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Noninvasive Analysis of Motor Unit Behavior in Pathological Tremor

A. Holobar, *Member, IEEE*, V. Glaser, J.A. Gallego, *Student Member, IEEE,* J.L. Dideriksen, *Student Member, IEEE,* and D. Farina, *Senior Member, IEEE*

***Abstract*— A robust surface EMG decomposition tool, referred to as tremor-optimized Convolution Kernel Compensation (CKC) technique, is described. This technique modifies and extends the previously published CKC method in order to circumvent the typical assumption on regularity and asynchrony of motor unit firings in normal condition and adapt to the discharge patterns in pathological tremor.**

The results on synthetic and experimental surface EMG signals demonstrate high performance of decomposition. In the case of simulated surface EMG with 20 dB SNR, excitation level of 20% maximum voluntary contraction (MVC) and simulated tremor frequency of 8 Hz, the newly proposed method identified 8 ± 2 motor units with sensitivity of motor unit discharge identification ≥ 95 % and false alarm and miss rates ≤ 5%. The performance worsened with increasing noise power, with 5 ± 2 motor units identified at 10 dB SNR and 3 ± 1 at 0 dB SNR. In 24 recordings of high-density surface EMG signals from four tremor-affected patients, the modified CKC technique identified 134 motor units (6 ± 4 motor units per contraction).

I. Introduction

TREMOR is the most common movement disorder that is strongly increasing in incidence and prevalence with ageing. Essential tremor affects approximately 4% of the population above 65 years of age whereas Parkinsonian tremor affects about 1% of the population over the age of 50 [1]. More than 65% of the population with upper limb tremor presents serious difficulties in performing activities of daily living.

Tremor is generated either at the central or peripheral level of the nervous system and its neurophysiological mechanisms are still poorly understood. The tools for in vivo quantification of the neural drive to a muscle during pathological tremor are required but currently lacking.

Due to a high safety margin at the nerve-muscle synapse, the neural drive to a muscle can be quantified from the surface EMG by identifying the discharge times of individual motor units [15]. Over the last decade, surface EMG decomposition received considerable attention and the progresses have been remarkable [9], [10], [13]. Although many of the proposed decomposition methods fail to classify motor unit action potentials (MUAPs) that occur at similar time instants (superimpositions of MUAPs) [10], [13], a few recently proposed methods have been demonstrated to identify complete motor unit discharge patterns in healthy subjects [11], [14].

Practically all EMG decomposition techniques (surface or intramuscular) assume regularity and asynchrony of motor unit firings in order to cope with a high complexity of interferent EMG pattern. In a healthy subject during static contractions, the motor unit fire regularly with discharge rates of 8 to 30 Hz, however in patients with essential tremor motor units may fire in bursts of up to 50 Hz, which are not sustained but are grossly grouped within each tremor cycle [7]. In pathological tremor, there is a further tendency for the discharges from individual motor units to synchronize over a shorter time span [2], [3], [4].

This study focuses on the non-invasive quantification of motor unit behavior in pathological tremor. Section II describes development and validation of a computer-aided source separation techniques capable of decomposing high-density surface EMG (HDsEMG) into contributions of different motor units during pathological tremor. Section III shows the decomposition results on both synthetic and experimental signals. Section IV discusses the results and limitations of the introduced decomposition technique.

II. Methods

A. Data Model

Suppose the surface EMG signals are detected with M detection points and denote by $\mathbf{x}(n)=[x_1(n)\dots\ x_M(n)]^T$ their sampled vector, with the n-th sample of i-th measurement in the i-th row. In the case of isometric muscle contractions, the measurements $\mathbf{x}(n)$ can be modeled as outputs of convolutive linear time-invariant multiple-input multiple-output (MIMO) model [11]:

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A. Holobar is with the Faculty of Electrical Engineering and Computer Science, University of Maribor, Maribor, Slovenia (e-mail: ales.holobar@uni-mb.si, phone: +38622207485; fax: +38622207272).

V. Glaser is with the Faculty of Electrical Engineering and Computer Science, University of Maribor, Maribor, Slovenia (e-mail: vojko.glaser @uni-mb.si).

J.A. Gallego is with the Bioengineering Group, Consejo Superior de Investigaciones Científicas, Madrid, Spain (e-mail: gallego@iai.csic.es).

J.L. Dideriksen is with the Center for Sensor-Motor Interaction, Department of Health Science and Technology, Aalborg University, Aalborg, Denmark (e-mail: jldi@hst.aau.dk).

D. Farina is with the Department of Neurorehabilitation Engineering, Bernstein Center for Computational Neuroscience, University Medical Center Göttingen Georg-August University, Göttingen, Germany (e-mail: dario.farina@bccn.uni-goettingen.de).

$$x_i(n)=\sum_{j=1}^{N}\sum_{l=0}^{L-1} h_{ij}(l)t_j(n-l)+\omega_i(n),\quad i=1,...,M \tag{1}$$

where $\omega_i(n)$ stands for zero-mean additive noise and N is the number of model inputs. Each model input $t_j(n)$ is considered a discrete binary motor unit discharge pattern, occupying the value of 1 whenever a motor unit discharge occurs and 0 otherwise:

$$t_j(n)=\sum_{r=-\infty}^{\infty}\delta\left(n-T_j(k)\right),\quad j=1,...,N \tag{2}$$

where $\delta(\tau)$ denotes the Dirac impulse and $T_j(k)$ stands for the time instant in which the k-th MUAP of the j-th motor unit appeared.

The channel response $h_{ij}(l);\ l=0,1,...,L-1$, corresponds to the L samples long MUAP of the j-th motor unit, as detected in the i-th measurement. In the convolutive mixing model, the channel responses $h_{ij}(l)$ can be of arbitrary shapes. Hence, any physiological property of the detected motor unit (e.g., its depth in the muscle tissue, MUAP propagation velocities, end-of-fiber effect), as well as the properties of the detection system (e.g., the spatial filter used) can be taken into account.

Model in Eq. (2) can always be rewritten in a matrix form:

$$\mathbf{x}(n)=\mathbf{H}\bar{\mathbf{t}}(n)+\boldsymbol{\omega}(n), \tag{3}$$

where $\boldsymbol{\omega}(n)=[\omega_1(n),....,\omega_M(n)]^T$ is a noise vector and the mixing matrix $\mathbf{H}$ comprises all the MUAPs as detected by the different surface electrodes [11], whereas the vector $\bar{\mathbf{t}}(n)=\left[t_1(n),t_1(n-1)...t_1(n-L+2)...t_N(n)...t_N(n-L+2)\right]^T$ stands for an extended form of a sample vector $\mathbf{t}(n)$.

B. Convolution Kernel Compensation (CKC)

The Convolution Kernel Compensation (CKC) decomposition technique [11] belongs to the class of blind source separation techniques and is inherently capable of resolving MUAP superimpositions. In contrast to the majority of previously proposed decomposition techniques, it builds on convolutive mixing model and does not rely on estimation of any morphological MUAP property, nor does it assume any particular MUAP shape. Instead, it focuses strictly on the properties of the motor unit discharge patterns, whereas the information about the MUAPs is cancelled out during the decomposition process. This is not a serious limitation, because the MUAP shapes can always be estimated by averaging the measurements in the vicinity of the reconstructed discharge patterns, that is, by using spike triggered averaging of surface EMG.

In the first step, the method blindly estimates the cross-correlation vector $\mathbf{c}_j=E(t_j(n)\mathbf{x}(n))$ between the j-th discharge pattern and all the measurements, where $E(.)$ stands for mathematical expectation. Holobar and Zazula proposed iterative gradient-based procedure for its blind estimation [12].

Gradient descent algorithm in [12] still requires a good initial approximation of $t_j(n)$ in order to converge to the genuine solution. As demonstrated in [12], the CKC approximation with $\mathbf{c}_j=\mathbf{x}^T(n_1)$ proves to be a good initialization point, where, without loss of generality, we assumed that the discharge of the j-th motor unit appeared at the time instant n_1. The required initial time instants n_1 can be selected from the so called activity index [11]:

$$I_A(n)=\mathbf{x}(n)^T\mathbf{C}_{\mathbf{xx}}^{-1}\mathbf{x}(n) \tag{4}$$

where $\mathbf{C}_{\mathbf{xx}}=E(\mathbf{x}(n)\mathbf{x}^T(n))$ is correlation matrix of $\mathbf{x}(n)$.

In the second step, the unknown mixing matrix $\mathbf{H}$ is compensated by calculating the linear minimum mean square error estimator of the j-th discharge pattern t_j [11]:

$$\hat{t}_j(n)=\mathbf{c}_j^T\mathbf{C}_{\mathbf{xx}}^{-1}\mathbf{x}(n) \tag{5}$$

The estimator (5) is asymptotically Bayesian optimal (in the least squared error sense) and has been thoroughly validated in more than 100 healthy subjects and approximately 15 different muscles with different anatomical properties (including fusiform, trapezoidal, pinnated and annular muscles). In all these tests, the CKC decomposition identified complete discharge patterns of up to 30 concurrently active motor units.

C. Adaptation of CKC to Pathological Termor

The CKC method builds on correlation matrix of EMG measurements ($\mathbf{C}_{\mathbf{xx}}$ in Eq. (5)) and relies on the assumption of independent discharge patterns. It is, thus, sensitive to motor unit synchronizations during tremor [11]. Generally speaking, the greater the motor unit synchronization, the less capable the CKC separation filters, defined in Eq. (5), are to discriminate different motor units. In order to overcome this problem and to increase robustness of the CKC method to motor unit synchronization, a procedure for automatic identification of time moments with synchronized motor unit discharges has been implemented. This procedure builds on higher-order statistics of the activity index, defined in Eq. (4):

$$I_{HOS}(n)=\mathbf{z}(n)^T\mathbf{C}_{\mathbf{zz}}^{-1}\mathbf{z}(n) \tag{6}$$

where $\mathbf{z}(n)=\mathbf{x}(n)\circ\mathbf{x}(n)$ and $\circ$ stands for Hadamard product.

For each pair of motor units with at least one perfectly synchronized discharge, a new artificial source (i.e., a new model input in Eq. (1)) is introduced into (6). This new source is a cross-term between the discharge patterns of both motor units and contains only those discharges that were perfectly synchronized in time (up to a single sample). Thus, it has much less discharges than original motor units.

As discussed in [11], the contributions of a source with fewer discharges have higher amplitude in the activity index than the contribution of a source with more discharges. Thus, time moments where motor unit synchronization appears can be directly detected by identifying high values of the activity index in (6). Without loss of decomposition accuracy, these less favorable time moments can be skipped when computing the correlation matrix $\mathbf{C}_{\mathbf{xx}}$. In this way, the required power of the CKC separation filters is maintained also in the case of relatively high motor unit synchronization, as demonstrated by the results in Section IV.

III. Experimental protocol

The newly proposed extension of the CKC technique was thoroughly tested on both synthetic and experimental surface EMG in presence of pathological tremor.

A. Synthetic surface EMG

Discharge patterns of synthetic motor units were generated by an advanced multi-scale model of a pair of antagonistic muscles during tremor [5], which is excited with a number of afferent and descending inputs. Tremor frequency of 8Hz was simulated and combined with four excitation levels (0%, 5%, 10% and 20% of maximum voluntary contraction - MVC). The distribution of recruitment thresholds for the motor neurons was modeled as described in [8], with an exponential function with many low-threshold neurons and progressively fewer high-threshold neurons. The number of motor units active at 5 % excitation level was 70 out of 120 simulated.

A muscle with elliptical cross-section (30(transversal) × 25.4(depth) mm) was simulated, with the 108,221 muscle fibers in total. A multilayer cylindrical volume conductor [6] was employed, comprising muscle, subcutaneous, and skin tissues. The recording system was a grid of 15×10 electrodes of circular shape (radius 1 mm) with 2.5-mm interelectrode distance in both directions. A bipolar recording was simulated for each longitudinal pair of adjacent electrodes. Results were averaged over 10 simulation runs. In each run, the locations of 200 simulated motor units were randomly distributed within the muscle.

B. Experimental signals

Four tremor-affected patients (3 with Parkinsonian termor, 1 with essential tremor, age: 72 ± 8 yrs) participated to the experiment. The subjects received a detailed explanation of the study and gave written informed consent prior to participation. The experiments were conducted in accordance with the Declaration of Helsinki and approved by the local ethics committee.

Surface EMG was recorded with 13×5 electrode grids (LISiN–OT Bioelettronica, Torino, Italy, interelectrode distance of 8 mm) from the distal portion of the wrist extensor during the three repetitions of the following two tasks (each in duration of 30 s):

1. RE: Rest the arm on the lap.
2. AO: Keep the arms outstretched against gravity.

Before the placement of the grid, the skin was lightly abraded using abrasive paste (Meditec–Every, Parma, Italy) and cleaned afterward. Reference electrode was put at the wrist of non-dominant tremor side. The surface EMG signals were amplified as bipolar recordings along the direction of the fibres, band-pass filtered (3 dB bandwidth, 10–750 Hz), and sampled at 2048 Hz by 12–bit A/D converter (LISiN–OT Bioelettronica, Torino, Italy).

C. Data analysis

Both simulated and experimental signals were decomposed with the modified CKC technique (Section II.C). The number of identified motor units and their discharge rate were extracted. The following signal-to-interference ratio (SIR) between the original EMG signals and the residue after subtraction of identified MUAP trains was calculated:

$$SIR(i)=\left(1-\frac{E\left[\left(x_i(n)-\sum_j z_{ij}(n)\right)^2\right]}{E\left[x_i^2(n)\right]}\right)\cdot 100\,\% \tag{7}$$

where $x_i(n)$ denotes the i-th EMG measurement and $z_{ij}(n)$ stands for the j-th motor unit's MUAP train reconstructed from the i-th EMG measurement.

For simulated signals only, the decomposition sensitivity and false alarm rate, as defined in Eq. (8) were calculated

$$Se_j=\frac{TP_j}{TP_j+FN_j},\qquad Fa_j=\frac{FP_j}{FP_j+FN_j} \tag{8}$$

where TP_j (true positives) denotes the number of correctly identified discharges for the j-th motor unit, FP_j (false positive) is the number of misplaced discharges and FN_j (false negatives) is the number of unidentified discharges. Discharge time tolerance was set equal to ± 0.5 ms.

IV. Results

Fig. 1 shows the average number of motor units identified from synthetic surface EMG with sensitivity ≥ 95 % and false alarm rates ≤ 5% as a function of SNR and excitation level. SIR as defined in Eq. (7) is also shown.

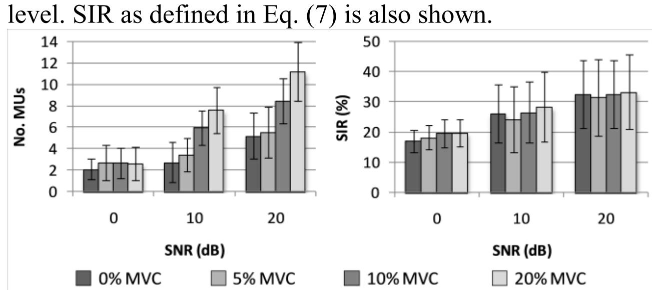

Fig. 1. Averaged number of motor units (No. MUs) with sensitivity ≥ 95 % and false alarm rate ≤ 5% (left panel) and SIR, defined in Eq. (7) (right panel), as a function of SNR and excitation level for tremor frequency 8 Hz. Mean values are depicted with bars, standard deviations with thick black lines. The results are averaged over 10 simulation runs.

Table 1 shows the numbers of motor units identified per contraction from four tremor-affected patients. The number of identified motor units ranged from 0 to 12 across different tasks and patients. All identified motor units exhibited tremor-related discharge pattern with at least one discharge per tremor cycle. In AO (arms outstretched) task, motor units were indentified in all the patients, whereas in the rest condition (RE) of patients 1 and 4 almost no motor unit was identified. Visual inspection of HDsEMG signals revealed no evident motor unit activity in these signals. In patients 2 and 3, relatively large number of motor units was identified in rest condition, indicating the presence of more severe rest tremor. Representative example of identified discharge patterns is depicted in Fig. 2.

Table 1. Number of motor units reconstructed from four tremor-affected patients during different experimental tasks (see Subsection III.B)

Task	Patient 1	Patient 2	Patient 3	Patient 4
RE 1	2	12	9	0
RE 2	1	7	9	0
RE 3	0	9	5	0
AO 1	10	8	4	4
AO 2	10	8	3	4
AO 3	9	9	2	9

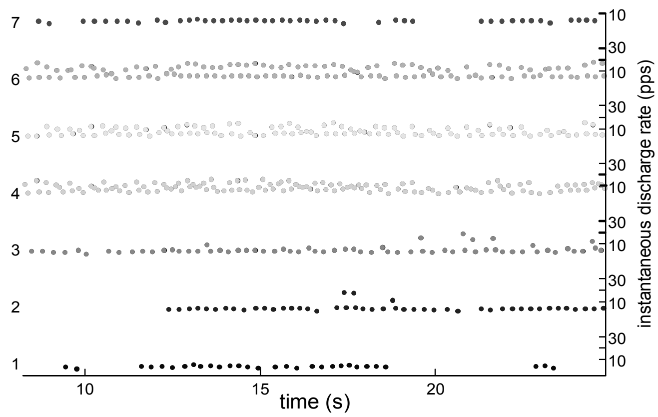

Fig. 2. Discharge patterns of motor units identified in tremor-affected patient. Each dot represents a discharge of individual motor units as identified by CKC decomposition of 64-channel surface EMG. Tremor-affected motor unit discharge patterns are clearly visible. Motor units 4, 5 and 6 exhibit so called paired motor unit discharges (typically, two motor unit discharges per tremor cycle appear).

V. Discussion

The results on synthetic signals demonstrate high performance of surface EMG decomposition. Except for SNR of 0 dB, the number of identified motor units increased significantly with the excitation level. In the case of excitation level of 20 % MVC and 20 dB SNR, the newly proposed method identified 11 motor units with sensitivity of motor unit discharge identification $\geq$ 95 % and false alarm rate $\leq$ 5%. This number decreased with increasing noise power and reached 8 motor units for 10 dB SNR and 2 motor units for SNR of 0 dB.

Along with the number of identified motor units, SIR, as defined in Eq. (7) also decreased significantly with SNR. In the case of 20 dB SNR, the MUAPs detected in the HDsEMG signal accounted for 30 % of the overall signal variance. No significant change of SIR was observed with decrease in excitation level, indicating that approximately the same portion of signal energy was identified in all excitation levels.

In experimental signals from four tremor-affected patients, the strict validation of decomposition results was not possible. Nevertheless, the identified discharge patterns were in agreement with the results published in [2], [3] and [4]. The modified CKC technique identified 134 motor units (6 ± 4 motor units per contraction). SIR, as defined in Eq. (7), ranged from 5% to 60 % (mean ± std. dev. = 24 % ± 17 %) across all tasks with at least one identified motor unit. In most of the cases, large MUAPs were successfully identified whereas the residual was mainly due to the large number of small MUAPs, representing the activity of small and/or deep motor units. This is in agreement with the results on healthy subjects [11].

In agreement with results published in [2], [3] and [4], motor units with paired discharges were frequently identified. Out of 134 motor units identified (Table 1), 41 motor units exhibited paired discharges, with the interdischarge interval ranging from 20 ms to 65 ms. This is in agreement with large variability of interdischarge intervals reported in [3] and [4].

In conclusion, a robust tool for decomposition of HDsEMG acquired during Parkinsonian and essential tremor has been developed and tested. The method demonstrates potential for physiological studies of motor unit behavior in pathological tremor.

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