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Technical Support of Intracranial Single Unit Activity Measurement

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***Abstract*—**The article deals with technical support of intracranial single unit activity measurement. The parameters of the whole measuring set were tested in order to assure the optimal conditions of extracellular single-unit recording. Metal microelectrodes for measuring the single-unit were tested during animal experiments. From signals recorded during these experiments, requirements for the measuring set parameters were defined. The impedance parameters of the metal microelectrodes were measured. The frequency-gain and autonomous noise properties of preamplifier and amplifier were verified. The measurement and the description of the extracellular single unit activity could help in prognoses of brain tissue damage recovery.

***Keywords*—**Measuring set; metal microelectrodes; single-unit; noise; impedance parameters; gain characteristics.

I. Introduction

INTRACRANIAL measurement of extracellular single unit activity (single-unit) can be useful for diagnostics. The measurement and evaluation of the local single-unit potential can inform us about an instantaneous neurophysiologic state of a brain tissue and its possible damage. Research on the field of neurophysiology deals with oxygen level effect on the brain physiological function [1]–[4].

The study of reversibility or irreversibility of the brain tissue damage in patients hospitalized at a shock trauma centre is the goal of this research. The results of this research might lead to a prediction of brain tissue recovery. Recently, not only improvement of blood oxygenation and carbon dioxide elimination is the main goal of the artificial lung ventilatory (ALV) support; nevertheless, joint effects of the ALV support upon the brain tissue and other physiological structures are in the centre of interest. This either short-time or long-time effects may result in a further damage of the brain tissue. The direct damage depends on the level of oxygenation, other arterial blood gases, metabolites, and many other parameters. The forced improvement in oxygenation regardless of an influence upon the other parameters can even cause damage to other organs. The main aim of the research is to specify criteria for application of a safe ventilatory strategy. The level of the brain tissue oxygenation has not only effect on a single-units appearance frequency, but on shape of the single-units as well. The effect alters the amplitude and time length of the single-unit [5]–[7]. The accurate description of the single-unit properties requires a suitable measuring apparatus. The aim of this article is to define technical criteria for intracranial measurement of the extracellular single unit activity. To assure the accurate measurement, it is necessary to focus on all individual parts of the measuring set.

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II. Methods

A projection of intracellular action potential to the extracellular space is referred to as single-unit. The shape of the single-unit, as it is for example presented by Nadasdy [8], contains both fast and slow changes of the potential. The most rapid change in amplitude, referred to as the fast sodium spike, is caused by current of the fast sodium channels. The consequent slower changes of the potential are produced by slow potassium channels. Exact measurement of both the high and low frequencies in single-unit spectra are necessary for analysis of the single-unit shape.

A set of single-units has been measured during animal experiments which were primarily intended for finding suitable electrodes for the extracellular measurement. The size of the fast sodium spike of the measured single-units can reach voltage of 150 μV. The typical duration of single-units was several milliseconds in average (Fig. 1).

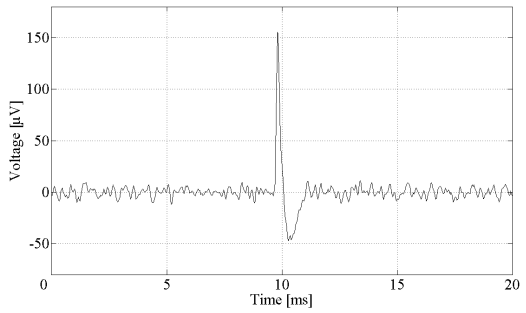

Fig. 1 Typical shape of single-unit recorded during the animal experiments in rats.

The spectral analysis of the measured single-units has been done. The biggest content of the single-unit energy in the frequency spectrum has been found in the frequency range

between 300 Hz and 6 kHz, with the maximum energy at 1 kHz approximately (Fig. 2). These parameters have been used for determination of basic requirements characterising the measuring set. Therefore, the following parameters of the set were measured and verified: impedance parameters of the metal microelectrodes, frequency-gain and autonomous noise properties of the preamplifier and amplifier.

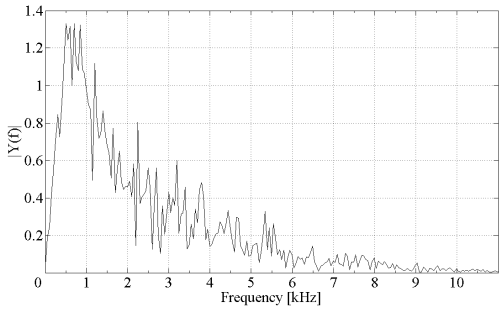

Fig. 2 The frequency spectrum of the measured single-unit presented in Fig. 1

A. Measuring System

The extracellular single unit activity was magnified by isolated preamplifier Alpha-IsP (ALPHA OMEGA ENGINEERING, Israel). The Alpha Omega Alpha-IsP is a low-noise isolated preamplifier. The dynamic input range of the preamplifier is ±400 mV. The input impedance of the preamplifier is 10 MΩ. The frequency response is within the range of 0.1 Hz and 10 kHz. The voltage gain of the preamplifier is 10. The isolation voltage of the preamplifier is 3500 V root-mean-square (RMS).

The isolated preamplifier Alpha-IsP was connected to signal amplifier MCP Plus 8 (ALPHA OMEGA ENGINEERING, Israel). The amplifier is intended for optimal measurement using extracellular microelectrodes. The dynamic range of the amplifier is ±10 V and the maximum value of amplification is 2500. The amplifier includes two Butterworth filters. The first of the filters is a high-pass 2-pole Butterworth filter with a cut-off frequency adjustable between DC and 1 kHz. The second filter is a low-pass 4-pole Butterworth filter with a cut-off frequency adjustable between 100 Hz and 10 kHz. The input impedance is 1 MΩ||2 pF. The noise RMS value of the amplifier within the frequency range of 1 Hz and 10 kHz is less than 10 mV.

B. Microelectrode Selection

The selection of the suitable metal microelectrodes impedance value was based on the minimization of noise in the measured intracranial signal recorded in living laboratory animals. The extracellular single unit activity was measured by metal microelectrodes TM33BXXKT (World Precision Instruments, Inc., USA) made of a compound of platinum and iridium. Electrodes impedance was between 0.1 and 2.0 MΩ. The frequency filter of the amplifier was set between 300 Hz and 6 kHz, its gain was set to 1000. The gained signal was digitalized using a 16-bit A/D convertor NI-DAQ 9215 (National Instruments Corporation, USA) at a sampling rate 30 kHz and the chosen voltage range was ± 1 V. The data were recorded by PC/AT computer using LabVIEW SignalExpress (National Instruments Corporation, USA) software. Processing and evaluation of the recorded data were conducted with Origin 6.0 (Microcal software, USA) and Matlab R2007a (The MathWorks, Inc., USA) software.

The animal experiments were approved by the Animal Care and Use Committee of the Institute of Physiology in order to be in agreement with the Animal Protection Law of the Czech Republic (fully compatible with European Community Council directives 86/609/EEC). Albio Wistar rats, weighing between 250 and 350 g, from the breeding station of the Institute of Normal, Pathological and Clinical Physiology were used in this study. They were maintained under standard conditions (light/dark cycles 12/12 h, humidity 60 %, temperature 23 ± 1 °C). The rats were anesthetized by intramuscular injection of a combination of ketamine (Narkamon 5 %, 100 mg/kg) and xylazine (Rometar 2 %, 16 mg/kg) [9]. According to the Swanson atlas, the stereotaxic coordinates of the introduced sensing electrode in the brain were: AP 3–5 mm, LL 1–2 mm and DV 1–3 mm to the bregma. A reference silver electrode was placed subcutaneously close to the left ear.

C. Impedance Parameters of the Microelectrodes

A microelectrode and physiological solution boundary was used during the microelectrode's impedance parameters measurement.

A 5-litre glass dish filled up with physiological solution (0.9 % NaCl solution in distilled water) was used for the impedance parameters measurement. A pair of the metal microelectrodes of the same nominal value of impedance was immersed in the solution. This nominal value of the electrode's impedance is declared by the manufacturer for the sinusoidal signal with a harmonic frequency of 1 kHz. The distance between the tips of the microelectrodes was 10 mm. A precision LCR Meter 4284A (Agilent, USA) was connected to the metal microelectrodes using a four-point (volt-ampere) impedance measuring method. The impedance parameters of the microelectrodes were measured within the frequency range of 20 Hz and 10 kHz.

D. Frequency-Gain of Preamplifier and Amplifier

The frequency-gain of preamplifier and amplifier was measured to verify the frequency pass-band declared by the manufacturer. The defined signal generator Sweep Function Generator 9205C (Protek, USA) was used as a source of the sinusoidal signal. The frequency range was set from 10 Hz to 10 kHz. The amplitude of the sinusoidal signal was adjusted to a value of 2.5 mV. The digital oscilloscope DSO3202A Oscilloscope (Agilent Technologies, USA) was used for displaying the measured signal from the amplifier and the generator. The band-pass of the amplifier was set from DC to 10 kHz. The total gain value of the preamplifier and amplifier pare was set to 1000.

E. The Autonomous Noise Parameters of the Preamplifier and Amplifier

The complete measuring set under the test was placed into an electromagnetic shielded chamber. The shielded chamber with the dimensions of 2x2x3 m is made of metal plates inlaid with ferrite absorbers. Its shielding efficiency value is 100 dB. The power supply line voltage intended for devices inside the chamber is filtered by an input-line filter. Furthermore, the power supply line voltage is brought to the Line Impedance Stabilization Network (LISN) inside the chamber. Any interference present in the power supply voltage is suppressed by LISN.

A 500 Ω resistor was connected to the preamplifier input. The active shielding input of the preamplifier was connected to the negative input of the preamplifier. Output of the amplifier was connected to a spectral analyzer Agilent E4440A (Agilent Technologies, USA) situated outside from the shielded chamber. The frequency range of the spectral analyzer is 3 Hz to 26.5 GHz. The absolute accuracy of the spectral analyzer is ±0.19 dB. The autonomous noise parameters of the preamplifier and amplifier were measured in the range from 10 Hz to 10 kHz.

III. Results

The metal microelectrodes seem to be suitable for measurement of the extracellular single unit activity. The metal microelectrodes yield a stable course of signal with a high signal-to-noise ratio. The impedance of the electrodes measured at 1 kHz harmonic signal fluctuated by 50 % of their nominal value declared by the producer. The electrode impedance 1 MΩ was found as the best value for the extracellular single unit activity measurement. Electrodes with this impedance have the best value of signal-to-noise ratio.

As illustrated in Fig. 3, the impedance of the microelectrode and physiological solution boundary wasn't higher than 2 MΩ within the tested frequency range.

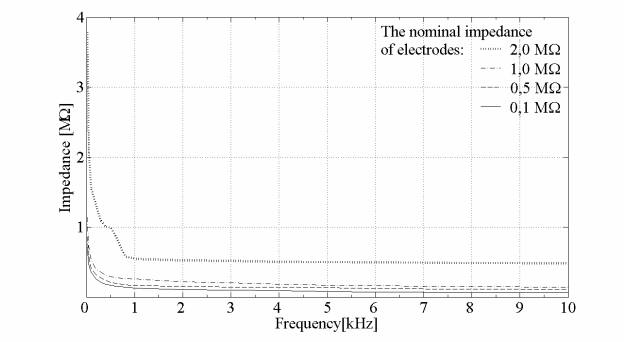

Fig. 3 The measured impedance of the metal microelectrodes of different nominal impedances.

Gain of the amplifier was flat within the whole frequency range of the single-unit and its value was 60 dB (Fig. 4).

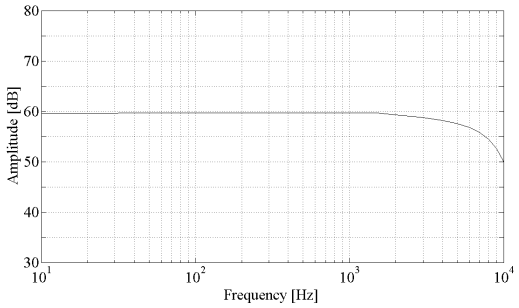

Fig. 4 Gain of the preamplifier and amplifier

The power spectrum was measured in order to determine the autonomous noise parameters of the preamplifier and amplifier. As presented in Fig. 5, the produced noise is frequency dependent with significant spikes at a frequency of 50 Hz (supply noise) and its corresponding high order harmonics. The mean value of the autonomous noise was −120 dBm, which is equivalent to a value of the power −150 dB. In contrast, the typical power of measured single-unit was −70 dB. Without the power supply interference, the signal-to-noise ratio of the amplifier with the preamplifier reached a suitable value of 80 dB. The effect of the autonomous noise of the preamplifier and the amplifier on the measured signal can be regarded as insignificant. The suppression of this supply noise is possible by suitable filters. The other possibility of filtering is using a software frequency filter in a computer. A suitable method for filtering the interference in a computer is an adaptive weight filter [10], [11].

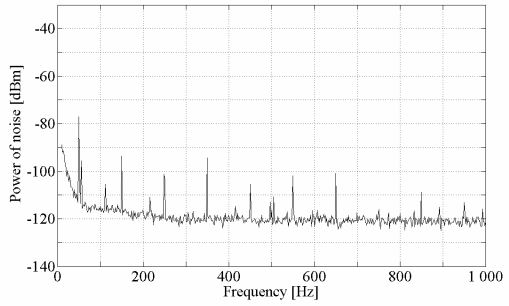

Fig. 5 Autonomous noise spectrum of the preamplifier and amplifier.

IV. Discussion

As described above, the unstable value of the metal electrodes impedance introduces an error into the measurement of single-units. This negative property of the metal microelectrodes may be caused by properties of the electrode and solution boundary.

As a result of a consultation with the producer of the metal microelectrodes, a methodology of electrodes preparation before the measurement was designed. It is necessary to de-oxidize the electrode first by passing a negative 3 volts across

the electrode. Hydrogen gas will evolve that will not only de-oxidize the surface but will clean it of any possible pollution. A calibration of the electrode impedance is suitable after this cleaning process.

Much stable impedance values are performed by conventional glass reference microelectrodes, but their big disadvantage is possibility of breaking the glass tip that, when it remains in the brain tissue, can cause serious problems.

V. Conclusion

Single unit activity was measured in laboratory animals in order to specify the technical requirements for a measuring set suitable for extracellular single-unit potential recording. With respect to these technical requirements, a measuring set was assembled and its parameters were verified. The final measuring system is suitable for extracellular monitoring of unit activity in the brain tissue.

References

[1] Dale, N., Pearson, T., Frenguelli, B. C.: *Direct measurement of adenosine release during hypoxia in the CA1 region of the rat hippocampal slice.* J Physiol, London, vol. 526, 2000, pp. 143–155.

[2] Pedata, F., Latini, S., Pugliesi, A. M., Pepeu, P.: *Investigations into the adenosine outflow from hippocampal slices evoked by ischemia-like conditions.* J Neurochem, vol. 61, 1993, pp. 284–289.

[3] Sattler, R., Xiong, Z., Lu, W-Y, MacDonald, J. F., Tymianski, M.: *Distinct roles of synaptic and extrasynaptic NMDA receptors in excitotoxicity.* J Neurosci, 2000, vol. 20, pp. 22–33.

[4] Nieber, K., Sevsic, J. a Illes, P.: *Hypoxic changes in rat locus coeruleus neurons in vitro.* J. Physiol., vol. 486, 1995, pp. 33–46.

[5] Englund, M., Bjurling, M., Edin, F., Hyllienmark, L., Brismar, T.: *Hypoxic Excitability Changes and Sodium Currents in Hippocampus CA1 Neurons.* Cellular and Molecular Neurobiology, vol. 24, no. 5, 2004, pp. 685–694.

[6] Sebastião, A. M., de Mendonc¸ A., Moreira, T., Ribeiro, J. A.: *Activation of Synaptic NMDA Receptors by Action Potential-Dependent Release of Transmitter during Hypoxia Impairs Recovery of Synaptic Transmission on Reoxygenation.* The Journal of Neuroscience, November 1, vol. 21, no. 21, 2001, pp. 8564–8571.

[7] Hansen, A. J., Hounsgaard, J., Jahnsen, H.: *Anoxia increases potassium conductance in hippocampal nerve cells.* Acta physiol. Scand., vol. 115, 1982, pp. 301–310.

[8] Nadasdy Z., Csicsvari J., Penttonen M., Hetke J., Wise K., Buzsaki G.: *Extracellular recording and analysis of neuronal activity: from single cells to ensembles.* In: Neuronal Ensembles: Strategies for Recording and Decoding, edited by Eichenbaum HB and Davis JL. New York: Wiley-Liss, 1998, pp. 17–55.

[9] Vaculín, Š., Franěk, M. and Rokyta, R.: *Dorsal Rhizotomy Changes the Spontaneous Neuronal Activity of Nuclei in the Medial Thalamus.* Physiological research, 49, 2000, pp. 279-283.

[10] Štork, M.: *Jednodimenzionální nelineární digitální filtry I.* AUTOMATIZACE, vol. 48, no. 6, 2005, pp. 382–385.

[11] Štork, M.: *Jednodimenzionální nelineární digitální filtry II.* AUTOMATIZACE, vol. 48, no. 7–8, 2005, pp. 446–450.