The 4th IEEE International Conference on E-Health and Bioengineering - EHB 2013
Grigore T. Popa University of Medicine and Pharmacy, Iaşi, Romania, November 21-23, 2013

Concentric Bipolar Active Electrode for Noninvasive Biopotential Measurement in Autonomic Nervous System

S. Hasegawa, Y. Aoki, S. Wada, A. Ueno
Department of Electrical and Electronic Engineering
Graduate School of Engineering, Tokyo Denki University
Tokyo, Japan
ueno@mail.dendai.ac.jp

Y. Fukuoka
Department of Electrical Engineering
Kogakuin University
Tokyo, Japan

G. Cauwenberghs
Department of Bioengineering,
Jacobs School of Engineering, UCSD
La Jolla, USA

Y. Shimizu, N. Nishimura, S. Iwase
Department of Physiology
School of Medicine, Aichi Medical University
Nagakute, Japan

***Abstract*— This study investigates a concentric bipolar active (CBA) electrode with ultra-high input impedance for non-invasive measurement of biopotentials from the autonomic nervous system (ANS). Experiments involving Valsalva maneuvers (VM) conducted with 4 male subjects showed spike-like potentials that resembled neural potentials recorded directly with microelectrodes from autonomic nerve. Spike-like bursts in two subjects showed a pattern similar to those observed in previous microneurographic studies following the changes in blood pressure during VM. Comparison of both spike-like potential and spectrogram detected by the CBA electrode with an electromyogram simultaneously recorded from neighboring muscles indicated independence between the signals from the CBA electrode and electromyogram. These results suggest that the biopotential signal recorded using the proposed electrode originates from nerve fascicles in ANS, indicating potential of the proposed electrode in noninvasive ANS measurement.**

Keywords*— *microneurography, noninvasive measurement, autonomic nervous system, concentric bipolar active electrode

I. INTRODUCTION

Action potentials of single nerve fibers in the autonomic nervous system (ANS) are typically recorded in direct contact with a tungsten microelectrode, inserted percutaneously into the nerve fascicles. This recording technique is employed not only in neurophysiological research [1] but also in clinical examinations [2] and for other neural interfaces [3]. Since the microelectrode is inserted into a nerve fascicle, this approach may cause algia and transient paresthesia along the nerve, particularly when adjustment of the electrode position takes considerable time by beginners. Also, some training and proper precautions are required for performing the measurement. Therefore noninvasive means to measure biopotentials originating from ANS nerve fascicles can be beneficial even with the limited spatial resolution falling short of individual fiber recording. Noninvasive techniques reduce the amount of training and risk of algia, and may be applicable to a wider range of ANS evaluations.

There are two challenges for realizing noninvasive recording of biopotential from nerve fascicles using surface electrodes: one is attaining high accuracy with high-impedance sensing over a larger frequency range (500-2000Hz) than electromyogram (EMG) measurement through insulating membranes that bundle the nerve fibers; and the other is exclusion of biopotentials not originating from neural activity. For the high-impedance biopotential sensing, we introduced a measurement technology used for an insulator electrode. Recently, Ohtsu et al. proved that an electrode coated wholly with insulating material and coupled capacitively with the body muscle was capable of sensing EMG using an ultra-high input impedance amplifier [4]. This implies biopotential from nerve fascicles may be detected by a similar measurement scheme, though the frequency component of neural action potential is higher than that of EMG. As for the exclusion of biopetential not originating from nervous activity, we adopted a configuration of concentric bipolar electrode. The concentric bipolar electrode is a type of Laplacian electrode [5]. It is known that body surface biopotential obtained with the Laplacian electrode is negatively proportional to the normal derivative of the normal component of current density at the body surface [6]. Accordingly, the Laplacian electrode is considered to be sensitive to the activity of a current source directly beneath the measurement site acting as a spatial filter. This implies that

This research was supported in part by a grant for Strategic Research Foundation Grant-aided Projects for Private Universities from MEXT, Japan, 2008 and in part by KAKENHI (24650300).

978-1-4799-2373-1/13/$31.00 ©2013 IEEE

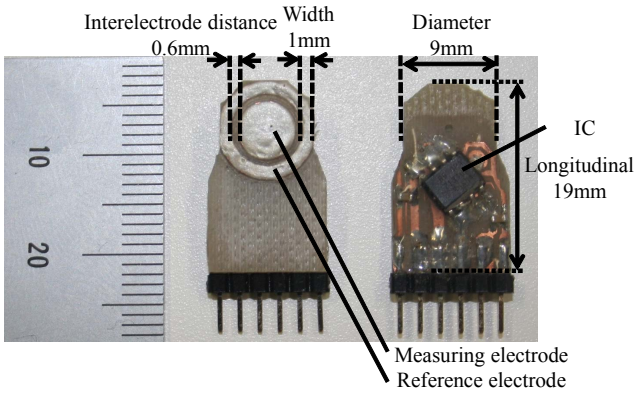


Fig. 1. Front view (left) and rear view (right) of the CBA electrode used in this study.

when an electrode is placed appropriately above a target nerve fascicle, the signal obtained with a concentric bipolar electrode is less susceptible to interferences caused by the activity of neighboring muscles than a conventional body surface electrode [7].

The present study aimed at exploring the potential of a concentric bipolar active (CBA) electrode with ultra-high input impedance for noninvasive biopotential measurement from nerve fascicles in ANS.

II. MATERIALS AND METHODS

A. CBA Electrode

Fig. 1 shows front and rear views of the fabricated CBA electrode. Concentric bipolar scheme consisted of measuring and reference electrodes, which are made of copper and coated with Ag/AgCl. Central disk and outer ring were assigned to the measuring electrode and the reference electrode, respectively. Two buffers were mounted on the back of the CBA electrode. A commercial IC, which incorporated two operational amplifiers with ultra-high input impedance (10TΩ // 2pF), was used. The two output signals were connected to a subsequent signal detection circuit.

B. Signal Detection Circuit

Fig. 2 shows a block diagram of the signal detection circuit. The differential amplifier was used to improve the common mode rejection ratio (CMRR). The cut-off frequency of the high-pass filter was set to 500 Hz to avoid interference by EMG from muscles neighboring the targeted nerve. The cut-off frequency of the low-pass filter was set to 2,000 Hz according to previous papers [8][9]. Total gain of the signal detection circuit was 20,000. CMRR ranged from 100 to 115 dB in the pass-band. Two sets of electrodes were used to increase success rate of the measurement.

C. Localization of Target Sites for Electrode Placement

Target sites on the body surface above median nerve of left forearm near cubital fossa were explored using an electrical stimulator (SEN-3401, Nihon Kohden Co.). The most sensitive two sites to the electrical stimulation were selected as the target sites. Intensity of the stimulation was set to the

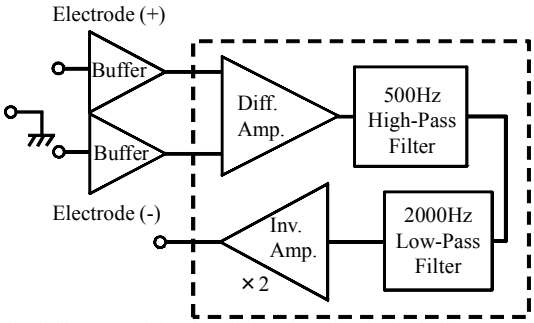


Fig. 2. Block diagram of the signal detection circuit (dashed square).

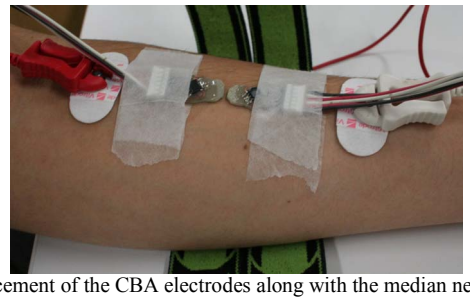


Fig. 3. Placement of the CBA electrodes along with the median nerve and of commercial disposable electrode for EMG detection.

sensation threshold of each subject. Since median nerve lies in a relatively shallow layer in forearms, little signal attenuation by mediated tissues was anticipated This provides convenient means to compare the obtained signal with previously reported results recording neural activity from the median nerve.

D. Measurement during Valsalva Maneuver Experiment

Four healthy male human subjects (ranging in age from 21 to 23 years) took part in the experiment. None of the subjects reported any history of neurological/cardiovascular disorder. This study was conducted in accordance with Helsinki Declaration guidelines and approved by the Institutional Review Board of Tokyo Denki University. The protocol was explained to the subjects prior to the experiment, and written informed consent was obtained from each subject.

All experiments were conducted in a shielded tent (SR403T, Tokyo Keiki Co.). Two CBA electrodes were placed side by side on the target sites as shown in Fig. 3. Target sites were determined by the method in Section II-C. Physiological saline water was applied on the target skin before electrode attachment. An Ag electrode (NE-155A, Nihon Kohden Co.) was placed on a fingernail with electrolyte paste as the reference electrode.

Valsalva maneuver (VM) was employed in the experiment to increase sympathetic nerve activity of the subjects. The subjects were instructed to perform VM for 15 s with expiratory effort against a closed airway at a constant intrathoracic pressure of 40 mmHg. A manometer (HT 1500N, Hodaka Co.) was used for monitoring the intrathoracic pressure. The normal physiological response during a VM consists of four phases: I) initial pressure rise, II) reduced venous return and compensation by blood vessel constriction, III) release of chest pressure and IV) return of cardiac output. Previous studies based on microneurography (MNG) revealed

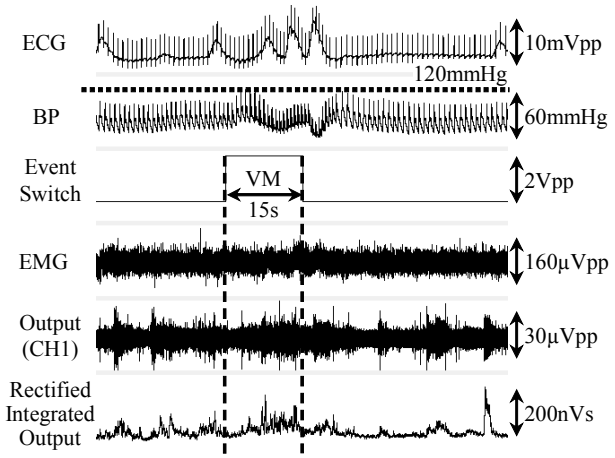


Fig. 4. Example of the measured signals in the subject #1. From top to bottom, the trace shown denotes ECG, BP, event signal generated during a Valsalva maneuver, EMG, output from one of the CBA electrodes, and integrated signal of the rectified output.

that muscle sympathetic nerve activity could be markedly enhanced in phases II and IV followed by a decrease in blood pressure [8].

Each experimental session began after enough resting period (more than 5 min) to ensure stable baseline measurements. Each subject performed VM twice in a session, during which an experimenter pressed an event switch to distinguish the VM period from the normal breathing period. Interval between the two VMs was 60 s or longer so that the blood pressure and heart rate returned to the normal before the second VM. Output signals recorded with the proposed CBA electrode, EMG, blood pressure (BP) and electrocardiogram (ECG) were measured simultaneously. Electrodes for EMG measurement were placed around the CBA electrodes to investigate whether or not muscle activity contaminated the outputs from the CBA. The BP was measured with a commercial continuous sphygmomanometer (Finometer MIDI, Finapres Medical Systems). All these signals were digitized with a 16-bit analog-to-digital converter (MP-150 System, BIOPAC System) at 10 kHz sampling.

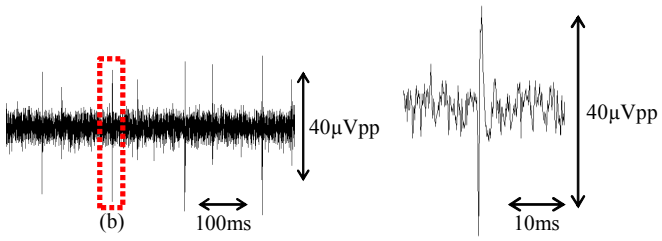
E. Measurement during Muscle Contraction Experiment

In order to examine an effect of muscle contraction (MC) on the output signal of the CBA electrodes, a measurement involving MCs was conducted for one of the subjects. The same measurement sites as in Section II-D were used for the CBA electrode and for EMG electrodes. The subject held a handgrip in the left hand and closed the hand for 10s in accordance with the experimenter's instruction. The experimenter pressed the event switch to distinguish the MC period from the normal holding period. The event signal and all other signals measured in Section II-D were recorded in the same manner.

III. RESULTS

A. Spike-like Potentials during VM Experiment

In order to examine an effect of muscle contraction (MC) on the output signal of the CBA electrodes, a measurement involving MCs was conducted for one of the subjects. The same measurement sites as in Section II-D were used for the CBA electrode and for EMG electrodes. The subject held a handgrip in the left hand and closed the hand for 10s in accordance with the experimenter's instruction. The experimenter pressed the event switch to distinguish the MC period from the normal holding period. The event signal and all other signals measured in Section II-D were recorded in the same manner.



(a) A period during VM (b) Enlarged period in (a)

Fig. 5. Example of the CBA electrode output in (a) a period during VM, and (b) an enlarged period of dashed area in (a).

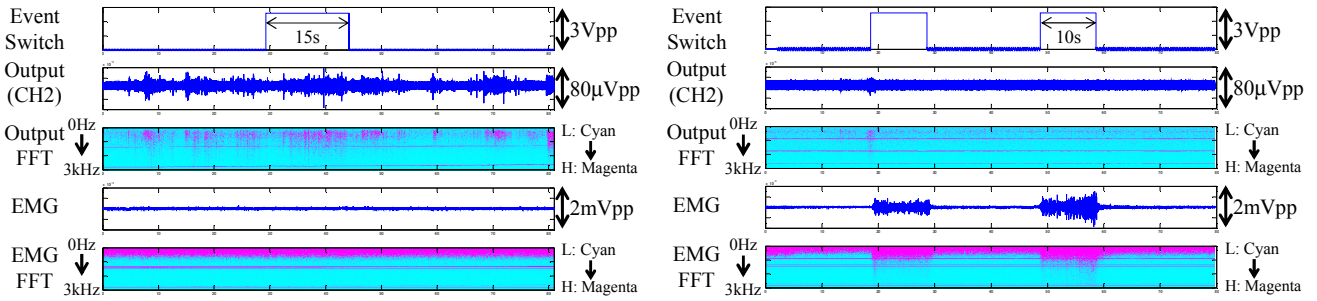
Fig. 5 shows an example of outputs of the CBA electrode in (a) a period during VM, and (b) enlarged period of the dashed area in (a). Some of the detected spikes had biphasic waveform with a duration of 2-3 ms as shown in Fig. 5(b), and the other presented bimodal waveform of similar duration. These waveforms resembled previous results of microneurographic studies in terms of form, amplitude and duration [8][9]. However, in some cases, their amplitude exceeded 200 μV and was relatively larger than that recorded in previous microneurographic studies.

B. Comparison between VM and MC Experiments

Fig. 6 is a comparison of both trace and spectrogram between VM and MC experiments. During the VM experiment in Fig. 6(a), the spectrogram of the CBA electrode output showed strong power (i.e. magenta color) in high frequency domain (> 1 kHz) at the times of spike generation. By contrast, the spectrogram of EMG in Fig. 6(a) indicated weak power (i.e. cyan color) in the high frequency domain except a power of harmonic noise at 1.3 kHz. On the other hand, during the MC experiment in Fig. 6(b), the spectral power of the CBA electrode output showed low intensity over the entire frequency range, and the power of EMG was larger in the frequency range below 500 Hz during MC. These comparisons suggest that output of the CBA electrode and EMG were independent from one another.

IV. DISCUSSION

As shown in Fig. 4 and Fig. 5, the proposed CBA electrode was successful in detecting spike-like potentials noninvasively from the skin surface above the median nerve for all subjects. Given that tissue impedance between the target nerve and the electrode is around a few MΩ due to a dense sheath with high impedance surrounding the nerve, the input impedance of measuring device should be larger than or comparable to 10 MΩ for stable signal detection. Since 16pF input capacitance corresponds to 10 MΩ reactance at 1 kHz,



(a) VM experiment (b) MC experiment

Fig. 6. Comparison of both trace and spectrogram between VM and MC experiments. From top to bottom, the time course variation shown denotes (1) event signal generated by the experimenter, (2) output from one of the CBA electrodes, (3) spectrogram of the above output, (4) EMG and (5) spectrogram of the above EMG; (a) during VM experiment, (b) during MC experiment.

adoptions of the operational amplifier IC having low input capacitance (2pF for the current IC) and of the active electrode structure, which eliminates stray capacitance of electrode lead, are critical for success of detection. Input capacitance of the proposed system was estimated around 20pF (i.e. 8 MΩ at 1 kHz), consistent with limitations in the results. In the measurement for subjects #3 and #4, where the detected spike-like potentials seemed not to be associated with VM, the impedance between autonomic nerve in the median nerve and the electrode might be close in value to the input impedance of the proposed system. Therefore a next challenge is to decrease the input capacitance of the measuring system so as to increase the success rate of measurement of biopotentials from ANS. One of the possible solutions is adoption of a newly developed IC for noncontact biopotential sensing which has only 60-fF input capacitance [11].

As mentioned in Section III-A, amplitude larger than 200 μV was observed in some of the detected spikes. This can be attributed to two potential reasons: one is summed and modulated potential from multiple nerve fascicles; and the other is artifacts by friction between the electrode and the skin. Since the large electrode area enabled the CBA electrode to detect biopotential not from a single nerve fiber but from multiple nerve fascicles, the detected potential might be elevated in a similar manner to that of EMG, in which amplitude of EMG increases with the number of muscle fibers recruited in the contraction. However, we cannot deny a possibility of friction artifact, because conductive paste was not applied on the surface of the CBA electrode. Further experiments are planned to verify the cause of the larger than anticipated amplitudes. Particularly, simultaneous measurement with microneurography will be essential for verification.

The spectrogram in Fig. 6(a) indicates that the detected spikes have frequency components higher than 1 kHz, which is one of the features of neural action potentials. Fig. 6(b) suggests muscle contraction of forearm does not affect the output of the CBA electrode. This may rely on the introduction of the concentric bipolar configuration to the electrode. These results support a potential that the output of the CBA electrode contains biopotentials originating from underlying nerve fascicles.

V. CONCLUSIONS

The present study proposed and tested a CBA electrode for noninvasive measurement of biopotentials from nerve fascicles in ANS. Experiments involving VM suggested its potential of detecting mixed and summed spike-like potentials which were assumed from one or multiple fiber bundles in the median nerve. Further experiments are required to investigate the correlation with microneurographically recorded nerve activity from ANS.

REFERENCES

[1] S.C. Gandevia and J.P. Hales, "The methodology and scope of human microneurography," J. Neuroscience Methods, vol.74, pp.123–136, 1997.

[2] Mano T, Iwase S and Toma S, "Microneurography as a tool in clinical neurophysiology to investigate peripheral neural traffic in humans," Clin Neurophysiol. vol. 117, no. 11, pp. 2357-2384, 2006.

[3] K. Takei, T. Kawano, T. Kawashima, K. Sawada, H. Kaneko and M. Ishida, "Microtube-based electrode arrays for low invasive extracellular recording with a high signal-to-noise ratio," Biomed. Microdevices, vol.12, pp. 41-48, 2010.

[4] M. Ohtsu, Y. Fukuoka and A. Ueno, "Underwater electromyographic measurement using a water-proof insulated electrode," Advanced Biomedical Engineering, vol. 1, pp. 81-88, 2012.

[5] B. Hjorth, "An on-line transformation of EEG scalp potentials into orthogonal source derivations," Electroenceph. Clin. Neurophysiol. vol. 39, pp. 526- 530, 1975.

[6] B. He and R.J. Cohen, "Body surface Laplacian ECG mapping," IEEE Trans. Biomed. Eng., vol. 39, pp. 1179–1191, 1992.

[7] S.P. Fitzgibbon, T.W. Lewis, D.M.W. Powers, E.W. Whitham, J.O. Willoughby, and K.J. Pope, "Surface Laplacian of central scalp electrical signals is insensitive to muscle contamination," IEEE Trans. Biomed. Eng., vol. 60, no. 1, pp. 4-9, Jan. 2013.

[8] J.P. Greenwood, J.B. Stoker and D.A.S.G. Mary, "Single-unit sympathetic discharge: quantitative assessment in human hypertensive disease," Circulation, vol. 100, pp. 1305-1310, 1999.

[9] A. Salmanpoura, L.J. Brown, J.K. Shoemakerb, "Spike detection in human muscle sympathetic nerve activity using a matched wavelet approach, " J. Neuroscience Methods, vol.193, pp.343-355, 2010.

[10] W.H. Cooke, J.R. Carter, and T.A. Kuusela, "Muscle sympathetic nerve activation during the Valsalva Maneuver: Interpretive and analytical caveats," Aviat Space Environ Med. vol.74, no.7, pp. 731-737, 2003.

[11] Y.M. Chi, C. Maier and G. Cauwenberghs, "Ultra-high input impedance, low noise integrated amplifier for noncontact biopetential sensing," IEEE J Emerg. Selected Topics in Circuits and Systems, vol. 1, no. 4, pp.526-535, Dec. 2011.