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Unipolar and bipolar signal acquisition to distinguish artifacts from nervous activity

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Abstract—The acquisition of nervous activity is a meticulous work which requires particular attention to validate the presence of the signal of interest and to distinguish it from electrical and physiological artifacts which are constantly added to the recordings even when the experimenters have taken care to clean the measurement environment as much as possible. In this article, we propose to analyze the bipolar and unipolar recordings from the same electrode contacts, to confirm the nervous nature of the recorded signal and distinguish it from artifacts on the vagus nerve. The metrics used for the analysis of these signals confirmed the recording of nervous activity and the ability of the measuring device to distinguish and separate the respiratory muscular artifact from the respiratory nervous activity even though they have very similar shapes.

Index Terms—Vagus nerve activity, Bipolar/Unipolar acquisition, Cuff electrode, Artifacts

I. INTRODUCTION

The nervous system transmits information from the periphery of the body to the brain and sends appropriate responses to the organs. It is the seat of autonomous regulation and adaptation to the environment. The signals passing through the nerves may be the signature of the functioning of a cohort of organs and changes in molecular nature or proportions. The recording and analysis of the activity of the nervous system is consequently a common interest of numerous studies [1]–[3] looking for markers to understand the functioning of biological mechanisms, detect changes that can characterize a transition to a pathological state and propose new therapies including neuromodulation.

In the specific context of peripheral nerve activity, two types of electrodes are proposed: extraneural electrodes and intrafascicular electrodes. Extraneural electrodes are often preferred for long-term applications since they are less invasive. Nevertheless, it has the disadvantage of being less selective and requiring greater sensitivity to capture nervous activity.

Correctly capturing nerve electrical activity is an essential step to draw conclusions reflecting the studied biological mechanism, but it represents a real challenge. Indeed, it is constantly disturbed by environmental electrical and physiological noise [1], sometimes making it difficult to detect the desired signal, or leads to an erroneous interpretation

when an artifact is confounded with the useful signal due to their similar shapes (e.g, respiratory bursts). Hence, it is necessary to set up acquisition protocols and analysis tools to distinguish and separate artifacts from the useful signal.

In this article, a comparison of unipolar and bipolar recordings performed on the same electrode contacts is proposed in order to confirm the presence of a nervous signal. Depending on the contact, the electrode can be more or less an antenna to environmental disturbances. Therefore, if the contact is modified during the experiment by changes of the conductive property of the contact due to dry out, by movement of the animal (respiratory under anesthesia) or by addition of a product such as lidocaine [1], [4], frequently used to block nervous activity, the captured artifact can also evolve over time. If we only have one signal, the observed changes could then be falsely interpreted as physiological. On the other hand, if the unipolar signal does not evolve while the bipolar recording changes, this indicates that the observed variations are not due to a modification of the contact leading to a different recording of the artifact but rather to an evolution of the nervous activity.

The criteria of temporal shift, change in amplitude and evolution of the content of the burst were chosen as arguments in favor of nervous information. We focused on the study of nervous respiratory activity conveyed by the vagus nerve. As the artifact of respiratory muscle contraction is often observed in the respiratory nerve activity recording, it provides a good example to test the ability of our approach to distinguish the artifact from the nerve signal.

II. ACQUISITION

All experimental procedure were approved by local (CIEPAL DAP # 597) and national (2019102917363112 (V7)) ethical committee. The rats were housed under a 12 h day/night cycle with controlled temperature and humidity and ‘ad libitum’ access to food and water. Anesthesia was induced using 2.5% isoflurane in 100% oxygen, then maintained at 2% during surgery and decreased to 1.5% during recording. The body temperature was controlled via a rectal probe and maintained thanks to a heat pad at 37.5 °C during all the procedure.

The cervical vagus nerve was separated from the carotid artery and de-sheated by gently removing over a small window the

connective tissue surrounding the nerve. A Cortec two-lead bipolar sling platinum-iridium cuff electrode with an internal diameter of 100 μm , a length of 1 mm and a distance between the two contacts of 0.35 mm, was immersed in a saline solution before placement around the nerve [5]. Using the biopotential headstage electrode board with dual input interface manufactured by Plexon, it is possible to record from the two cables connected to the two contacts of the electrode both the electronic bipolar signal, i.e not computed by software, and the unipolar signals. The ground was placed in the animal's leg. Signals were first amplified using an 8 channels biopotential analog headstage for peripheral nerve recording with a bandpass [120 Hz 2 pole, 12 kHz 1 pole] filter and a gain of 50. The headstage is connected to a mini DigiAmp which is primarily intended for complementing the gain of the headstage. It provides a choice of three gain values (50, 250, and 1000). We worked with a gain of 1000 (adjust from the software). The mini DigiAmp then performs a 16-bit A/D conversion at 40 kHz per channel. The latter is connected to the Omniplex chassis, itself connected to the computer.

The rats were placed in a Faraday cage during recording. Lidocaine was applied to induce a change in nerve activity. The experimenters used a cream to minimize its spread to other parts of the animal's body and took care to place it downstream of the electrode on the de-sheated surface of the nerve without touching the electrode. The recordings are managed using the Omniplex software and are stored in ".plx" format, to be opened in Matlab using the Matlab Online Client Development kit 32 and 64 bits. Basal nerve activity was observed for two minutes and showed a stable amplitude. The presented recording was started immediately after the application of lidocaine. The amplitude at the start of the recording corresponds to that of basal activity.

III. PROCESSING METHODS

All codes were created in Matlab R2022b.

Data was first filtered using a second-order Butterworth filter [300, 3000 Hz] [6]. The amplitude is next divided by 50 to take into account the headstage gain (the gain of the mini DigiAmp is directly taken into account since it is adjusted from the software), and multiplied by 1000 to obtain μV (the original file being in mV). In the following, the statistical significance will be assumed for a p-value < 0.01 . Accordingly, the significancy will be noted with the symbol *.

A. Removal of cardiac artifacts

Unipolar recordings contain cardiac artifacts that must be minimized before studying the signals. In our experiments, electronic bipolar acquisition eliminates cardiac peaks as they are sufficiently shared by the two measurement channels. The method proposed below can be also generalized to different signal removal.

As the amplitude of R peaks greatly exceeds that of respiratory

bursts, it is possible to detect them using a threshold crossing technique. Cardiac activity peaks were extracted using windows centered on the R peak and stored in a matrix M.

A singular values decomposition (SVD) applied to $M=USV'$ was used to estimate each individual cardiac activity peak C_i using the combination of V_1 and V_2 , the two first singular vectors associated with the two greatest singular values λ_1 and λ_2 . The choice of the two first singular vectors improved the modeling under the assumption of small delays between cardiac activity peaks. Each cardiac peak was therefore estimated by

$$C_i = U_{i,1}S_{1,1}V_1 + U_{i,2}S_{2,2}V_2 \quad (1)$$

and then subtracted from the signals.

B. Study of burst envelopes

The unipolar and bipolar envelopes were calculated using a sliding window applied to the filtered signal and taking the average of the absolute values in each window. In order to delineate the envelope around zero, a second order polynomial was fitted on the envelope values and then subtracted.

For a first estimate of the amplitude evolution over time, the peaks of each envelope were detected by imposing a minimum width constraint. However, this method is subject to changes of the density of the nervous activity present in the burst and not only to changes of the magnitudes of the activity.

Then, to measure the time shift between the unipolar and bipolar envelopes, cross-correlation was applied.

C. Detection of respiratory bursts and analysis of compound action potentials

In order to study the potential change in burst content by the action of lidocaine, we must first segment the action potentials which is composed by the activity of different fibers as we used an extraneural electrode (i.e which surrounds the nerve). These action potentials will thus subsequently be called compound action potentials (CAPs). It should be noticed that the shape and magnitude of the CAP are modified by the synchronicity and number of the depolarizing fibers.

We used the time location of the burst provided by the calculation of the width of the envelope peaks to segment bursts. Then, an adaptative threshold, taking a certain percentage of the maximum value in each burst, was applied to find the location of the peaks of the compound action potentials. A window centered on each of this peaks was used to extract the CAPs.

With the aim to confirm the change in amplitude observed on the envelope, we used all the raw values of the CAP peaks in each burst and for all the bursts. To observe the potential effect of lidocaine, we performed a linear regression applied to all of these values. The regressors are the burst index (from 1 to 206 in our example). Model statistics were used to

determine if the computed trend was significant. The F-test tests whether the regression model fits significantly better than a degenerate model consisting of a single constant term.

One way to see the narrowing or widening of the CAPs over time is to study the evolution of the width of the peaks calculated on the normalized CAPs. This normalization was carried out by dividing each CAP window by the maximum value identified in this window. Normalization allows us to focus on the shape. For this analysis, we also used linear regression and the statistics of the model found to determine if a trend was present. The regressors and significance threshold were the same as those indicated above.

Finally, we were interested in the variation of the number of peaks over time. We counted the number of peaks per burst in the bipolar signal as well as in the unipolar recording. These values were very noisy from one burst to another. We therefore chose to average over the number of peaks calculated for each burst using a sliding window of fifty bursts.

IV. RESULTS

The presence of respiratory activity in our signals was confirmed by the spectrum of the envelope showing a first harmonic of 1.3Hz (Fig. 1) which is within the respiratory frequency range of the anesthetized rat.

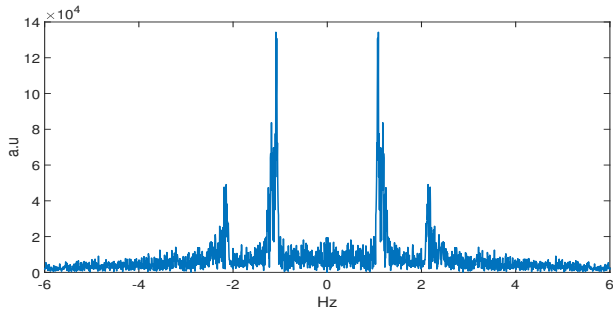


Fig. 1. FFT of the bipolar signal envelope where the first and second harmonics are visible.

The unipolar signals are free of cardiac peaks thanks to the appropriate modeling obtained from the SVD (Fig. 2). This method could also be used for the elimination of other artifacts.

The comparison of the amplitude evolutions between the bipolar and unipolar envelopes shows that it decreases over time in the former case (a result expected with the application of lidocaine which reduces nervous activity) while it seems relatively stable for the latter (Fig. 3). In addition, the cross-correlation indicates a gap of 81 ms between the two envelopes. This shift is moreover visible when the envelopes are superimposed (Fig. 4). The envelope of unipolar bursts precedes that of bipolar ones.

The content of the bursts was then analyzed. Firstly, the evolution of the amplitude of the peaks of CAPs in the bipolar

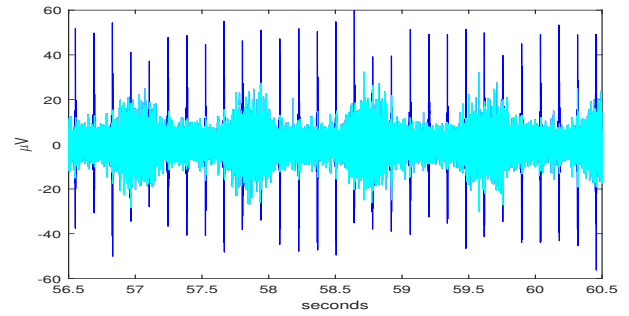


Fig. 2. Removal of cardiac artifacts. Unipolar signal before SVD processing (blue), after processing (cyan).

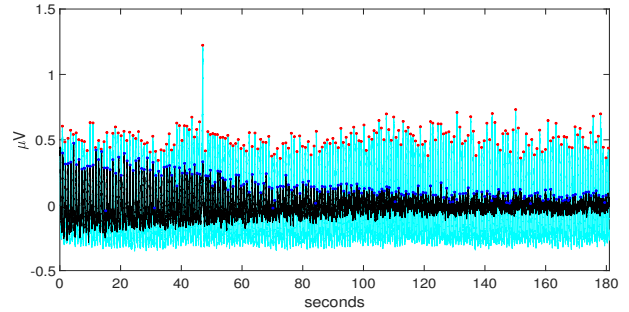


Fig. 3. Evolution of the amplitude of the bipolar envelope (black) and the unipolar envelope (cyan). The amplitude of the unipolar envelope has been divided by 5 to facilitate visual comparison.

bursts was compared to the evolution of the peaks of CAPs in the unipolar bursts. We see that the amplitude of the bipolar CAP peaks decreases over time (Fig. 5). The trend found by linear regression is significantly more representative than a model using a single constant term, with an F-value of $4.71e+03^*$. In the unipolar signal, the amplitude does not seem to evolve (Fig. 6). We cannot conclude that the model found is significantly different from a constant with an F-value of 0.78.

The same trend analysis could be carried out on the evolution of the widths of the CAP peaks detected within the bursts. We also observe a decrease in the bipolar signal with a significant trend (Fig. 7) indicated by an F-value of 792^* while the unipolar signal does not show any significant

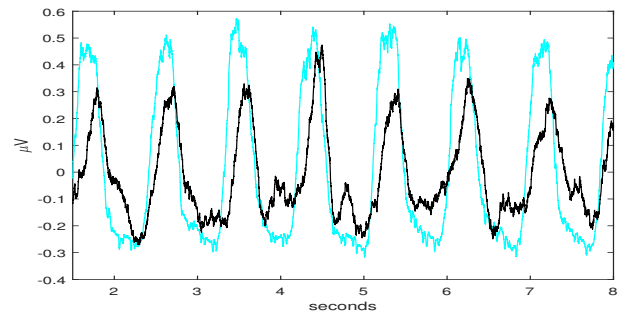


Fig. 4. Zoom in on the envelopes to observe the time shift. Bipolar envelope (black) and unipolar envelope (cyan).

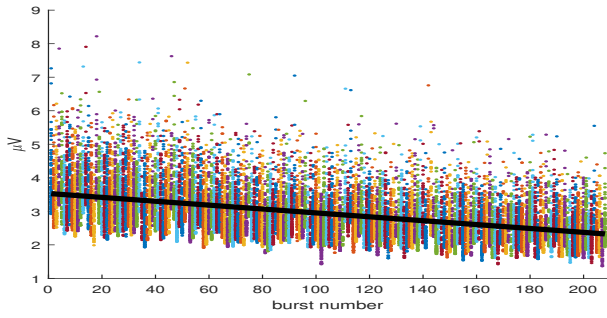


Fig. 5. Evolution of the amplitude of the CAP peaks in each burst and for all the bursts in the bipolar signal. For each burst, the amplitudes of the CAPs are represented on the ordinate. The trend is in black.

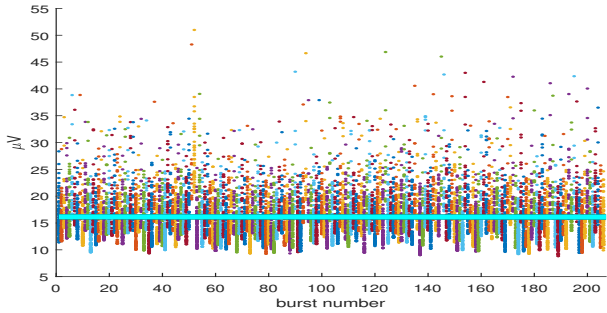


Fig. 6. Evolution of the amplitude of the CAP peaks in each burst and for all the bursts in the unipolar signal. For each burst, the amplitudes of the CAPs are represented on the ordinate. The trend is in cyan.

evolution with an F-value of 1.83. In addition, in line with the previous result, the number of detected CAPs (not depicted in this paper) decreases over time in the bipolar signal only.

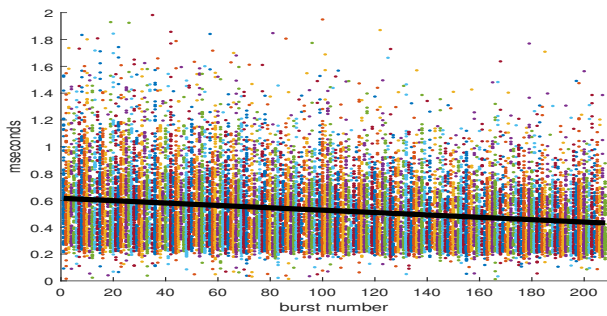


Fig. 7. Evolution of the width at half height of the CAP peaks in each burst and for all the bursts in the bipolar signal. For each burst, the widths of the CAPs are represented on the ordinate. The trend is in black.

V. DISCUSSIONS AND CONCLUSION

In contrast to the unipolar records, the decrease in amplitude, CAP width and CAPs number on the bipolar signal, seems to indicate that the observed evolution is not due to a modification of the contact of the electrode but indeed to a change in the respiratory nervous activity of the vagus nerve caused by the application of lidocaine on the surface of the nerve. Furthermore, these decreases can be

explained physiologically. The decrease in amplitude is linked either to less active fibers or to desynchronization. If we had the same number of fibers and desynchronization, the width of the CAPs and/or their density would have to increase. We observe the opposite, which indicates a decrease in the number of active fibers, therefore a reduction in nervous activity. The stability of the measurements on the unipolar signal and the time shift of the unipolar and bipolar envelopes provided by cross-correlation seem to demonstrate that the unipolar bursts correspond to the artifact of respiratory muscle contraction. The envelope of unipolar bursts precedes that of bipolar bursts. Consequently, it can therefore be assumed that the recorded respiratory nerve signal corresponds to afferent feedback signals sent by pulmonary stretch receptors. The nerve signal is contained in the unipolar recordings, since it is from these pathways that the bipolar signal is obtained, but it is drowned out by the respiratory muscular artifact of higher amplitude. Bipolar acquisition makes it possible to greatly decrease these artifacts, notably through the efficiency of the common mode rejection rate of the amplifier.

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