Electrohysterographic conduction velocity estimation

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Abstract— **Monitoring and analysis of the fetal-heart and the uterine-muscle activity, referred to as electrohysterogram (EHG), is essential to permit timely treatment during pregnancy. While remarkable progress is reported for monitoring of the fetal cardiac activity, the EHG measurement and interpretation remains challenging, and limited knowledge is available on the underlying physiological processes. In particular, little attention has been paid to the analysis of the EHG propagation, whose characteristics might indicate the presence of coordinated uterine contractions leading to intrauterine pressure increase. Therefore, this study focuses for the first time on the noninvasive estimation of the conduction velocity of EHG action potentials by means of multichannel EHG recording and surface high-density electrodes. A maximum likelihood algorithm, initially proposed for skeletal-muscle electromyography, is modified for the required EHG analysis. The use of clustering and weighting is introduced to deal with poor signal similarity between different channels. The presented methods were evaluated by specific simulations, proving the combination of weighting and clustering to be the most accurate method. A preliminary EHG measurement during labor confirmed the feasibility of the method. An extensive clinical validation will however be necessary to optimize the method and assess the relevance of the EHG conduction velocity for pregnancy monitoring.**

I. INTRODUCTION

Statistics confirm that first-time births to women in their 30s are rapidly becoming the norm. As a result, mother and child face increasing risks for miscarriage, premature delivery, birth defects, and health problems later in life. Ten to twenty percent of all pregnancies are complicated by hypertension, preterm delivery, and fetal growth retardation, often causing death or permanent damage to the newborn child [1]. Pregnancy monitoring techniques are essential to assess the key risk factors and permit timely medical intervention.

Next to fetal heart rate monitoring, detection and evaluation of the uterine contractions is of major importance. Typical techniques adopted in clinical practice involve the use of either a tocodynamometer, which provides a non invasive indication of contraction onset timing based on external strain gauges, or an intrauterine pressure catheter, which provides the uterine pressure value by the intrauterine insertion of a catheter [1]. The latter technique provides quantitative information, but it is invasive and applicable only during labor.

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In the past few years, a noninvasive alternative technique is being proposed that promises to provide quantitative information on the uterine activity without the use of intrauterine catheterization. Quantitative information on the myometrium (uterine muscle) is in fact derived from the analysis of its electrical activity, referred to as electrohysterogram (EHG). Several techniques have been proposed for the analysis of the EHG. Some authors have proposed reliable techniques for the noninvasive estimation of the intrauterine pressure [2], while other authors could distinguish between two different EHG frequency components [3], possibly being able to predict the course of pregnancy. The ultimate goal and main challenge remains the prediction of preterm delivery. While the presented techniques are invariably based on single channel measurements, we believe that important information for monitoring and predicting the progress of pregnancy resides in the EHG propagation characteristics.

In this study we focus on the conduction velocity (CV) of the EHG action potential (AP), i.e., the electrical activation of the myometrial cells. The EHG is measured by high-density multichannel recording on the lower abdominal surface. Differently from skeletal muscles, which are striated and present an anatomical direction of propagation of the APs, the myometrium is a smooth muscle; as a result, the AP direction of propagation is unknown and depends on the the specific pattern of gap-junction connections between the cells, which are dynamically formed during each contraction. Therefore, we performed our measurements by bi-dimensional high-density surface electrodes, which permit to estimate all the possible CV directions along the abdominal plane underneath the electrodes.

Several methods are available from the electromyography literature for the measurement of the AP CV. Due to the nature of signals measured from skeletal (striate and voluntary) muscles, these methods use monodimensional information, as the direction of propagation can be derived from the muscle fiber orientation. These methods can be divided in four major categories [4]: cross-correlation, phase difference, maximum likelihood (ML), spectral multidip. A four electrode implementation of the multidip approach, leading to an analytical solution, has been presented [5], which can also be extended to larger dimensions. However, more extensive validation is required before adapting the system to our EHG measurements.

Among the remaining three methods, the phase difference method and the ML method, both implemented in the frequency domain, permit CV measurements that are not limited by the time sampling rate [4]. Given the EHG frequency content, usually lower than 1 Hz [2], this characteristic is

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highly desirable, permitting low sampling rates and, therefore, reducing the complexity of the acquisition/analysis system. The ML approach [6], compared to the phase difference method, permits a complete exploitation of our multichannel measurements because it uses all the available acquisition channels, leading to an increased robustness to a low signal-to-noise ratio (SNR).

In conclusion, the ML method has been chosen for the EHG analysis. In order to improve the method performance, a subset of signals is automatically selected based on the signal similarity by minimum spanning tree clustering [7]. The signal similarity is determined by analysis of the cross-correlation function. In addition, the method has been improved by integration of weights in the mean square error minimization; the weights are automatically determined based on the signal similarity. The algorithm is applied in two perpendicular directions. The resulting CV estimate is therefore a vector determined by two perpendicular components in the abdominal plane. A preliminary test of the method feasibility was performed with a woman in labor.

II. METHODOLOGY

In this Section, more detailed information is provided on the proposed CV-estimation methods. These methods are based on the characteristics of the measured signals, depending on the measurement system, presented in Section II-A, as well as on the implemented preprocessing steps, presented in Section II-B. The adopted ML algorithm and the proposed improvements are then presented in Sections II-C and II-D, respectively.

A. Measurement

One measurements was performed at the Máxima Medical Center in Veldhoven (the Netherlands) on a women in labor who signed an informed written consent. The sensors were placed as described in Fig. 1 after skin preparation with an abrasive paste for impedance reduction. The EHG was recorded by a Refa system (TMS International, Enschede, the Netherlands) comprising a multichannel amplifier for electrophysiological signals and a grid of 64 (8x8) high-density (HD) electrodes (1 mm diameter, 4 mm inter-electrode distance). The HD electrode grid was placed on the mid-line of the abdomen below the umbilicus; the ground (GRD) electrode was positioned on the right hip. An external tocogram was employed to support the assessment of the contraction period.

B. Data preprocessing

Given the narrow-band nature of the EHG signal, the acquired signals were band-pass filtered by a sixth order Butterworth filter with low and high cut-off frequencies at 0.3 and 1 Hz, respectively. This permitted to suppress most of the noise introduced by the respiration, the maternal electrocardiogram, and the abdominal electromyogram [8]. The filtered signals could therefore be downsampled from 1024 to 16 Hz without introducing aliasing and reducing significantly the computational complexity of the following analysis. This result is particularly desirable when dealing with 64 parallel channels. Fig. 2 shows an EHG AP sequence registered by a column (8 channels) of the acquisition matrix after filtering and downsampling.

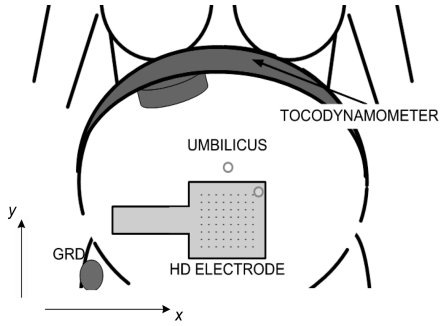

Fig. 1. Scheme of the measurement setup.

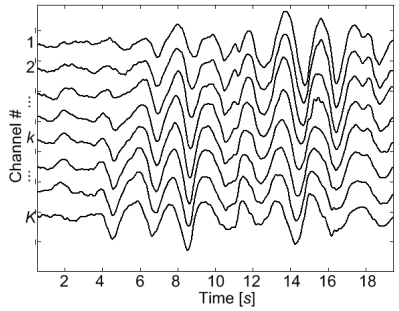

Fig. 2. Example of EHG APs recorded by one column of the acquisition matrix after filtering and downsampling.

C. Maximum likelihood method

Focusing on either one column or one line of the acquisition matrix, the adopted ML method is developed under the hypothesis that the measured multichannel signal can be modeled as

$$x_k(n) = s(n-(k-1)q) + a_k(n), \tag{1}$$

where $x_k(n)$ is the signal measured at the k^{th} electrode ($k \in [1,2,...,K]$) of any column (or row) of the high density matrix, n indicates the time sample, $n \in [1,2,...,N]$, q is the integer number of time samples by which the signal is delayed between two subsequent channels, $s(n)$ is the reference signal shape (delayed in each channel k by $q \cdot (k-1)$), and $a_k(n)$ is white Gaussian noise with variance σ_a^2. Similarly to all CV measurement methods that are reported in the literature on electromyography, the major assumption is that the same signal shape, $s(n)$, is measured at each channel. The CV estimation requires the estimation of q, representing the integer number of sampling periods that the signal is delayed between adjacent channels. The estimate of q can be seen as the maximization of the probability $p(q|x_k(n),s(n))$. The shape function $s(n)$ can be estimated as the average $x_k(n)$ for all channels after alignment, i.e.,

$$\hat{s}(n) = \frac{1}{K}\sum_{k=1}^{K} x_k(n+(k-1)q). \tag{2}$$

Using Bayesian inference and assuming $p(q)$ uniform, the maximization of $p(q|x_k(n),s(n))$ corresponds to the maximization of $p(x_k(n)|q,s(n))$. Given the model in (1), with the assumption of white Gaussian noise, $p(x_k(n)|q,s(n))$ can be expressed as

$$p(x_k(n)|q,s(n)) = \frac{1}{(2\pi)^{\frac{N}{2}}\sigma_a^N} \cdot e^{-\frac{\sum_{n=1}^{N}[x_k(n)-s(n-(k-1)q)]^2}{2\sigma_a^2}}. \quad (3)$$

The probability function in (3) can be extended to the vector $\underline{x}(n)$ including all channels k. The ML estimation of q corresponds to the maximization of $\ln(p(\underline{x}(n)|q,\widehat{s}(n)))$ [9]. Therefore, focusing on a selected time window $t(n)$, the estimation of q reduces to the minimization of the cost function

$$\varepsilon^2(q) = \sum_{k=1}^{K}\sum_{n=1}^{N}[t(n)\cdot(x_k(n) - \frac{1}{K}\sum_{m=1}^{K}x_m(n+(m-k)q))^2]. \quad (4)$$

Since the signals x_k are only available for discrete values of q, minimization of (4) results in a discrete estimate of the optimum q, which depends on the sampling rate. By using the Parseval's equality, (4) can be transformed in the frequency domain, where q becomes a continuous multiplicative factor of the phase and can be estimated without resolution limits. The resulting cost function is

$$E^2(q) = (\frac{2}{N})\sum_{f=1}^{\frac{N}{2}}|T(f)*X_k(f) - \frac{1}{K}\sum_{m=1}^{K}[T(f)*X_m(f)e^{j2\pi f(m-k)\frac{q}{N}}]|^2, \quad (5)$$

where f represents the discrete frequency and $T(f)$ is the fourier transform of $\sqrt{t(n)}$.

Since the derivatives of the cost function in (5) with respect to the delay parameter q can be calculated analytically, gradient based iterative methods can be used very efficiently to minimize $\varepsilon^2(q)$. We have tested the least mean squares (LMS) algorithm, which requires the first derivative only, and the Newton's method, which requires the first and second derivative [10]. The Newton's method shows a much faster convergence (only few iterations are required), although it requires an accurate initialization to avoid convergence to local minima. Therefore, the Newton's method is adopted and combined with a preliminary grid search to determine a proper initialization.

D. Channel clustering and weighting

The proposed method is based on the assumption, implicit in (1), that the signals registered at different channels are delayed versions of the same reference shape $s(n)$. This assumption, already weak for skeletal muscles [11], is even weaker for the myometrium, where differences in the volume conductor and cell-to-cell conduction path underneath the electrodes may cause shape variations of the propagating APs [3]. The proposed approach can therefore measure the average CV underneath the acquisition matrix. In order to increase the robustness of the CV estimation with respect to AP shape variations, the method is improved by automatic selection of a cluster of channels showing "similar" APs and by proper weighting of the cost function in (4).

Both clustering and weighting are based on the quantification of the signal similarity and, therefore, the definition of their distance. To this end, two approaches are considered, based on signal time correlation and spectral coherence, respectively. By these two approaches, the similarity ξ_{ij} between two signals $x_i(n)$ and $x_j(n)$ is defined as either the maximum of the cross correlation function, normalized with respect to the product of the signal standard deviations, or the correlation coefficient of the amplitude spectra. In both cases, $-1 \le \xi_{ij} \le 1$, with $\xi_{ij} = 1$ for $x_i(n) = x_j(n)$ (best case). The second approach is not limited by the sampling rate; however, the missing phase information makes it less sensitive to shape variations. Therefore, the first approach is chosen to define the distance d_{ij} as $d_{ij} = (1-\xi_{ij})/2$.

A distance matrix $[D]$ is defined that collects all the mutual distances d_{ij} of the signals measured at different channels. Clustering is obtained by applying the Prim's algorithm on the distance matrix $[D]$ and, therefore, by growing the minimum spanning three until all electrodes are connected [12]. The resulting tree defines different clusters of similar electrodes. The largest clusters are considered for further analysis. Clusters can include rows and columns. Eventually, the ML algorithm is applied on the row and the column with the largest clusters. In general, if two clusters have the same size, then the cluster with the smallest length (sum of distances) is chosen.

A further improvement of the ML algorithm consists of introducing proper weights, w_k, in the cost function $\varepsilon^2(q)$. In addition, the estimated reference shape $\widehat{s}(n)$ in (2) can also be improved by weighting the sum of functions $x_k(n)$ depending on their similarity with the other functions in the same column or row. Equation (4) can then be formulated as

$$\varepsilon_w^2(q) = \sum_{k=1}^{K}\sum_{n=1}^{N}w_k[t(n)\cdot(x_k(n) - \sum_{m=1}^{K}w_m\cdot x_m(n+(m-k)q))^2], \quad (6)$$

with

$$w_k = \frac{\sum_{i=1,i\neq k}^{K}\xi_{i,k}}{\sum_{i=1}^{K}\left(\sum_{j=1,j\neq i}^{K}\xi_{i,j}\right)}.$$

Notice that $\sum_{k=1}^{K}w_k = 1$. With the same procedure used to obtain (5), (6) is transformed in the frequency domain in order to obtain an estimate of q in the continuous domain by minimization of $E_w^2(q)$. Clustering and weighting should not necessarily be combined. In fact, clustering can be viewed as a form of binary weighting.

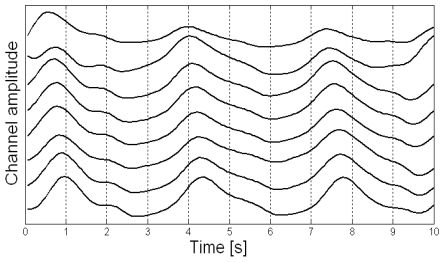

Fig. 3. Example of preprocessed simulated signals with SNR varying from -1 to 25 dB.

TABLE I

DELAY ESTIMATES BY DIFFERENT METHODS.

Method	Estimates of 49.8 ms	Estimates of 149.4 ms
ML	51.3 ± 4.3 ms	150.0 ± 5.8 ms
ML+clust.	50.5 ± 1.9 ms	149.8 ± 4.2 ms
ML+weights	50.8 ± 3.7 ms	149.9 ± 5.4 ms
ML+clust.+weights	50.5 ± 1.5 ms	149.5 ± 3.4 ms

III. RESULTS

The presented CV-estimation methods are evaluated by means of simulations based on real signals. A time interval of 10 s including a complete EHG AP was extracted from a real EHG recording. This signal was then artificially delayed to simulate the measurement of the same AP by the other electrodes lying along the same line. Two different delays, equal to 49.8 and 149.4 ms, respectively, were considered. After downsampling at 16 Hz, these delays corresponded to a fraction of the sampling frequency. For the inter-electrode distance of the adopted electrode matrix, the simulated delays corresponded to velocities of 8.0 and 2.7 cm/s, within the physiological range of the EHG CV [3].

The simulated signals were first tested to evaluate the effect of the number of electrodes on the accuracy of the CV estimation by the ML approach. White Gaussian noise was added to each simulated signal with a SNR equal to 10 dB. The added noise, viewed as the shape difference between the signals, corresponded to the average SNR in the measurement. As expected, the results confirm an increased accuracy for increased number of electrodes. The standard deviation of the CV estimates with 100 different noise sequences was calculated simulating 2, 4, 6, and 8 electrodes. For a delay of 49.8 ms, the standard deviations were equal to 4.2, 1.4, 0.59, and 0.36 ms, respectively. For a delay of 149.4 ms, the standard deviations were equal to 4.3, 1.3, 0.86, and 0.6 ms, respectively. The mean bias was always smaller than 2% of the real CV.

The simulation with eight electrodes was then used to evaluate the different methods for the CV estimation. In this simulation, the SNR of each channel was randomly varied, ranging between -1 and 25 dB. An example of simulated signals, after preprocessing, is shown in Fig. 3. The CV-estimates were calculated by the ML method alone, and after the addition of clustering, weighting, and the combination of clustering and weighting. 100 different noise sequences were used. The mean values and the standard deviations are reported in Table I.

The measurement feasibility was also tested with one woman in labor. A time segment of 50 s during a contraction was visually inspected and five subsequent APs were determined. The method combining clustering and weighting was applied on the entire 8x8 electrode matrix. The estimated velocity components for the horizontal and vertical directions (x and y directions in Fig. 1) were 4.3 ± 0.4 cm/s and -7.4 ± 1.5 cm/s. These estimates are within the expected physiological range [3].

IV. DISCUSSION AND CONCLUSIONS

The EHG CV measurement by high-density multichannel recording is proposed for the first time. A ML approach, reported for the CV estimation in skeletal muscles, is chosen for the measurement. The algorithm is further improved by means of clustering and weighting, based on the signal similarity between different channels. Our simulations prove that the combined use of weighting and clustering produces the most accurate results; on average, the variance diminished by 23% becoming less than 3.4% of the measured value. The use of an electrode matrix permits estimating the CV vector in two dimensions. In fact, differently from electromyographic CV measurements, the EHG CV direction is not known a priori. The method feasibility was confirmed by a preliminary test with a woman in labor. After a more extensive validation, the method might open new possibilities for future clinical studies aimed at assessing the CV-vector dynamics and its value for prediction of the pregnancy course and, in particular, preterm delivery.

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