The spread of muscle fiber conduction velocity
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Chapter 4

Muscle fiber conduction velocity estimation using surface EMG: validation of a new method using model simulations

Fiete Lange, Han van der Hoeven, Natasha Maurits in preparation
Abstract

**Background** The muscle fiber conduction velocity (MFCV) and the spread of conduction velocities (SpCV) are regarded as useful variables in the study of normal and pathological muscle function. However, using surface EMG (sEMG) determination of MFCV, it is generally held not possible to determine the spread of muscle fiber conduction velocities between different motor unit action potentials, especially in an interference pattern. In a previous paper we reported a new method, the interpeak latency (IPL) method, to determine absolute values, and the spread of MFCVs, at different levels of recruitment, using sEMG measurements. In this paper, we use a (sEMG) simulation model, to validate the IPL method with respect to the mean and spread of MFCV.

**Methods** In the model, the action potentials are generated by simple monopoles. Important input parameters for the model such as the spread of MFCV and the mean MFCV are systematically varied. The myoelectric signal is measured by three surface electrodes, arranged in line. MFCV values resulting from the IPL method are compared to model inputs and - for mean MFCV - the cross-correlation method.

**Results** We found a good correlation between results from the cross-correlation method and the IPL method with respect to the mean MFCV. The IPL method proved to be capable to estimate the spread in MFCVs. The reliability of the IPL method can be improved by rejection of outliers in multiple measurements.

**Conclusion** The IPL method is capable of accurately estimating the (spread of) MFCV even in a sEMG interference pattern. When taking systematical errors into account, it can be used for clinical practice.

Introduction

The mean muscle fiber conduction velocity (MFCV) as well as its variability are regarded as indicators for neuromuscular disease (Vogt and Fritz, 2006). The variability can be expressed as the standard deviation of all measured MFCVs (SpCV, spread of conduction velocities). Muscle fibers can become hyper- or hypotrophic, in the course of neuromuscular disease, and as a result of training or disuse. Invasive and
surface measurements of MFCV are therefore regularly used in clinical diagnostics and research (Andreassen and Arendt-Nielsen, 1987; Farina et al., 2004; van der Hoeven and Lange, 1994; van der Hoeven et al., 1993; Huppertz et al., 1997; Ramaekers et al., 1993; Sadoyama et al., 1988). We designed a new method, called the Inter Peak Latency (IPL) method (Lange et al., 2002), to estimate MFCV and SpCV from surface EMG recordings. We have shown that, based on two channel sEMG recordings, it is possible to determine MFCV and SpCV without the necessity of invasive measurements. The distribution can be expressed as the standard deviation of all MFCVs measured (SpCV, spread of conduction velocity). At lower levels of force the spread as determined by the IPL method is comparable with invasively obtained values (Lange et al., 2002). However, at higher force levels, it is generally held not possible to determine the spread of MFCV due to the interference pattern. To validate the IPL method in this situation, we performed a computer model simulation study at various, lower as well as higher, levels of recruitment. Important input parameters for the model such as the spread of MFCV and the mean MFCV are systematically varied.

**Material and Methods**

We designed a computer model to simulate bipolar sEMG recordings, based on the work of Stegeman et al (Stegeman et al., 2000). The IPL method uses the peaks within the sEMG signal to calculate the MFCV and its spread. The computer model yields an EMG signal with multiple peaks, depending on the level of recruitment. The model allows to systematically vary MFCV and SpCV.

**Physiological model**

The force generating units in human skeletal muscles are the muscle fibers. Groups of muscle fibers are innervated and activated by the axon of one anterior horn cell, together called the motor unit. Muscle force results from a combination of recruitment and frequency modulation of the motor units. Our model is based on the detection of motor unit action potentials as those potentials can be detected at the surface. Firing rate,
distance of the motor units from the electrodes and conduction velocity of the motor units can be varied in our model. All simulations were done using twenty simulated MUPs. The depolarization-repolarisation sequence in the physiological model is one of the most important parameters with respect to the exact waveform and source of the electric field of the sEMG signal. However, since the main goal of the present study was to simulate the peaks in the surface EMG, the exact waveform of MUPs was not carried on into the model.

**EMG Model**

The action potential depolarization and repolarization zones are the sources of an electric field in the surrounding volume conductor. These zones are propagating along muscle fibers, and can be modeled as multiple moving monopolar current sources and sinks. From Poisson’s equation, the surface \((z=0)\) potential contribution \(P\) at position \((x,0,0)\) and at time \(t\) resulting from each point source moving along a line parallel to the electrode alignment \((y=0)\) is given by:

\[
P(x,0,0,t) = \frac{I}{4\pi \sigma R(x,t)}
\]

Here, \(I\) is the source strength in mA, \(\sigma\) is the conductivity of the volume conductor in \(\Omega^{-1} \text{m}^{-1}\) (fixed at 0.5 in our simulations) and \(R(x,t)\) is the instantaneous distance from \((x,0,0)\) to the moving point source. The volume conductor is assumed to be purely resistive. The overall surface potential distribution at time \(t\) is given by the summation of \(P\) over all muscle fibers and all point sources per fiber. Figure 1 illustrates the resulting simulated signals.

**Calculation of MFCV: inter peak latency method and cross correlation**

*Inter peak latency method:* We described this method in detail before. In short, up-going (i.e. negative) peaks were identified and marked in an interference pattern of a two channel sEMG recording simulations. We assume a peak where the derivative of the EMG signal \((d\text{EMG})\) crosses
the zero line. dEMG has to be > 0 for at least 15 earlier and < 0 for at least 15 later samples (to identify solitary peaks only), while the EMG signal has to be negative at dEMG = 0. Assuming a range of physiologically occurring conduction velocities (CVs) between 2.9 and 5.5 ms⁻¹, we defined a window of CV (1.8 - 6.5 ms⁻¹) which corresponds to a latency difference of 5.55 - 1.56 ms at a fixed inter-electrode distance of 10 mm. For each negative peak in the first channel we searched for negative peaks with a latency between 1.56 and 5.55 ms in the second (more distal) channel. In case of a single (or solitary) peak we determined the latency between the peaks in the two channels. For clear visual presentation we defined classes (bins, bin-width 0.3 ms⁻¹) of CVs. The conduction velocity for each pair of peaks was calculated and counted for the above mentioned bin. Next, the mean CV (CV_IPL) and the standard deviation of CV for each measurement were calculated. We expressed the spread of CV (SpCV_IPL) as 1 SD of CV_IPL. **Cross correlation method:** We used the method as described by Nishizono (Nishizono et al., 1979). In short: the two EMG-signals were cross-correlated. The peak in the correlogram represents the displacement of the two signals in relation to each other, indicating the time shift between the two signals. CV was calculated as time shift divided by interelectrode distance.
Table 4.1: Simulation parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Unit</th>
<th>Used in Simulations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of simulated MUPs</td>
<td></td>
<td>20</td>
</tr>
<tr>
<td>Simulation interval</td>
<td>ms</td>
<td>205</td>
</tr>
<tr>
<td>Interelectrode distance</td>
<td>mm</td>
<td>10</td>
</tr>
<tr>
<td>Signal sample frequency</td>
<td>Hz</td>
<td>20000</td>
</tr>
<tr>
<td>Physiological CV window</td>
<td>ms(^{-1})</td>
<td>1.8-6.5</td>
</tr>
<tr>
<td>Input conduction velocities (mean)</td>
<td>ms(^{-1})</td>
<td>2.9-5.5</td>
</tr>
<tr>
<td>Action potential fire frequencies</td>
<td>Hz</td>
<td>14±4</td>
</tr>
<tr>
<td>Depth sources (uniform distr.)</td>
<td>cm</td>
<td>0.5-1.5</td>
</tr>
<tr>
<td>Source strengths</td>
<td>mA</td>
<td>1.0±0.2</td>
</tr>
<tr>
<td>Motor endplate zone</td>
<td>cm</td>
<td>0±0.09</td>
</tr>
</tbody>
</table>

A range is indicated by a score (-). Firing rates, source strength and the dimension of the motor endplate zone are expressed as mean values with standard deviations (±SD). The simulation interval, the inter-electrode distance and the signal sample frequency were chosen to be equivalent with historic measurements of our laboratory. Input conduction velocities and firing rates were chosen to meet physiological values.

**IPL Method: validation and error analysis**

Force generation of the muscle is achieved by the combination of rate coding and recruitment of motor units. We focused on simulations based on an interference pattern generated by a fixed number (20) motor unit action potentials. The following parameters of the model were systematically varied (Table 1): mean conduction velocity and spread of conduction velocity, as well as the firing rate. The firing rate was varied within physiological limits, i.e. between 8 and 20 Hz. The input conduction velocity (CV\(_{\text{input}}\)) and spread (SpCV\(_{\text{input}}\)) were based on physiological measurements (van der Hoeven, 1995; Zwarts, 1989). A random sample of the distribution of conduction velocities was taken and fed into the computer program as input for the model. For a summary of all simulations in this study see Table 2.
Validation

First we performed multiple simulations to validate the correct estimation of CV\textsubscript{IPL} at different fixed spreads. We compared the CV\textsubscript{IPL} to the mean input of CVs (CV\textsubscript{input}). CV\textsubscript{input} was varied between 1.8 - 6.5 ms\(^{-1}\). For each input spread (SpCV\textsubscript{input}, range 0.1 - 0.5 ms\(^{-1}\), step 0.1 ms\(^{-1}\)) we performed 154 simulations. For each simulation a new random sample of twenty CVs was created, serving as input CV\textsubscript{input}. Next we did 770 simulations with variable CV\textsubscript{input} and variable spread. After that SpCV\textsubscript{input} was compared to SpCV\textsubscript{IPL}. Again CV\textsubscript{input} was fixed between 1.8 - 6.5 ms\(^{-1}\).

Error analysis

Next we performed an analysis of errors or discrepancies between SpCV\textsubscript{input} and SpCV\textsubscript{IPL}. The error SpCV\textsubscript{error}, defined as the difference SpCV\textsubscript{input} - SpCV\textsubscript{IPL}, was calculated for each simulation. Furthermore we calculated the error CV\textsubscript{error}, defined as the difference CV\textsubscript{input} - CV\textsubscript{IPL}. SpCV\textsubscript{error} was compared to SpCV\textsubscript{input} as well as to CV\textsubscript{error}.

To analyse discrepancies between SpCV\textsubscript{input} and SpCV\textsubscript{IPL}, the distribution of SpCV\textsubscript{error} was calculated and statistically compared to the expected Gaussian distribution. For this purpose we grouped all SpCV\textsubscript{input} values and all SpCV\textsubscript{error} values using bins (bin width of 0.05 ms\(^{-1}\)). For each bin value of SpCV\textsubscript{input} we also calculated the distribution of the associated SpCV\textsubscript{error}. The analysis of the distribution of SpCV\textsubscript{error} revealed a skewed or binominal distribution (see Results section). Therefore we recalculated the relation between SpCV\textsubscript{input} and SpCV\textsubscript{IPL} with all but the two most extreme SpCV\textsubscript{error} per SpCV\textsubscript{input}-bin. In the last step we tried to eliminate the influence of electrophysiologically (nearly) invisible simulated motor unit potentials (MUP\textsubscript{sim}). MUP\textsubscript{sim} far away from the electrodes and low-voltage MUP\textsubscript{-1} have a very low or near zero amplitude and therefore can not be detected by the surface EMG methods. Those MUP\textsubscript{sim} do contribute to the input however and will influence IPL\textsubscript{input} and SpCV\textsubscript{input} whereas the surface EMG will not represent those distant or low-voltage MUPs. Therefore we performed additional simulations with fixed parameters for MUP\textsubscript{sim}, thus removing the confounders depth and strength of MUP\textsubscript{sim}. Only CV\textsubscript{input} and therefore the spread was varied.
Finally the influence of the CV window settings was evaluated. The width of the window used by the IPL method determines the range of CVs that can be found by this method. \( \text{SpCV}_{\text{IPL}} \) is dependent of the range of CVs and the relation between the width of the window and \( \text{SpCV}_{\text{IPL}} \) has to be investigated. The relation between the CV window setting (a parameter of the IPL method) and \( \text{SpCV}_{\text{error}} \) was investigated by comparing simulations at standard window setting (1.8 - 6.5 ms\(^{-1}\)) to simulations at a wide (0.5 - 8.0 ms\(^{-1}\)), respectively narrow (mean ±5 SD) window.

**Statistical analysis**

The results of the simulations were compared to the cross-correlation technique and analyzed by linear regression analysis. \( \text{CV}_{\text{input}} \) and \( \text{CV}_{\text{IPL}} \) were compared using correlation analysis. The frequency and distribution of \( \text{SpCV}_{\text{error}} \) was analyzed for each \( \text{SpCV}_{\text{input}} \)-bin and tested for normality by non linear regression analysis using the equation for Gaussian distribution

\[
\frac{A}{2\pi\sigma^2}e^{-0.5\left[\frac{X - \mu}{\sigma}\right]^2}
\]

as fit function. Here \( A \) the area, \( \sigma \) the standard deviation and \( \mu \) the mean as fit parameters. The results of these tests were expressed using goodness of fit (\( r^2 \) value). Statistical significance was accepted at \( p<0.05 \).

**Table 4.2: Summary of Simulations**

<table>
<thead>
<tr>
<th>Aim</th>
<th>Simulations (N)</th>
<th>Input CV</th>
<th>Input spread</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simulation I</td>
<td>Correct estimation of CV</td>
<td>154</td>
<td>1.8-6.5 ms(^{-1})</td>
</tr>
<tr>
<td>Simulation II</td>
<td>Correct estimation of spread</td>
<td>770</td>
<td>1.8-6.5 ms(^{-1})</td>
</tr>
<tr>
<td>Simulation III</td>
<td>Correct estimation of spread</td>
<td>55</td>
<td>Constant depth, constant strength</td>
</tr>
<tr>
<td>Simulation IV</td>
<td>Error reduction</td>
<td>770</td>
<td>Reuse simulation II, reject 2 most extreme outlyers</td>
</tr>
</tbody>
</table>
Figure 4.1: The first figure (B) represents an in vivo measurement with a bipolar rigid array of surface electrodes. Figure B shows one simulation. The duration of the signal displayed here is 0.34 seconds. Note the similarity of phase-shift and morphology of the signals. The difference between the signal in EMG channel 1 and EMG channel 2 signals is bigger in the in vivo measurements.

Results

Conduction velocity

$CV_{IPL}$ was calculated for different $SpCV_{input}$, ranging from 0.1 ms$^{-1}$ to 0.5 ms$^{-1}$. We found a good correlation between $CV_{input}$ and $CV_{IPL}$ ($r^2 = 0.97-0.99$, Figure 2). At higher $SpCV_{input}$, there was a tendency to overestimate low CVs and underestimate high CVs. We also found that correlation coefficients decreased with higher $SpCV_{input}$, implying slightly decreased accuracy in IPL-estimates for higher CVs.
Spread

Simulations were conducted in which the spread of conduction velocities was varied between 0.1 ms\(^{-1}\) and 0.5 ms\(^{-1}\). For this range of values the correlation between SpCV\(_{\text{input}}\) and SpCV\(_{\text{IPL}}\) was \(r^2 = 0.50\). The majority of these simulations resulted in values along the x=y line (Figure 3, x = SpCV\(_{\text{input}}\) and y = SpCV\(_{\text{IPL}}\)), indicating the similarity of SpCV\(_{\text{input}}\) and SpCV\(_{\text{IPL}}\). Above this line we found scattered points, implying that there was a systematical overestimation of SpCV by the IPL-method for certain simulations.

Analysis of errors and discrepancies between SpCV\(_{\text{input}}\) and SpCV\(_{\text{IPL}}\)

We found no correlation between SpCV\(_{\text{input}}\) and SpCV\(_{\text{error}}\) (Figure 4A). To analyse the distribution of errors for each SpCV\(_{\text{input}}\), the range of SpCV\(_{\text{input}}\) was divided into eleven bins, each of width 0.05 ms\(^{-1}\). In seven bins (0.05 - 0.099 up to 0.35 - 0.399) we found a skewed distribution of SpCV\(_{\text{error}}\). The skew was caused by simulations in which the IPL-method overestimated SpCV\(_{\text{IPL}}\) (Figures 4B and 4C show a representative case). For values of SpCV\(_{\text{input}}\) between 0.4 and 0.6 ms\(^{-1}\) (bins 0.40-0.449 up to 0.549-0.6, figure 4C) we found a normal distribution. After identifying the skewness in the distribution of SpCV\(_{\text{error}}\) we either had the possibility to
Figure 4.3: A: $\text{SpCV}_{\text{input}}$ vs $\text{SpCV}_{\text{IPL}}$ ($r^2=0.50$). Indicated are the linear regression line (thin drawn line) with its 95% confidence intervals (dashed lines). Note the thick, drawn line marked ‘$y=x$’. B: demonstration of $\text{SpCV}_{\text{IPL}}$ vs $\text{SpCV}_{\text{input}}$ ($r^2=0.76$) after post-measurement rejection of the two most extreme outliers.
do further analysis using the median instead of mean values or rejecting outliers to obtain normal distributions of $SpCV_{error}$. After rejecting the two most extreme outliers of series of ten simulations we found a much better correlation ($r^2 = 0.76$, figure 3B) between $SpCV_{IPL}$ and $SpCV_{input}$.

We did 55 simulations with variable $SpCV_{input}$ but constant depth and constant strength of $MUP_{sim}$. We found a good correlation ($r^2 = 0.76$) between $SpCV_{input}$ and $SpCV_{spread}$.

There was no relation between $SpCV_{error}$ and $CV_{error}$. We found that $SpCV_{IPL}$ depended on IPL window settings. At maximum window settings (0.5 - 8.0 $ms^{-1}$) we found no correlation between $CV_{input}$ and $SpCV_{IPL}$, whereas with a dynamic, relatively narrow window around the mean input CV (window centered at mean input CV, lower limit -5 SD, upper limit +5 SD; SD = standard deviation of mean input CV) the correlation was higher ($r^2 = 0.35$).

**Discussion**

In this paper a simulation technique was used to validate the IPL method for two-channel bipolar surface EMG recordings. The IPL method employs the peaks in the surface EMG to estimate mean of en spread in MFCV. Visual comparison of the simulations with in vivo obtained two-channel surface EMG signals revealed no differences between simulated and real signals, and similar peak morphology.

**Model**

The peaks in the surface EMG are the cornerstone of the IPL method and consist of (a summation) of motor unit action potentials. Motor units contain several to many muscle fibers, that can vary in diameter. In our model we did not include this variability. Theoretically, increased variability in fiber diameter would result in lower amplitudes in the surface EMG, and in fewer peaks. The amplitude of those peaks in relation to the electric activity before and after the peak depends on the interelectrode distance in bipolar recordings, the distance of the source (i.e. the closest of those fibers that generate the MUAP) to the electrode, and the
Figure 4.4: SpCV$_{\text{error}}$ (SpCV$_{\text{input}}$ - SpCV$_{\text{IPL}}$) vs SpCV$_{\text{input}}$ and frequency distribution of SpCV$_{\text{error}}$. We counted the number of errors (Y-axis) within specified bins (X-axis). This was done for a wide range of SpCV$_{\text{input}}$ and we here show two representative figures. Upper frame: goodness of fit using non-linear regression analysis with Gaussian equation was $p = 0.0002$, implying a significant difference with the Gaussian equation. Lower frame: $p > 0.1$, implying a good fit with the Gaussian equation.
distance over which the membrane depolarizes. MUAPs can be modeled using linear quadrupole (i.e. two back-to-back dipoles + − +) current sources, which can also be described as a tripole (+ = +), with the centered, negative poles fused (Stegeman et al., 1997). In our simulations use a monopole similar to the center negative part of the more advanced tripole model. The positive leading and trailing parts of the MUAP are thus not explicitly simulated. However, the amplitudes of the positive leading and trailing parts of the MUAP are relative small compared to the high amplitude negative peaks and we therefore conclude that the monopolar model is sufficient to test the reliability of the IPL method. Based on visual comparison with in vivo measurements we also conclude that the simulation model has the capability to generate peaks that are comparable to those in a physiological surface EMG signal.

All tests used the same number of simulated MUAPs. The IPL method was able to find a sufficient number of peaks in each simulated signal. In all simulations it was possible to determine $CV_{IPL}$. We found a very good correlation between $CV_{\text{input}}$ and $CV_{IPL}$. This implies that the mean MFCV can be estimated accurately by the IPL method. A difference with real-life measurements is the absence of noise, which we did not introduce into the signal given the aim of the study. Theoretically, noise could influence the ability of the IPL method to identify peaks in the signal. Therefore investigators using the IPL method should be alert for noise in case the method fails to detect any peaks.

In our model, MUAPs follow a straight line parallel with the electrodes. A possible influence of multiple fiber directions within the muscle was not investigated. In that case lower correlation coefficients are expected using the cross-correlation method. The IPL method will detect and associate (multiple) possibly non-related peaks, resulting in inaccurate $CV_{IPL}$ values. The use of the cross correlation method, together with the IPL method, and optimization of the correlation coefficient by replacement of electrodes could be a strategy to minimize the problem of non-parallel fiber direction.

The spread of conduction velocities calculated by the IPL method correlates highly with input spread. However, $SpCV_{\text{input}}$ and $SpCV_{IPL}$ did not match perfectly even in the absence of noise. Our analysis of the errors/discrepancies revealed no systematic relation between $SpCV_{\text{error}}$
and the SpCV_{input}. This could be explained by a random error in detecting peaks, caused by the association of physiologically unrelated peaks in the two channels. To further clarify the discrepancies we also analyzed the distribution. This analysis indicated that the majority of the errors followed a Gaussian i.e. random distribution. However, we also detected another systematic component resulting in an overestimation of spread in some measurements. This raised the question of preventing overestimation of the spread within a collection of measurements performed under unchanged conditions. Within our dataset we were able to demonstrate that rejection of the two most extreme outliers within consecutive series of ten simulations resulted in less overestimation of the spread.

In our search for other systematical errors, we focused on our use of a uniform distribution of strength and depth of simulated MUAPs. Theoretically the deep and weak MUAPs could be missed in the surface signal. Hogrel et al. (2008) used a model to shown that surface EMG has a limited capacity to detect motorunits with low conduction velocities and therefore low amplitudes in the interference pattern. The limited detection of distant and low voltage MUAPs will influence the CV_{IPL}. Generally spoken, surface EMG with a low number of electrodes is limited to detecting MUAPs mainly from the superficial layers of the muscle. Deep MUAPs and MUAPs with low amplitudes could influence the value of CV_{input} but surface EMG probably will fail to detect those MUAPs. In our model this could result in a discrepancy between estimation of the CV_{IPL} and CV_{input}. We performed additional simulations to analyze the influence of these deep and low amplitude MUAPs using a fixed number of MUAPs at constant depth and strength. These simulations indeed revealed a much better correlation between SpCV_{input} and SpCV_{IPL} compared to variable strength and depth simulations. We therefore conclude that part of the errors in the IPL method can be explained by the presence of MUAPs not detectable to surface electrodes. Since this is a problem of detection and not of analysis all methods to estimate MFCV of SpCV based on limited number of sEMG signals will have the same bias towards superficial motor unit action potentials.

In the present study we were also able to illustrate the influence of the window setting in the IPL method on the estimate of SpCV_{IPL}. Increasing the width to e.g. 0.5 ms\(^{-1}\) - 8.0 ms\(^{-1}\) increases the chance of detecting
peaks that are physiologically not. As a result CV\textsubscript{IPL} and SpCV\textsubscript{IPL} will be less reliable. In our previous paper we had good results with a window width of 1.8 ms\textsuperscript{-1} - 6.5 ms\textsuperscript{-1}. This window should work fine in case of routine measurement and in fatigue research. Here we demonstrated that when the window is narrowed to a range of five SD (lower edge -5 SD, upper edge +5 SD) around the expected or measured mean CV, the estimate of SpCV is improved. We suggest that the center of the window can be preset or optimized using the CV from the cross correlation method.

**Conclusion**

We found a good correlation between the cross correlation method and the IPL method with respect to the mean MFCV. The IPL method proved to be capable to estimate the spread in MFCVs in model simulations. A major enhancement of the IPL method can be achieved by using multiple measurements and rejecting outliers. Furthermore, window settings have a key influence on the results of the IPL method. Centering the parameter window-width on the cross-correlation method mean MFCV can improve the determination of SpCV\textsubscript{IPL} in surface EMG.
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Hogrel JY, Ledoux I et al. Reliability of muscle fibre conduction velocity distribution estimation from surface EMG. *Biomedical Signal Processing and Control* 3 118–125, 2008


