Published in final edited form as:

IEEE Biomed Circuits Syst Conf. 2018 March 29; 2017: 1–4. doi:10.1109/BIOCAS.2017.8325216.

Acquisition of Bioelectrical Signals with Small Electrodes

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Abstract

Although the mechanisms of recording bioelectrical signals from different types of electrogenic cells (neurons, cardiac cells etc.) by means of planar metal electrodes have been extensively studied, the recording characteristics and conditions for very small electrode sizes are not yet established. Here, we present a combined experimental and computational approach to elucidate, how the electrode size influences the recorded signals, and how inherent properties of the electrode, such as impedance, noise, and transmission characteristics shape the signal. We demonstrate that good quality recordings can be achieved with electrode diameters of less than 10 μm , provided that impedance reduction measures have been implemented and provided that a set of requirements for signal amplification has been met.

I Introduction

Advances in microfabrication technology enable the integration of various sensing functionalities into monolithic microelectronic microsystems. For diagnostic applications, it is conceivable that integrated microelectronic systems are so small ($< 10^3 \mu\text{m}^3$) that they may even freely move with blood circulation in a human body while they record signals. Such systems would require sensing electrodes that are as small as possible. The electrode properties (size, material, etc.) greatly influence the quality of the recorded signals [1]. A common assumption is that large electrodes (diameter $> 50 \mu\text{m}$) are well suited for recording low-frequency signals, such as cardiac signals, while smaller electrodes (diameter $< 20 \mu\text{m}$) are prevalently used to detect signals of higher frequency, such as neuronal extracellular action potentials [2]. The effects of the electrode size on the performance of neural recording has reported in [3], however the boundary conditions and limitations for using smaller electrodes ($< 10 \mu\text{m}$ diameter) and considering the full recording chain have not yet been studied in sufficient detail.

The obvious question is, how small can electrodes be designed to achieve good signal quality and information content, given the constraints imposed by the applied technology. We approach this question by first assessing how a signal evolves during recording. Figure 1 shows the bioelectric signal recording chain and the respective noise sources. Two main factors influence the recording performance of microelectrodes: (1) signal attenuation due to spatial averaging, which depends on the electrode size, and due to the impedance characteristics of the recording electrode; and (2) thermal noise of the electrode. The bioelectrical signals of interest are attenuated along the overall recording chain and may be

compromised by noise until they are digitized and stored for analysis. Through experimental and computational approaches, we characterized the effects of electrode size and of the readout channel characteristics on the quality of the recorded signals.

This paper is organized in 4 sections. Section II presents the effects of electrode size and impedance on signal attenuation. Section III describes the noise characteristic of electrodes of various sizes and impedance reduction methods. Section IV concludes the paper.

II Signal attenuation

A Spatial-averaging determined by the electrode size

Spatial-averaging of the signals due to the electrode size influences the level of detail of bioelectrical signals that can be extracted. We quantified the spatial-averaging in dependence of the electrode size by using a stimulating micropipette (square-wave stimulation, 1000 Hz, 50 nA) in saline solution close to the electrode as a known point current source, as shown in Figure 2a. To measure the signal spreading at micrometer scale, we recorded the signal of the micropipette, which was moved parallel to the planar electrode surface (Figure 2b) from the center of the electrode to up to 20 μm distance. To record the signals from the electrodes, onchip amplifiers in the HD-MEA [4] were used. The recordings were done for two electrode sizes $e11$ (86 μm^2) and $e14$ (11 μm^2). We also simulated (in Matlab) the signal spreading by using the method of images (MoI), which was used to fit the measurements as shown in Figure 2c. The closer the source was to the electrode, the larger was the effect of spatial averaging by the electrode. For example, when the signal source was at an x-y distance of 1 μm , a 25% signal amplitude attenuation was detected for using an 86 μm^2 electrode as compared to a 11 μm^2 electrode. However, if the signal source was at 20 μm distance, both electrode sizes (11 μm^2 and 86 μm^2) provided almost the same signal amplitude.

B Effect of electrode impedance on signal recording

The electrode size or surface area directly influences the impedance of the electrodes, which is another contributor to signal attenuation in the signal recording chain. The ratio of electrode impedance (Z_{el}) to amplifier-input impedance (Z_a) and the routing (or shunt) capacitance influence the recorded signal magnitude [5]. Figure 3a shows the equivalent-circuit model of a recording channel, from the signal source (here a neuron) to the amplifier input, adapted from [6]. Parasitic capacitances (C_p) largely contribute to signal attenuation due to the long connections between electrodes and amplifiers. The effective input impedance of a voltage amplifier is mainly dependent on the amplifier configuration. In the case of a closed-loop type amplifier [7], a large input capacitance (C_i) and a small feedback capacitance (C_f) are used to achieve a high gain, which results in a low effective input impedance ($Z_a = 1/\omega \cdot (C_i + C_a)$). In contrast, the input impedance of an open-loop amplifier [8] is mainly depending on the input transistor gate capacitance (C_a), which is usually an order of magnitude lower than C_i .

The signal attenuation in dependence of the impedance ratio (Z_{el}/Z_a) was simulated for bright Pt and Pt-black electrodes for electrode sizes from $100 \times 100 \mu\text{m}^2$ down to $1 \times 1 \mu\text{m}^2$

and confirmed through measurements (Figure 3b-c). Pt-black has been electroplated onto the electrodes to reduce their impedance, as it effectively increases the overall electrode surface area while the geometric area is preserved. Four electrode sizes were used for the measurements. An artificial signal, an alternating voltage of 1 mV peak to peak at 1 kHz was applied to the saline solution, and the resulting signals were acquired from each type of electrode. The recording voltage amplifier was used in closed-loop configuration with an input capacitance of 3.8 pF (41 MΩ at 1 kHz). For simulation, an estimated unit capacitance of 0.2 pF/μm² was used for bright Pt electrodes and 30 pF/μm² was used for Pt-black electrodes [9]. As expected, the ratio between Z_{el} to Z_a played an important role for signal recording. We saw significant attenuation (70%) in the measured signals for the smallest electrode el4 (bright Pt), which is due to the fact that the electrode impedance is comparable to the input impedance of the voltage-recording amplifier (Figure 3b-c). By reducing the absolute electrode impedance through Pt-black deposition, the signal attenuation effect was reduced to < 2% for all four different electrode sizes. For the case of the simulated 1×1 μm² electrode, the signal attenuation was reduced from > 95% to < 5% through Pt-black deposition. We found that the signal attenuation was below 5%, if the electrode impedance was 10 times lower than the amplifier input impedance. In the measurement setup, the parasitic capacitance (C_p) was estimated to be 0.5 pF. To see the effects of the parasitic capacitance on signal attenuation, C_p was swept (from 0.1 to 10 pF) while keeping the same amplifier input impedance (3.8 pF). A lower impedance ratio (realized through Pt-black deposition or the use of larger electrodes) was needed to cope with the higher parasitic capacitances.

Small electrodes (with diameters of less than 5-10 μm) have high impedance and require amplifiers with very high input impedance, which is usually hard to realize in experimental setups. A suitable impedance ratio (Z_{el}/Z_a) needs to be established (by applying impedance reduction techniques like Pt-black deposition) for optimizing the electrode-amplifier interface matching.

III Noise characteristics of the electrode

Two main types of noise interfere with the signals recorded by microelectrodes: (1) the inherent thermal noise of the electrodes and (2) the noise of the recording amplifiers. The quality of recordings and the signal-to-noise ratio (SNR) depend on how well the signal of interest can be acquired in the presence of noise from the various sources in the recording chain. Thermal noise adds to the recorded signal at each electrode. Decreasing the size of microelectrodes results in an increase in their impedance—the major contributor of their intrinsic thermal noise [6][10]. The equivalent thermal noise can be calculated as follows:

$$v_n = \sqrt{4kT\text{Re}(Z_e') \cdot \Delta f} \quad (\text{eq. 1})$$

where k is the Boltzmann constant, T is the absolute temperature, $\text{Re}(Z_e')$ is the real part of the effective electrode impedance, and Δf is the noise bandwidth. The real part of the impedance was measured for all electrode sizes (Figure 4a-b), and the equivalent integrated noise over different frequency bands was estimated (using the eq. 1) as shown in Figure 4c.

Both, bright Pt and Pt-black electrodes show higher noise at low frequencies and a plateauing of the noise level (dominated by the thermal noise of spreading resistance, R_s) at higher frequencies. The noise of bright Pt electrodes was generally higher across all frequency bands, especially in the low-frequency band. Lowering the electrode impedance reduced the electrode-size dependence of the noise and turned out to be extremely important for low-frequency signal acquisition (e.g., cardiac signal recoding). Low electrode impedances can be achieved through applying coatings, which increase the overall surface area while preserving a small geometric electrode area, such as Pt-black or poly-3,4-ethylenedioxythiophen (PEDOT) [11] [12].

IV Conclusion

We have shown, through experimental and computational analysis, how sub-10 μ m electrode diameters influence the quality of bioelectrical signal recordings. We investigated and quantified the effects of signal attenuation, caused by spatial-averaging effects, which depend on the electrode area and the impedance ratio of electrode and amplifier input impedance. To keep the attenuation low, an impedance ratio $Z_{el}/Z_a < 0.1$ is sufficient for electrodes of less than 10 μ m diameter. Electrode-impedance reduction (e.g., through Pt-black deposition) was of pivotal importance to achieve low noise values, especially in the low-frequency band. Our results showed that good-quality recordings can be achieved with electrode diameter of less than 10 μ m.

Acknowledgments

The authors thank A. Stettler and Albert Martel, ETH Zurich for the electrode post-processing. This work was supported by the European Community through the European Research Council Advanced Grants 267351 'NeuroCMOS' and 694829 'neuroXscales', as well as the Swiss National Science Foundation through Grant 205321_157092/1. Felix Franke acknowledges individual support through an Ambizione Grant PZ00P3_167989.

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Figure 1. Bioelectrical signal recording chain.

The electrical signals of interest are attenuated along the overall recording chain and compromised through noise until they are digitized and stored for analysis. The surface area of the electrode determines the impedance of the electrode (Z_{el}), and the impedance determines the electrode noise (n_{el}); the ratio of electrode impedance to amplifier input impedance ($Z_{el}:Z_a$) directly affects signal attenuation.

Figure 2. Spatial signal averaging according to electrode size.

a) Schematic side view of the experiment, where the stimulating pipette constituted a known point source at a z -distance of $7 \mu\text{m}$ from the electrode array in saline solution. The pipette was kept at the same z -distance during movements in the x - y plane. **b)** Pt electrodes of four different sizes (el1: $86 \mu\text{m}^2$; el2: $44 \mu\text{m}^2$; el3: $22 \mu\text{m}^2$; el4: $11 \mu\text{m}^2$) fabricated on a CMOS high-density microelectrode array [4]. **c)** Simulation of four electrode sizes (el1-4) and experimental recordings (el1, el4) of the signal amplitudes, as detected by the recording electrodes, while the pipette was moved in the x - y plane.

Figure 3. Electrode impedance and effect on signal attenuation.

a) Equivalent-circuit model of a metal microelectrode for electrophysiology recordings as adapted from Robinson (1968). Figures **(b, c)** show the attenuation of the recorded signal through bright Pt and Pt-black electrodes for different electrode sizes. The amplifier input capacitance was taken as 3.8 pF based on measurements, and the shunt capacitance was swept between 0.1 pF to 10 pF as shown in the figures. The measured signal attenuation due to electrode size/impedance is shown for 4 electrode sizes. Blue lines represent bright Pt electrodes, and black lines represent the Pt-black electrodes.

Figure 4.

(a, b) Electrode impedance of electrodes of various sizes as a function of frequency. (c) Integrated noise of bright Pt electrodes and Pt-black electrodes computed from the real part of the measured electrode impedance.