Sensors & Transducers, Vol. 220, Issue 2, February 2018, pp. 45-50

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Sensors & Transducers

Published by IFSA Publishing, S. L., 2018
http://www.sensorsportal.com

Low-cost Electrode Arrays for Recordings of Neural Activity

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Received: 14 February 2017 /Accepted: 16 February 2018 /Published: 28 February 2018

Abstract: Recordings of neural activity with further data interpretation and analysis are helping to discover underlying processes of the brain's functioning. These studies can have a huge impact on the development of modern highly promising technologies such are: cognitive computing, machine learning and artificial intelligence, human-machine interfaces, bionic prosthetic devices and etc. This has remarkably increased the interest in electrophysiological recordings. Although the technology and techniques of these recordings are being continuously improved, there are still many obstacles in getting high quality recorded data due to its complicated nature, small signal amplitudes and inherited noises. Every node in the recording system is crucial for getting meaningful and precision data.

In this paper, a method for manufacturing of low-cost electrode arrays for electrophysiological recordings is described. The proposed electrode arrays are easy-to-replicate and can be easily modified, which gives flexibility for customized probe preparation. The testing shows that these probes have low electrical impedances and can be used for neural spike registration.

Keywords: Electrophysiological recording, Neural spike registration, Electrode array, Impedance measurement, Electrode manufacturing.

1. Introduction

The electrical recording of extracellular signals of brain remains basic tool for investigation of neural activity due to its high temporal resolution, usability in chronic experiments and opportunity of parallel recording from multiple regions of the brain as well as from multiple sites of the same region [1].

But what can be inferred by recording brain activity is a link-question that bring us to system neuroscience, where recording methods become a data supplier and tool for data mining.

To investigate the problems of system neuroscience by revealing ongoing electrophysiological processes in brain, one should have sufficient interpretable data of high quality [2]. Electrophysiological recordings contain data that is complex by its nature and its quality largely define what can be extracted and inferred by the data mining techniques [3].

The mission of system neuroscience is to give findings about the system by revealing patterns of its internal and external interactions and creating simulation models of that systems. The key to the solution of the first task is hiding in a data that should contain sufficient interpretable information about the system. To make an information interpretable, recordings must be carried in well controlled

conditions and be done in certain regions of the brain that are known to be reactive to given external or internal stimuli [4]. Another data related issue is its reliability that requires low noise, high precision recording systems and appropriate data processing techniques [5].

Currently a wide range of recording and neural interfacing systems are present in the market and hardware improvement methods are introduced in various articles [6-12]. But still the gain of high quality data with low-cost and easy-to-implement custom systems is an obstacle for neuroscientists. The neural interfacing is the first step in a recording chain and a lot of physical limitations are related to this stage. First of all is the limited number of neurons that can be captured by implanted electrode and number of electrodes that can be implanted in a one brain for multi-scale recording [13].

For more than a century electrophysiological recordings has been conducted with different types of metallic electrodes and arrays. Insulated metal tetrodes and microwire arrays have been widely used and described for their low-cost, feasibility to conduct and biocompatibility [14-16]. But these electrodes inherently have high impedance which is a concern to have a better signal-to-noise ratio, less signal distortion and heat dissipation.

In nowadays dense multisite recordings the state-of-the-art silicon probes allow high-quality chronic recordings from awake animals [17-18]. Silicone probes with various geometry can be manufactured at the specific facilities requiring experts in the field and time resources to establish the method and test the quality of probes which results in high-cost of these non-reusable probes [19].

Further stages of analog signal conditioning are signal amplification and filtering that make signal detectable by acquisition cards and improve signal to noise ratio. On the other hand, it has been shown that these stages may distort the signal causing frequency dependent phase shifts, as well as loss of ‘‘meaningful’’ signals [20].

The resolution and sensitivity of present acquisition systems may justify the simplification of the system, which reduce cost and time for setting up the experiment and potentially can prevent signal distortions [21].

Latest researches show that for reaching minimal distortions of registered electrophysiological signals the used electrodes must have much less impedance compared with the input impedance of registration devices [20].

In this paper we describe a method for manufacturing of low-cost electrode arrays for electrophysiological recordings, which have low electrical impedance and are easy-to-replicate.

We were able to directly register neural spikes with the designed electrodes by NI PXI-4462 dynamic signal acquisition device without using external amplifiers and filters.

2. Methods

2.1. Electrode Design

As the electrodes for electrophysiological recordings should be implanted very precisely, the best solution is to have an array of the electrodes. To have a low-cost electrodes we have simplified their design to have minimum number of elements. For these reasons we have designed our probes in the shape of a comb that has known separations between electrode tips (Fig. 1).

The designed probes have 7 electrode tips that are 100 μm wide and 5 mm long and have separations between tips 600 – 800 μm. On the top side of the electrode there is a connector with 8 pins for easy wiring. Each pin is electrically connected to one of the electrodes and there is one extra pin for connecting external reference wire if needed.

In the Fig. 1 the conducting metallic parts of the probe are shown with red color and pins are shown in green.

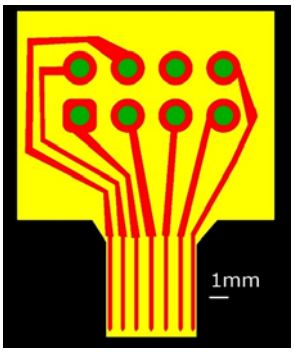

Fig. 1. Design of probes for electrophysiological recordings.

2.2. Electrode Fabrication

As a base material for our probes we have chosen glass-reinforced epoxy material (FR-4) with laminated copper foil that has 35 μm thickness. FR-4 is a common material for printed circuit boards.

To manufacture (cutout) our probes from FR-4 plate we have used a LPKF ProtoMat S62 circuit board plotter. This high-speed plotter provides unequaled precision and performance for quickly and easily milling and drilling circuit board prototypes [22]. It provides 2.5D milling of PCB’s with 0.25 μm resolution and 1μm repeatability. This parameters easily fulfill the demands of designed probes.

For probe manufacturing we have designed electrodes in LPKF CircuitPro software. After drawing electrodes and defining available manufacturing tools, this software automatically calculates the paths of milling. For providing fine clearances between electrode tips we have used “RF

End Mill" manufacturing tool which provides as fine as 400 μm clearance.

After manufacturing probes with LPKF ProtoMat S62 plotter (Fig. 2) we electrochemically coated the electrode tips with gold. This was done for increasing the conductivity of electrodes and making probes biocompatible for chronic recordings.

At the next stage we have soldered a connector to the probe (Fig. 3).

The last stage in the manufacturing of probes is isolation with a layer of dye of the conductive parts of electrodes except their tips.

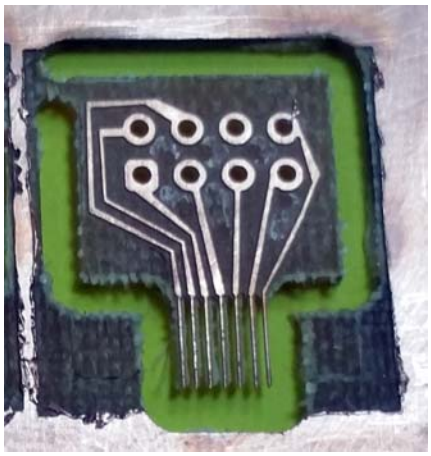

Fig. 2. The probe for electrophysiological recordings manufactured from FR-4 plate.

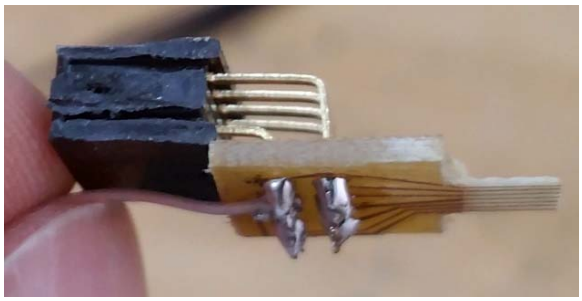

Fig. 3. The designed probe with a connector soldered to it.

2.3. Recording System

Modern recording systems of neural activity use preamplifiers and analog filters to be able to register signals. But that additional circuits distort signals. To show that our probes can be used even for recordings without the use of preamplifiers we have chosen NI PXI-4462 dynamic signal acquisition device. It provides four-channel dynamic signal acquisition for making high-accuracy frequency-domain measurements. NI PXI-4462 is a PXI module with four analog inputs that have 24 bit voltage resolution and 37 nV sensitivity in the range of ±316 mV. This module provides up to 204.8 kS/s sampling rate and have 1 MΩ || 217 pF input impendence.

To build the registration circuit we have put the NI PXI-4462 module in a NI PXIe-1082 chassis with a NI PXIe-8135 controller.

We have written a computer program in LabVIEW programming environment to control the data acquisition process of the system. The program configures the PXI-4462 dynamic signal acquisition module, reads data from it, graphically displays the data on a computer monitor and saves the recordings in a computer file.

To test the noise level of the built system we short connected the wired inputs of the system and started recording. This recordings were done in differential mode with 25 kS/s speed. The overall noise level of the system was established from the recordings to be ±3 μV (Fig. 4).

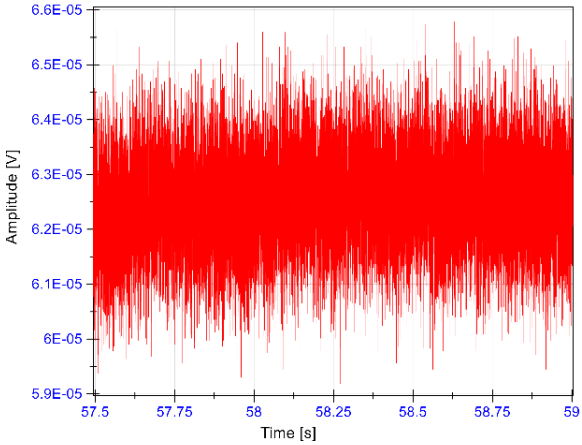

Fig. 4. The noise of the system.

3. Animal Surgery and Probe Implantation

The designed probe has been chronically implanted to albino rats weighted 300-350 g. The bregma-lambda distance has been measured and the stereotactic coordinates has been calculated according to the atlas [23].

The rats were anesthetized with pentobarbital (50 mg/kg) and xylazine (5 mg/kg). Lydocaine spray has been applied locally and dexametazone (0.2 mg/kg) has been injected i/m to prevent brain swelling. Ketoprofen (5 mg/kg) was injected to prevent post-surgical pain.

A window has been drilled 4mm*6mm and the electrode has been slowly inserted in AP 4.9, and ML (1-6) coordinates, i.e. the electrode comb having length of 5 mm has been inserted parallel to sagital suture, 4.9 mm to the right. And the reference wire was placed on the scalp. The probe has been fixed by dental acrylic and the animals were left to recover for 3-7 days.

The animals were kept under standard laboratory conditions with 12 h light regimen (7:00-19:00) and the experiments were conducted according to

European Communities Council Directive (86/609/EEC) and were approved by the institutional ethical committee.

4. Measurements

4.1. Electrode Impedance Measurements

The impedance of implanted electrodes has a critical role in gathering high quality data. Lower electrode impedances results in lower noises and less signal distortions. To measure the impedances of designed electrodes we have used NI ELVIS II+ laboratory workstation.

We have connected the implanted probe to the measuring device and made two type impedance measurements: impedance between one of electrodes and reference wire and impedance between two electrodes. These measurements were done with testing signal frequencies from 1Hz to 30 kHz.

Fig. 5 shows the results of impedance measurements of the implanted probe. The lower blue curve represents the impedance between one of electrodes and reference wire and the upper red curve represents impedance between two electrodes.

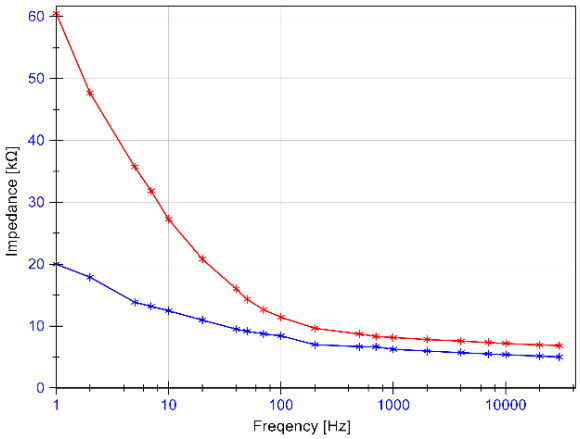

Fig. 5. Measured impedances between one of electrodes and reference wire (blue curve) and impedance between two electrodes (red curve).

The results of impedance measurements of the implanted probe show that the designed electrodes have much lower electrical impedances compared to commercially available electrodes. More specifically, commercial electrodes have 200 kΩ – 10000 MΩ impedances at 1000 Hz, whereas our electrodes have 6 kΩ – 8 kΩ at the same frequency. This gives advantage of gathering signals with lower noises and less distortions in the same measurement conditions [16].

The amount of distortions of registered electrophysiological signals depends on a ratio of impedances of electrodes and input impedance of registering device. Frequency-dependent attenuation and phase shifts of registered signal are present when electrode impedance is not negligible relative to input impedance of registering device [20].

The NI PXI-4462, which we use to register neural activity, has 1 MΩ || 217 pF input impedance that varies with the signal frequency. To estimate the input impedance for frequencies of our signals, we have calculated these values for frequency range from 1 Hz to 30 kHz. As a result we have plot a curve showing the dependence of input impedance of the registering device from frequency of signals (Fig. 6).

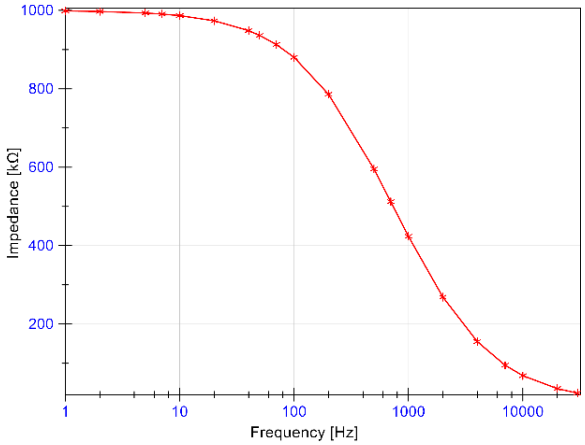

Fig. 6. The dependence of input impedance of the NI PXI-4462 from frequency of registered signals.

Fig. 5 and Fig. 6 show that the input impedance of our registering device is significantly higher than the impedance of the designed probes. In particular, the input impedance of NI PXI-4462 module is about 420 kΩ at 1000 Hz, whereas our electrodes have 6 kΩ – 8 kΩ at the same frequency.

4.2. Recordings of Neural Activity

The recordings of neural activity were performed after 3 days of recovery from surgery. The anaesthetized rat was placed in a Faraday cage with 50 cm × 50 cm × 80 cm dimensions. Each recording session lasted 5-10 minutes.

The NI PXI-4462 was configured to make simultaneous measurements from 4 analog inputs in differential mode with 25 kS/s sampling rate. The "+" terminal of each input channel was connected to one of the electrodes of the implanted probe. The "–" terminals of all input channels were connected to the reference wire of the probe.

The written computer program reads data from analog inputs of NI PXI-4462, graphically displays the data on a computer monitor and saves the recordings in a TDMS file.

To find neural spikes we have done post-processing of recorded data in NI DIAdem program. More specifically, we have done digital high-pass filtering of recorded data with 530 Hz cutoff

frequency. The filter was configured as: 1st order digital high-pass Butterworth filter.

The filtered signals are shown on Fig. 7 and Fig. 8.

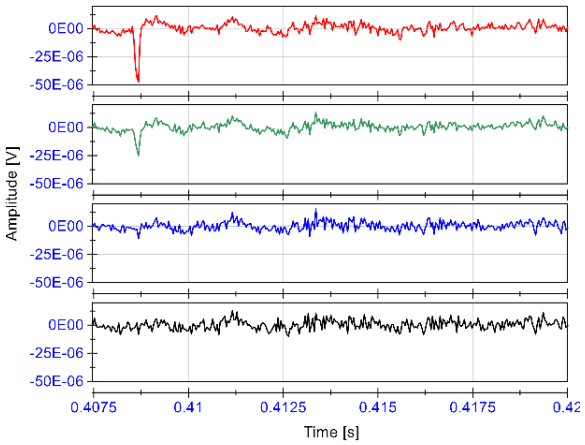

Fig. 7. Traces of a neural spike on the first and second channels of recorded data after digital high-pass filtering.

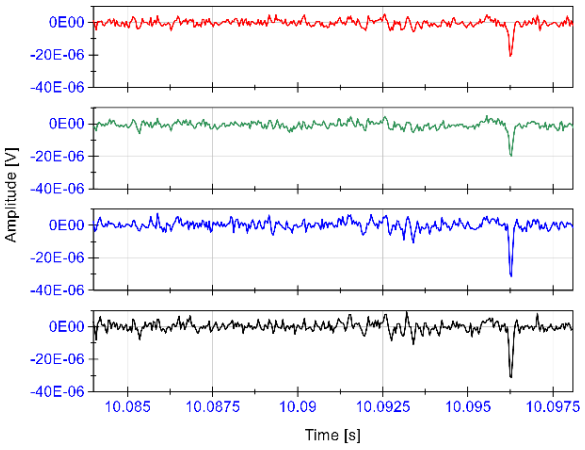

Fig. 8. Traces of a neural spike on all channels of recorded data after digital high-pass filtering.

On Fig. 7 and Fig. 8 traces of neural spikes are clearly seen on recorded data. The registered spikes have about 1ms durations. These spikes are reflected differently on each channel depending on a proximity of the origin of a spike to the corresponding electrode. In our recordings the amplitudes of registered spikes vary from 20μV to 50μV.

5. Conclusion

The designed probes can be easily manufactured from FR-4 plates with means of commercial circuit board plotters. The manufacturing process is relatively easy and can be done in a short amount of time. This results in low cost of the probes.

The geometry of the proposed probes can be easily modified and extended, which gives flexibility for customized probe preparation.

The manufactured electrodes have low impedance, which makes them suitable for use even with relatively low input impedance registering devices. We were able to register neural spikes with designed probes without using preamplifiers and analog filters.

Acknowledgements

The surgeries were conducted in Yerevan State Medical University and the recordings have been done in Armenian National Engineering Laboratories (ANEL) with a support from ISTC research grant program.

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