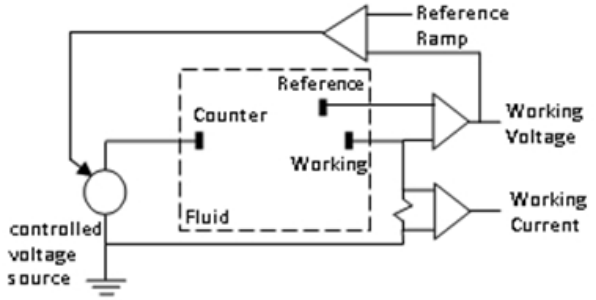


Fig. 4: EAS GUI

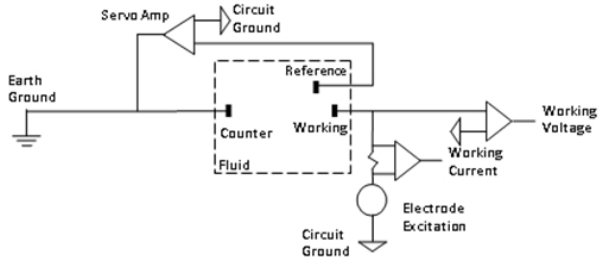
via the standard HTTP web protocol to a web browser for visualization. This way no special software needs to be installed to analyze and view the data, and the electrode measurement data can be shared among researches anywhere, running different computer systems as long as a web browser is available.

C. EAS 2.0

Though the current EAS system improves the efficiency of electrode testing over manual methods, it still performs the measurements in series, one electrode at at a time. This is acceptable for current pulsing measurements, since each electrode takes around 20 seconds to measure. But the Gamry CV (e.g. at 50mV/s) and EIS measurements (e.g. of multiple frequency points) can add up to 5–10 minutes per electrode. With an array of 16 electrodes, that amounts to 80–160 minutes testing time. It gradually becomes impractical to test all of the implanted electrodes (e.g. 96) in a live animal on a regular basis without seriously affecting the progress of the intended experiment by the researcher.



(a) common working electrode topology



(b) common counter electrode topology

Fig. 7: Potentiostat Cicruit Topology

One solution is to measure CV and EIS in parallel for all electrodes within an array. The traditional single channel potentiostat uses the common working electrode topology (Fig. 7a), which prevents multiple channels from running in parallel. EAS 2.0 will adopt the common counter electrode topology (Fig. 7b), which allows multiple working electrode channels to be independent of each other, provided that simultaneous CV and EIS measurements won't interfere with each other.

Since there is no need for an external potentiostat and scope. It greatly reduces the cost of the system. The data collection and batch experiment software becomes much easier to develop as well.

III. EAS 1.0 TEST RESULTS

As an example of the application of EAS 1.0, we plot the CV (50mV/s) of the AIROF microelectrodes measured *in vitro* (Fig. 5), and the inter-pulse voltage of the same microelectrodes measured *in vivo* (Fig. 6). A 16-electrode-array was characterized in PBS and then chronically implanted in the cortex of a Starling [3]. EAS 1.0 was used to take CV, EIS and current pulsing data daily, for a continuous period of 37 days after implantation. The inter-pulse voltage measures the electrode voltage waveform when the cathodic current switches to zero, prior to the onset of the anodic phase. It is a direct indication of the extent of polarization of the electrode caused by the cathodic charge delivery. he electrode polarization is an important parameter for assessing and confirming the electrochemical integrity of the electrode-tissue interface.

In this experiment, Electrode E2–E12 had AIROF coating, which greatly enhanced their charge delivery capacity, whereas E14–E16 were bare iridium electrodes to begin with. The AIROF electrodes show a stable inter-pulse voltage over time, except electrode E9. Electrode E9 experienced film delamination on Day 18, which can be diagnosed not only from this plot, but CV and EIS measurements as well. Its inter-pulse voltage drops to the bare iridium electrode level. This illustrates the use of the EAS system to diagnose an electrodes failure during the course of an experiment and distinguish this failure from a shift in stimulus threshold.

E14 and E15 were modified by growing an AIROF film, using ESA 1.0, *in vivo* at Day 25 and Day 35 respectively. They showed the expected lift of inter-pulse voltage, which is consistent with the acquired AIROF due to activation. It indicates the success of *in vivo* AIROF activation.

These measurements show the versatility and diagnostic capability of an EAS system. With the development of EAS 2.0, this powerful tool will become more readily available to a wider range of neuroscience researchers.

IV. CONCLUSION

EAS has been extensively used for electrode testing in our neural engineering laboratory. The earlier system "glues" together various external instrument with software to accomplish automatic and efficient measurements. The next implementation, EAS 2.0 will aim to integrate the CV, EIS and current pulsing measurement capability into a single instrument, using a custom integrated circuit as the hardware engine. That will reduce both hardware and software cost. To reduce the experimental time for multiple arrays, the key technology is to be able to make potentiostat measurements in parallel [4], [5].

The web-based data processing and visualization is hoped to make possible remote diagnosis of electrode integrity, and encourage data sharing among neural science researchers, as well as electrode manufacturers. EAS can measure each single electrode from its birth till its retirement from use, and keep track of the lifetime data.

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