MOTOR UNIT FIBER DENSITY ESTIMATION USING ARTIFICIAL NEURAL NETWORKS

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Abstract: An estimator for the motor unit fiber density (MUFD) is proposed, using artificial neural networks and motor unit action potential (MUAP) parameters as inputs. Training and evaluation sets of MUAPs were simulated using muscle, needle and signal models, varying three physiological parameters (MUFD, variance of the innervation point and variance of muscle fiber diameter), and allowing random placement of the needle. Additionally, a new MUAP parameter was defined to improve the performance of the estimator under variations of the placement of the needle. Multivariate statistical methods were employed to detect structural patterns and to perform dimensionality reduction on the sample data. Most parameters were found to be interdependent and highly correlated with either MUFD, variance of the innervation point or irregularity of the MUAP. Input parameters were chosen according to the information gathered with multivariate statistical analysis. Estimator performance was evaluated using maximum and RMS error. Network architecture and training algorithm selection was done to minimize estimation error and computational complexity.

Introduction

Neuromuscular pathologies may cause changes in the number of fibers of motor units (MUs) produced by loss of fibers, as in miopathies, and/or reinnervation processes, as in neuropathies. Useful information about the structure and functioning of a MU may be obtained from the motor unit action potential (MUAP), a record of the electrical activity of the MU perceived in a needle electrode placed into the MU territory. Several MUAP parameters have been defined to describe the MUAP quantitatively [1-3], and are commonly used in daily diagnosis. We can find parameters related to MUAP size (area, amplitude, duration...) shape (number of turns, phases, irregularity...) and frequency components. MUAP size parameters are concerned with measurement of bigger or smaller MU, mainly related to MUFD, while shape parameters are related to synchronization of the different single fiber action potentials (SFAPs) forming the MUAP.

Those characterizing parameters have a great variability, since there are many factors affecting them. One factor is the placement of the needle, as insertion determines the distance between the electrode and the sources (muscle fibers). Another factor is the difficulty of the parameter measurement itself, as in duration. Finally, the main source of intrinsic variability in the parameters is the nature of the MUAP, formed by a delayed summation of the SFAPs, influenced by innervation point dispersion, MF diameters, MF positions, etc. All this variability difficults the setting of normality thresholds, and the discrimination accuracy between normal and pathological muscles is compromised. A desirable property of new parameters is the robustness, making them less dependent from all the sources of variability.

This study is concerned with the estimation of the motor unit fiber density (MUFD), which measures the number of muscle fibers (MFs) of a MU per mm^2. In our approach, we use artificial neural networks (ANNs) to estimate MUFD from MUAP parameters. This estimator, as calculated from MUAP parameters, can also be viewed as a new MUAP parameter.

Materials and Methods

We used a MUAP simulator to generate synthetic MUAPs related to certain muscle and insertion conditions. MUFD is a physiological parameter that is unreachable *in-vivo*, as its measurement implies dissection of the muscle under study. However, simulation techniques are generalized and accepted as a research tool [4,5].

Our simulator makes use of models for the muscle [6,7], the needle and single fiber action potential [8]. To simulate the muscle, several physiological parameters defining the MUs (MUFD and mean and variance of diameter), the MFs (length and mean and variance of diameter), innervation point (mean and variance of longitudinal placement, mean and variance of fire delays) can be controlled. For the electrode, the insertion position of the needle and the accuracy of the numerical integration can be controlled. Finally, for the SFAP model the Dimitrov-Dimitrova convolutional model is employed, and we used normative parameters, even that some of them can also be varied [9].

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We simulated 10,000 muscles according to available morphological measurements about Vastus Medialis muscle, varying three physiological parameters: the MUFD (between 5 and 45 fibers/mm^2), the variance of the innervation point (IP) (between 0 and 16 mm) and the variance of the MF diameter (between 0 and 25 μm). To do this, we took 100 regularly spaced intervals for the MUFD and 10 for both IP variance and MF diameter variance. In each of the 10,000 cubes defined in the parameter space, we generated 50 independent MUs, with a random selection of the three parameters among the cube limits, and with an homogeneous distribution of muscle fibers. Needle insertion points were located in a random position inside the motor unit territory and all the muscle's length, simulating a random needle placement.

We selected those three physiological parameters to be varied to have a sample were all the pathological conditions, implying some loose or increase of muscle fibers were represented. We included random placement of the needle to obtain a good estimator robust to changes in recording conditions, especially under proximity to the neuromuscular junction and tendons areas.

To better agree with real potentials we established amplitude and rise-time criteria over simulated MUAPs. Only those with amplitude greater than 50 μV and rise-time smaller than 500 μV/ms were accepted. If some potential did not match the criteria it was rejected and another one was simulated instead. As a result, we had a sample of 500,000 simulated MUAPs.

MUAPs were characterized using a set of 17 parameters previously defined in quantitative EMG literature [1-3] (duration, amplitude, area, thickness, size-index, number of phases, number of turns, turns to phases ratio, irregularity, spike duration, spike area, rise time, slope, maximum slope, maximum frequency, median frequency and mean frequency), and a new parameter defined for this study: the pre-spike duration, defined as the time from the beginning of the MUAP to the beginning of the spike.

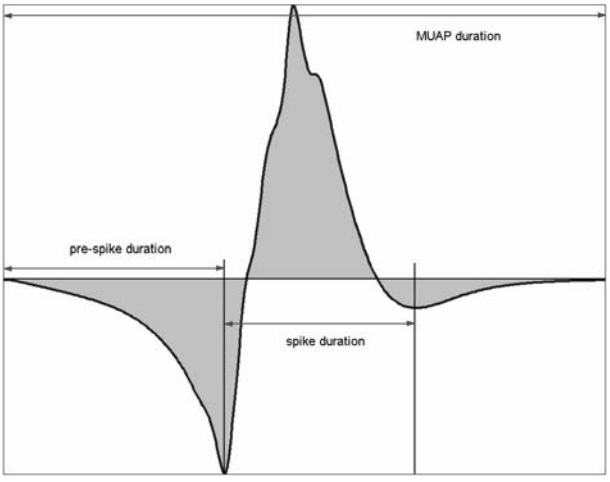

Figure 1: Pre-spike duration and its relation with other duration parameters: MUAP and spike duration

The available data were separated in two sets for training and evaluation respectively. A previous multivariate study [10] was done with the training sample. We studied the relations between physiological and MUAP parameters, and among MUAP parameters themselves, with multivariate techniques looking for structural patterns in the data set. We calculated univariate correlations and canonical correlations (CC) among MUAP and physiological parameters to detect dependencies. We applied principal component analysis (PCA) to check the dimensionality of the MUAP parameters data set, applying Kaiser and Cattel's Scree criteria over resulting eigenvalues. We applied factor analysis (FA) to the MUAP parameters data set varying the number of factors from 10 to 4, trying to detect structural patterns by commonalities, considering significant the parameters with a factor loading greater than 0.5.

We designed an ANN-based MUFD estimator after having analyzed several backpropagation (BP) and radial basis (RB) ANN configurations [11], and compared different training algorithms, number of layers and number of neurons. The previous multivariate statistical study helped us to select the right inputs for the ANN, since we knew we were looking for an estimator capable of making predictions under different IP variance and MF diameter variance, and changing needle placement conditions.

To evaluate estimation quality we calculated maximum, mean and RMS errors in function of MUFD, to have a picture of estimation quality at different densities, and for the whole evaluation data set at time, to have a numerical merit figure to compare the different approaches. We chose the number of neurons in the hidden layer of BP networks so that the relationship between estimation quality and computational complexity was optimized.

Results

Univariate correlation analysis gave us correlations among MUAP and physiological parameters. The parameters with a greater correlation with MUFD were amplitude (ρ=0.68, $p<0.001$), area (ρ=0.83, $p<0.001$), spike area (ρ=0.81, $p<0.001$) and size-index (ρ=0.83, $p<0.001$); the more correlated with IP variance were number of turns (ρ=0.61, $p<0.001$), rise time (ρ=0.67, $p<0.001$), thickness (ρ=0.67, $p<0.001$), slope (ρ=0.68, $p<0.001$) and maximum slope (ρ=0.63, $p<0.001$); the more correlated with longitudinal position of the electrode were pre-spike duration (ρ=0.97, $p<0.001$) and duration (ρ=0.62, $p<0.001$); finally, no parameter was correlated with MF diameter variance neither to radial position of the electrode more than 0.3.

Canonical correlation analysis detected the linear combination of MUAP parameters that maximize the correlation with physiological parameters. Analyzing the correlations among CCs and physiological and MUAP parameters (figure 2), we observed that the 1st CC explains the MUFD (ρ=0.96, $p<0.001$) with a

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combination of area and size-index; 2nd CC explains the longitudinal position of the electrode (ρ=0.91, $p<0.001$) in terms of pre-spike duration; 3rd CC explains a mixture of MUFD and IP variance in terms of amplitude, area, thickness, spike duration and slope; and the rest of CCs offered a mixture of both physiological and MUAP parameters hardly interpretable, even more, without a significant correlation among them.

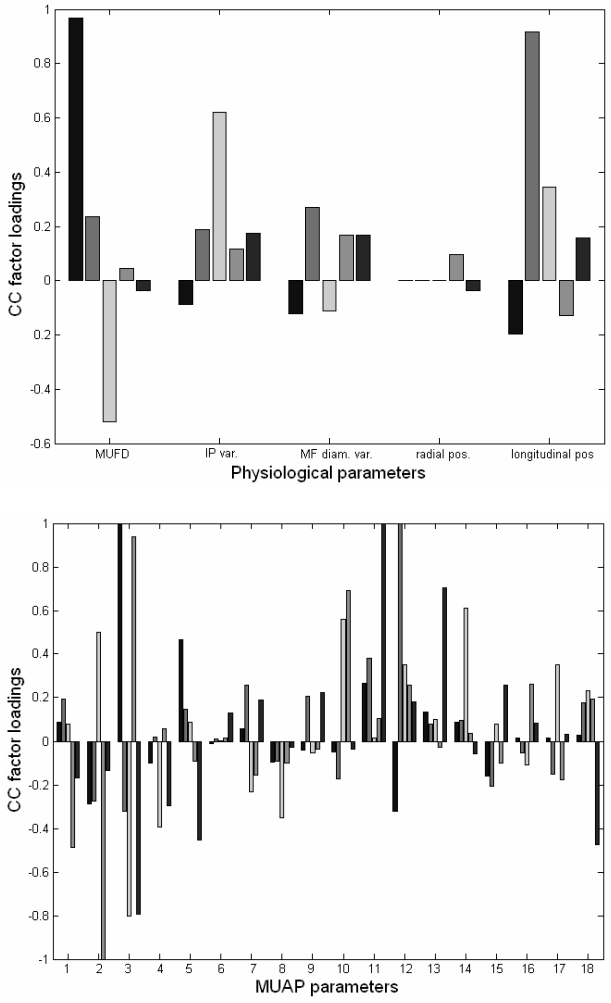

Figure 2: Correlation coefficients among CCs and physiological and MUAP parameters. Each parameter contains 6 bars corresponding to the correlations with the 6 CCs. MUAP parameters are labeled as follows: 1 - duration, 2 - amplitude, 3 - area, 4 - thickness, 5 - size-index, 6 - phases, 7 - turns, 8 - T/F ratio, 9 - irregularity, 10 - spike duration, 11 - spike area, 12 - pre-spike duration, 13 - rise time, 14 - slope, 15 - maximum slope, 16 - maximum frequency, 17 - median frequency, 18 - mean frequency

As a result of PCA, we observed that the first 6 principal components (PCs) could explain 90% of input data variance. Applying Kaiser criterion, 5 PCs were enough to represent the data. Attending to Cattel's Scree criterion, only 4 PCs were sufficient. To evaluate the information that PCs brought about physiological parameters, we calculate their correlations. The 1st and 2nd PCs, were highly correlated with the MUFD (ρ=0.73, $p<0.001$ and ρ=0.65, $p<0.001$ respectively), the 3rd PC was highly correlated with the longitudinal position of the electrode (ρ=0.69, $p<0.001$), and the 4th PC, with the variance of the IP (ρ=0.53, $p<0.001$). None of the PCs was appreciably correlated with variance in the MFs diameter.

The results of factor analysis depend on the number of common factors extracted. For a 6 factors FA (figure 3), the 1st factor depended on amplitude, area, size-index, spike area, slope and maximum slope, which are indeed parameters highly correlated with DFUM; the 2nd factor included the duration, thickness, spike duration and rise time, which are parameters highly correlated with the IP variance; the 3rd factor was formed by irregularity, number of phases, turn to phases ratio and mean frequency, which are parameters that depend on the complexity of the wave form; the 4th factor is mainly formed by the pre-spike duration, parameter related to the longitudinal position of the needle; the 6th factor is the number of turns, and the rest of factors did not present any loading factor greater than 0.5.

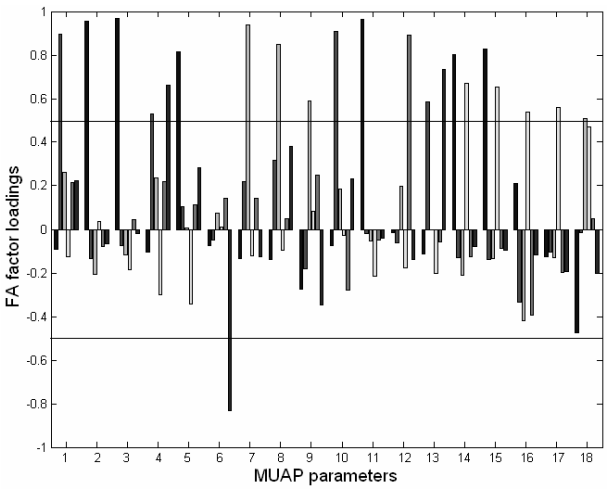

Figure 3: Factor loadings of MUAP parameters in a 6 factors FA. Each parameter contains 6 bars corresponding to the loading in each factor. MUAP parameters are labeled as in figure 2.

For a 4 factors FA, results showed a reordering in the factor loadings. The 1st factor remains unchanged, while the 2nd includes the slope and maximum slope, the 3rd factor includes now the number of turns in this complexity dependent group, and the 4th factor is now only represented by the pre-spike duration.

Considering this study, we chose three different sets of parameters as inputs of the ANN (table 1) to evaluate the estimation capabilities of each group. The three groups are formed by one (or two in set III) parameter(s) correlated with MUFD (spike area and/or size-index), another one correlated with the variance in the IP (spike duration), an index of MUAP irregularity (number of phases), and finally our estimator of the longitudinal needle placement (pre-spike duration).

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Table 1: Input parameters sets

Set	Input parameters
I	spike area, spike duration, number of phases, pre-spike duration
II	size-index, spike duration, number of phases, pre-spike duration
III	spike area, size-index, spike duration, number of phases, pre-spike duration

After evaluation of accuracy of the different sets (table 2), we observed that the set that includes the size-index (II) is slightly superior, both in maximum and RMS errors, to the one that includes the spike area (I) as MUFD dependent parameters. Further quality improvement can be obtained if the two parameters are included in the same set (III).

Table 2: Estimation evaluation with different sets of input parameters

ANN – Input parameters	e_{max} (%)	e_{RMS} (%)
Set I	10.94	2.41
Set II	9.81	2.37
Set III	8.46	2.12

Table 3: Estimation evaluation with different algorithms

ANN – Training settings	e_{max} (%)	e_{RMS} (%)
BP – Momentum Gradient	9.01	2.41
BP – Lèvenberg-Marquardt	8.46	2.12
RB – 25 neurons	8.36	2.07
RB – 15 neurons	8.26	2.03

Regarding the estimation quality, RB with 15 neurons appeared as the best ANN. From a computational point of view, BP networks were the least demanding in memory requirements and computation time. In a trading between estimation quality and computational cost, BP with Lèvenberg-Marquardt training algorithm seems to be the best solution.

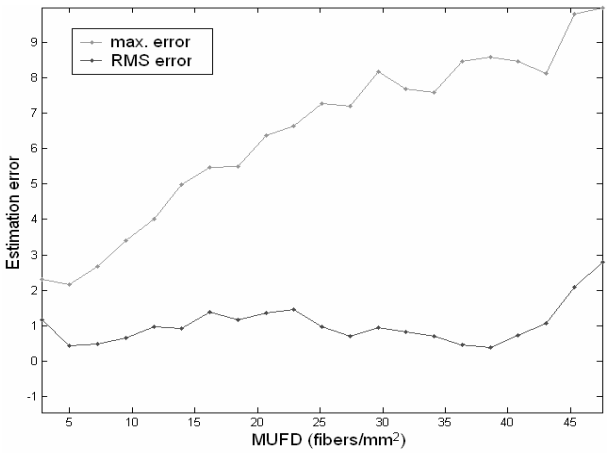

Figure 4: Performance of MUFD estimator

Discussion

Estimation capabilities of physiological and anatomical dimensions of a MU are very limited if just one MUAP parameter is employed. Multivariate approaches are more effective [1,12] since they are capable of bringing out more information about the numerous variables implied in the generation and acquisition of the MUAP. The ANN-based approach [13], multivariate in essence, is very effective and allows reaching very accurate estimates due to the nonlinear relations extracted from the training data.

Accurate estimates of MUFD are obtained when four network inputs are used, correlated respectively to the MUFD, the IP variance, the irregularity of the MUAP wave form and the longitudinal position of the electrode. Further improvement of accuracy is obtained if another MUFD dependent parameter is included.

That means that, in terms of MUAP parameters, and in what it attains to MUFD or size of the MU, information brought by the 18 parameters considered can be condensed in 5 or 6.

It is interesting to see that one of the parameters needed to perform an accurate estimation is the newly formulated pre-spike duration. Its correlation with longitudinal position of the needle helps to reduce the uncertainty of the estimation.

With this methodology, estimation with simulated signals is simple and effective. However, simulation itself has its own limitations. Even if simulators are widely accepted as a research tool, validation studies are not sufficient to ensure the adequacy of simulated signals.

Physiological data that feed the simulator are taken from anatomical studies [14-16] not always complete neither free from contradictions. Moreover, muscles are different from each other and may suffer changes, apart from pathological, due to aging or other circumstances.

The next step should be evaluating the ability to discriminate between normal and pathological muscles with real MUAPs, what will require further researches.

To apply this technique to real signals, as well as normative parameters are calculated for the different human muscles in quantitative EMG, a different ANN should be trained with MUAP generated from physiological parameters according to that muscle, to obtain a good MUFD estimator for each muscle.

If the accuracy in real signals was the same that in simulated ones, this estimator would help to reduce the range of normative values, increasing discrimination capacity among normal and pathological muscles, this way increasing diagnostic capabilities of quantitative EMG.

Conclusions

The use of ANN to estimate MUFD seems an adequate solution to the problem of estimation MUFD from the MUAP parameters. High estimation accuracy is reached with relatively low computational

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complexity. It seems to be a promising technique that, if it is proved to be as efficient in real signals, could increase diagnostic abilities of quantitative needle EMG techniques. Further research has to be done in this way.

In addition, information gathered by the MUAP parameters already defined can be condensed in a few set, as long as we can extract all the physiological information available from them. The pre-spike duration parameter seems to be a good option to obtain information about the needle insertion that was not considered earlier.

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