Modeling and Identification of the Electrohysterographic Volume Conductor by High-Density Electrodes

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Abstract—The surface electrohysterographic (EHG) signal represents the bioelectrical activity that triggers the mechanical contraction of the uterine muscle. Previous work demonstrated the relevance of the EHG signal analysis for fetal and maternal monitoring as well as for prognosis of preterm labor. However, for the introduction in the clinical practice of diagnostic and prognostic EHG techniques, further insights are needed on the properties of the uterine electrical activation and its propagation through biological tissues. An important contribution for studying these phenomena in humans can be provided by mathematical modeling. A five-parameter analytical model of the EHG volume conductor and the cellular action potential (AP) is proposed here and tested on EHG signals recorded by a grid of 64 high-density electrodes. The model parameters are identified by a least-squares optimization method that uses a subset of electrodes. The parameters representing fat and abdominal muscle thickness are also measured by echography. The mean correlation coefficient and standard deviation of the difference between the echographic and EHG estimates were 0.94 and 1.9 mm, respectively. No bias was present. These results suggest that the model provides an accurate description of the EHG AP and the volume conductor, with promising perspectives for future applications.

Index Terms—Action potential, electrohysterography, high-density (HD) electrodes, parameter estimation, smooth muscle, subcutaneous tissue thickness, volume conductor.

I. INTRODUCTION

THE SEQUENCE of contraction and relaxation of the uterine muscle (myometrium) results from the cyclic depolarization and repolarization of the muscle–cell membranes [1]. The spontaneous electrical activity of the myometrium, which can initiate in any cell (pacemaker) and then excites surrounding regions, consists of bursts of action potentials that can be measured at the abdominal surface (electrohysterogram) [2], [3]. Uterine contractions are often the first sign of labor; therefore, when occurring preterm, they need to be promptly suppressed by tocolytics. During labor, a coordinated and strong uterine activity is required for the effective expulsion of the fetus at the end of delivery. Accurate monitoring of the uterine activity is therefore essential. The methods currently employed in clinical practice for uterine activity monitoring, such as internal and external tocographies, cervical change evaluation by digital or ultrasound examination, and the measurements of biomarkers (e.g., fibronectine) in symptomatic women, could support the selection of patients at higher risk of preterm delivery within few days, but they are either invasive or not sufficiently accurate for effective prognosis and, therefore, prompt treatment of premature birth [4]–[6].

During a contraction, the electrohysterographic (EHG) signal can be recorded noninvasively by standard Ag–AgCl contact electrodes placed on the abdomen. Many studies demonstrated that the analysis of the EHG signal may play a key role for accurate monitoring of the uterine contractions, prediction of labor, and improvement of perinatal outcome [7]–[11]. However, many issues related to the conduction pattern of electrical activation are still unsolved [12].

An important contribution for studying noninvasively the conduction properties of EHG signals and the development of novel monitoring technology can be provided by modeling techniques. At the myometrium level, the cellular action potential (AP) generation and the excitation–contraction coupling have been recently accurately modeled as a function of a large number of electrophysiological parameters related to ionic concentrations [13], [14]. Instead, the myometrium-skin volume conductor has been only partially investigated, and it is typically considered as a homogeneous infinite layer [13], [15]. As a result, the myometrium-skin conduction properties are assumed only dependent on the distance between source and recording site. Nevertheless, a complete understanding of the volume conductor effect on the measured signals is fundamental to support the development of accurate prognostic and diagnostic tools based on the EHG signal analysis.

In this study, a myometrium-skin conduction model is developed that consists of a four-layer model obtained by extension of simulation studies reported in the literature for the skeletal electromyogram [16]. The volume conductor effect is formalized in the spatial frequency domain by a transfer function that accounts for the physical and geometrical properties of the biological tissues interposed between the source of electrical current in the myometrium and the recording site on the skin. The intracellular AP is mathematically modeled by a Gamma probability density function [17]. After model reduction, the potential recorded on the skin surface depends on five parameters, of which three are...
related to the source signal shape and two are given by the thickness of the fat and the abdominal muscle. The model parameters are estimated from EHG measurements performed by a grid of 64 high-density (HD) electrodes on five pregnant women at term with uterine contractions. For comparison, the values of fat and abdominal muscle thickness were also measured by echography.

II. METHODOLOGY

A. Background

The contractile element of the uterus is the myometrium, which is composed of billions of smooth muscle cells. The sequence of contraction and relaxation results from a cyclic depolarization and repolarization of the muscle cells in the form of APs. The intracellular AP results from time-dependent changes in the membrane ionic permeability caused by hormonal changes or cell-to-cell excitation. Due to changes in the permeability, ions diffuse across the membrane according to their electrochemical gradients and a transmembrane ionic current is established. APs occur in bursts; they arise in cells that act as pacemakers and propagate from cell to cell through gap junctions, which are low-resistance electrical connections [2]. It has been shown that gap junctions are present between myometrial cells in pregnant animals only during parturition [18]. Due to a lack of evidence [19], many authors concluded that no classical linear propagation of single APs, similar to the myocardium, could be assumed for the myometrium, and that only a global propagation of the whole burst envelope could be measured [19], [20]. However, more recently, extensive measurements of the electrical activity of the guinea pig uterus using a grid of extracellular electrodes clearly demonstrated that also for the myometrium, similarly to the myocardium, a linear propagation of single electrical spikes occurs and can be measured [12], [21], [22].

In this study, the potential recorded on the skin surface is formalized as a function of the transmembrane ionic current and the properties of the volume conductor between the myometrium and the skin. For identifying the model parameters, single surface APs are visually selected from the bursts recorded during contractions. We assume that, below the recording electrodes, the current source can be approximated by a planar wave that propagates, as hypothesized in [13], either along the longitudinal or the circumferential axis of the uterus.

B. System Modeling

1) Volume Conductor Modeling: The biological tissues interposed between the electrical source at the myometrium and the recording site on the skin act as a volume conductor, producing a spatial low-pass filtering effect. Similarly to the study reported in [16] for skeletal muscles, the volume conductor between the myometrium and the skin is considered as made of parallel interfaces separating the tissue layers. As the abdominal curvature is negligible in a limited region, the interfaces can locally be approximated by infinite parallel planes. The biological tissues involved in the conduction of EHG signals are represented in Fig. 1 and consist of myometrial tissue [see (a) in Fig. 1], where the source is placed at a depth \( y = y_b \), a \( \Delta h_b \) thick abdominal muscle layer [see (b) in Fig. 1], a \( \Delta h_c \) thick fat layer [see (c) in Fig. 1], and a \( \Delta h_d \) thick skin layer [see (d) in Fig. 1].

The general relation between the potential and the current density source in a nonhomogeneous and anisotropic layer is expressed by the Poisson equation [23] as

\[
- \frac{\partial}{\partial x} \left( \sigma_x \frac{\partial \phi(x, y, z)}{\partial x} \right) - \frac{\partial}{\partial y} \left( \sigma_y \frac{\partial \phi(x, y, z)}{\partial y} \right) - \frac{\partial}{\partial z} \left( \sigma_z \frac{\partial \phi(x, y, z)}{\partial z} \right) = I_V(x, y, z)
\]

(1)

where \( I_V(x, y, z) \) is the volume current source (in amperes × cubic meter inverse), \( \phi(x, y, z) \) is the potential (in volts), and \( \sigma_x, \sigma_y, \) and \( \sigma_z \) (siemens per meter) are the conductivities of the medium in the \( x-, y-, \) and \( z- \) directions, respectively.

Skin, fat, and myometrial tissue can be considered isotropic, i.e., the value of conductivity does not depend on the direction of propagation, and therefore, \( \sigma_x = \sigma_y = \sigma_z = \sigma \), while the abdominal muscle is anisotropic, i.e., \( \sigma_x = \sigma_y = \sigma, \) \( \sigma_x \neq \sigma_z = \sigma_{zh} \) [16]. In the \( y- \) direction, \( \sigma_y = \sigma_{yz} = \sigma_{zh} \) if the muscle fiber orientation is parallel to the \( z- \) axis, and \( \sigma_{yz} = \sigma_{zh} \) if it is parallel to the \( x- \) axis. All the tissues can be regarded as homogeneous. In the myometrium, the relation in (1) becomes

\[
-\sigma_a \left( \frac{\partial^2 \phi_a}{\partial x^2} + \frac{\partial^2 \phi_a}{\partial y^2} + \frac{\partial^2 \phi_a}{\partial z^2} \right) \phi_a(x, y, z) = I_V(x, y_0, z) \delta(y - y_0)
\]

(2)

with \( \phi_a(x, y, z) \) and \( \sigma_a \) being the potential and the conductivity, and \( I_V(x, y, z) \) the current source at depth \( y_0 \).

All the other layers contain no current source. In the anisotropic muscle layer \( b \), we have

\[
\left( \frac{\partial^2 \phi_b}{\partial x^2} + \frac{\partial^2 \phi_b}{\partial y^2} + \frac{\partial^2 \phi_b}{\partial z^2} \right) \phi_b(x, y, z) = 0
\]

(3)

where \( \phi_b(x, y, z) \) is the potential in this layer. In the isotropic fat layer \( c \), with potential \( \phi_c(x, y, z) \), and similarly in the layers \( d \) and \( e \), with potentials \( \phi_d(x, y, z) \) and \( \phi_e(x, y, z) \), respectively, relations of the form

\[
\left( \frac{\partial^2 \phi_c}{\partial x^2} + \frac{\partial^2 \phi_c}{\partial y^2} + \frac{\partial^2 \phi_c}{\partial z^2} \right) \phi_c(x, y, z) = 0
\]

(4)
hold. The solution of (2)–(4) can be obtained in the spatial frequency domain by calculating the 2-D Fourier transform in the \(x\) and \(z\)-directions. Indicating by \(k_x\) and \(k_z\) the spatial angular frequencies in the \(x\) and \(z\)-directions, due to the Fourier transform properties, the second derivatives in the \(x\) and \(z\)-directions become, in the spatial frequency domain, \(-k_x^2\) and \(-k_z^2\), respectively, by multiplications. Furthermore, we define

\[
k_y = \sqrt{k_x^2 + k_z^2}
\]

Therefore, indicating by \(\Phi_a\), \(\Phi_b\), and \(\Phi_c\) the Fourier transform of the potentials \(\phi_a\), \(\phi_b\), and \(\phi_c\), respectively, in the spatial frequency domain, (2)–(4) become

\[
\left(\frac{\partial^2}{\partial y^2} - k_y^2\right) \Phi_a(k_x, y, k_z) = \frac{I_V(k_x, y, k_z)}{\sigma_a} \delta(y - y_0)
\]

\[
\left(\frac{\partial^2}{\partial y^2} - k_y^2\right) \Phi_b(k_x, y, k_z) = 0
\]

\[
\left(\frac{\partial^2}{\partial y^2} - k_y^2\right) \Phi_c(k_x, y, k_z) = 0
\]

respectively. Equations of the same form as (7), which refers to layer \(a\), also hold for the skin layer, \(d\), and the air, \(e\). In order to obtain the expression of the potential on the skin surface, all the obtained partial differential equations can be solved by adding the boundary conditions at the four interfaces, namely the continuity of the current in the \(y\)-direction, the continuity of the electrical field in the \(z\)- and \(x\)-directions, and the decay to zero of the potential for \(y \to \pm \infty\).

The expression of the potential \(\Phi_a(k_x, y, k_z)\) in the spatial frequency domain on the skin surface \((y = h_d)\) as a function of the current source \(I_V = I_V(k_x, y_0, k_z)\) and the volume conductor properties can then be derived as given in (8), as shown at the bottom of this page, using the following conventions:

1. \(R_a = \sigma_a / \sigma_{xb}\);
2. \(R_b = \sigma_b / \sigma_{xb}\);
3. \(R_c = \sigma_c / \sigma_{xb}\);
4. \(R_d = \sigma_d / \sigma_{c}\);
5. \(\alpha_1(k_x, k_z) = k_y \cosh(\Delta h_b k_y b) R_a + k_y b \sinh(\Delta h_b k_y b)\);
6. \(\alpha_2(k_x, k_z) = k_y \sinh(\Delta h_b k_y b) R_a + k_y b \cosh(\Delta h_b k_y b)\).

In the following, the expression of the surface potential, which has been formalized in two dimensions for completeness, is simplified and addressed as a one-dimension problem. Due to the planar wave assumption, the use of a two-dimension model is not expected to provide additional relevant information. The \(z\)-axis is considered the main component (horizontal or vertical) of the electrical activity propagation velocity. The spatial angular frequency in the \(x\)-direction, \(k_x\), is set to zero and a single line

\[
\Phi_c(k_x, h_1, k_z) = \left(1 - R_d\right) \left\{ k_y b \alpha_1(k_x, k_z) \cosh[(\Delta h_e - \Delta h_d)k_y] - R_c k_y b \alpha_2(k_x, k_z) \sinh[(\Delta h_e - \Delta h_d)k_y] \right\} / 2e^{k_y y_0} I_V(k_x, y_0, k_z) k_y b / \sigma_{xb}
\]

\[
+ \left(1 + R_d\right) \left\{ k_y b \alpha_1(k_x, k_z) \cosh[(\Delta h_e + \Delta h_d)k_y] + R_c k_y b \alpha_2(k_x, k_z) \sinh[(\Delta h_e + \Delta h_d)k_y] \right\} / 2e^{k_y y_0} I_V(k_x, y_0, k_z) k_y b / \sigma_{xb}
\]

\[
\cdot \left(\int_0^{\infty} \frac{z^{\alpha - 1} e^{-z / \beta}}{\beta^{\alpha} \Gamma(\alpha)} d\zeta,\ z \geq 0\right)\]

\[
\cdot 0,\ z < 0
\]

As also suggested for skeletal muscles [17], the intracellular AP (IAP) at the myometrium, IAP\((z)\), can be suitably described in the space domain by a function that has the shape of a Gamma probability density function

\[
IAP(z) = \left\{\begin{array}{ll}
\frac{z^{\alpha - 1} e^{-z / \beta}}{\beta^{\alpha} \Gamma(\alpha)}, & z \geq 0 \\
0, & z < 0
\end{array}\right.
\]

where \(\Gamma\) is the Gamma operator, \(\alpha \in \mathbb{R}^+\) is a dimensionless shape parameter, and \(\beta \in \mathbb{R}^+\) is a spatial scale parameter.

The example of the function IAP\((z)\) modeled by (10) in Fig. 2(a) refers to a propagation velocity \(v_z\), parallel and opposite to the \(z\)-axis. Considered the relation in (9) between the

Fig. 2. (a) Example of intracellular AP and (b) volume current source modeled in the space domain by a Gamma probability density function and its third derivative, respectively. The IAP propagation direction is parallel and opposite to the \(z\)-axis. Assuming a propagation velocity of about 10 cm/s, the depicted example corresponds to an AP duration of 150 ms.
spatial and temporal properties of a waveform, when compared to the intracellular APs depicted in the literature [24], [25], the shape of the modeled AP in Fig. 2(a) represents of microelectrode recordings of uterine activity.

As from (1), the source of our model, \( I_V \), is a volume current source density; being a measure of the current outflow per unit volume, \( I_V \) can then be obtained by the divergence of the current density \( \mathbf{J}(x, y, z) \), in amperes per meter square, i.e.,

\[
I_V = \nabla \cdot \mathbf{J}(x, y, z) = \frac{\partial}{\partial z} (\mathbf{J}(z))
\]

(11)

where the last equality results from the hypothesis of a single propagation direction along \( z \). Assuming the core-conductor model [23], the transmembrane ionic current density \( \mathbf{J}(z) \) is proportional to the second spatial derivative of the IAP profile [23]. In the spatial frequency domain, the volume current source \( I_V(k_z) \) of the model in (8) is therefore given as

\[
I_V(k_z) = \mathcal{F} \left\{ \frac{A \partial^3 \text{IAP}(z)}{\partial z^3} \right\} = \frac{A ik_z^3 \left( -ik_z + \frac{1}{2} \right)^{-\alpha} \beta^{-\alpha}}{\sqrt{2\pi}}
\]

(12)

where \( \mathcal{F} \) indicates the Fourier transform, \( A \) is an amplitude scaling factor that accounts for the number of cells simultaneously active during the contraction, and \( i = \sqrt{-1} \).

3) Model Reduction: The surface potential \( \phi_s(k_z, b_3, k_z) \) in (8) depends on the tissue thicknesses and conductivities, the source depth \( y_0 \), and the parameters \( \alpha, \beta, \) and \( A \) in (12). The tissue conductivities are, however, relatively invariant and the values reported in the literature are used [26]–[28]. For APs propagating in the direction parallel to the abdominal muscle fiber orientation, i.e., \( z \) parallel to the vertical line of the abdomen, by assuming a uterine conductivity \( \sigma_a = 0.2 \text{ S} \cdot \text{m}^{-1} \) [26] and a transversal muscle conductivity \( \sigma_{ab} = 0.09 \text{ S} \cdot \text{m}^{-1} \) [27], we obtain \( R_a = 2.2, R_b = 5, R_c = 0.5, \) and \( R_d = 20 \) [28]. For APs propagating horizontally, \( \sigma_{ab} \) is the longitudinal abdominal muscle conductivity; therefore, \( \sigma_{ab} = 0.4 \text{ S} \cdot \text{m}^{-1} \) [27], \( R_a = 0.5, R_b = 0.2, \) and \( R_c = 0.225 \).

A further reduction of the model parameter number is obtained by setting the skin tissue thickness, \( \Delta h_d \), to a constant value. A low intersubject variability of the skin thickness, demonstrated already in previous studies [29], is also suggested by 15 echographic measurements performed at the Máxima Medical Center, Veldhoven, The Netherlands, from 12 pregnant and three nonpregnant women. In agreement with the values employed in other modeling approaches [28] and those measured for dermatological investigations on the abdomen [29], we measured a skin thickness equal to 2 mm in 87% of the cases. Therefore, the model is identified by assuming a constant skin thickness \( \Delta h_d = 2 \text{ mm} \).

An additional model reduction also concerns the source depth \( y_0 \). Assuming the source to be close to the myometrium-abdominal muscle interface, \( y_0 \to 0 \) and, therefore, the exponential term in (8) can be approximated by a McLaurin expansion \( e^{k_y y_0} \to 1 \).

C. Experimental Data Recording and Preprocessing

The measurements were performed at the Máxima Medical Center after approval by the ethical committee of the hospital. Five women in labor, admitted to the hospital with contractions, were enrolled in the study after signing an informed consent. The sensors were placed as described in Fig. 3 after skin preparation for contact impedance reduction. The EHG was recorded using a Refa system (TMS International, Enschede, The Netherlands), comprising a multichannel amplifier for electrophysiological signals and a grid of 64 (8 \( \times \) 8) HD electrodes (1 mm diameter, 4 mm interelectrode distance). The sampling frequency was 1024 Hz. The electrodes have a flexible support, which can be fixed to the skin by a double-sided adhesive tape mask that covers the interelectrode space and leaves the sensing surface recessed in a cavity. The cavity can be filled by electrolyte gel. The combined use of flexible and recessed electrodes contributes to the reduction of movement artifacts [30].

The HD electrode grid was placed on the midline of the lower abdomen immediately below the umbilicus. By analyzing a set of previous measurement performed with electrodes distributed on the abdomen, the signals recorded by electrodes placed in this region resulted less affected by movement artifacts, such as respiration, than the signals recorded by electrodes placed in other locations [31]. The common reference for the monopolar EHG signals recorded by the HD electrode was placed on the right hip, close to the ground (GRD) electrode. The external tocogram, simultaneously recorded due to medical prescription, was employed to support the assessment of the contraction period. An accelerometer was fixed on the HD electrodes to detect movements and exclude from the analysis signal segments affected by motion artifacts. An Aloka ultrasound scanner was employed to measure the thickness of the fat and the abdominal muscle layers underneath the HD electrode. Two echographic images were recorded: one during the quiescent period and one at the contraction peak. The values of thickness were then measured on the echographic image by two independent observers.

The uterine EHG signal can be affected by various noise sources, e.g., electrocardiographic (ECG) signals, electromyographic (EMG) interference generated by the contraction of abdominal muscles, and different motion artifacts. It has been
extensively reported that the EHG signal does not have significant frequency components outside the frequency band 0.1–5 Hz [20]. The interference due to the EMG signal has a dominant frequency component of about 30 Hz [8], the main frequency of respiration is up to 0.34 Hz, and the lower frequency of the ECG signal is given by the heart rate, which can be as low as 1 Hz [32]. In the literature, either narrow bandpass filtering (i.e., between 0.34 and 1 Hz) [10] or maternal ECG subtraction combined with bandpass filtering between 0.1 and 3 Hz was proposed to improve the EHG SNR [11]. In this paper, a sixth-order Butterworth bandpass filter with cut-off frequencies at 0.1 and 0.8 Hz is used. The example of AP in Fig. 4, filtered between 0.1 and 5 Hz and between 0.1 and 0.8 Hz, in fact, suggests that low-pass filtering below 0.8 Hz does not affect the signal shape while removing the ECG interference at the heart rate. Due to the electrode typology and position, low-frequency oscillations due to the respiration are not visible in the recorded signals.

D. Model Parameter Identification

For each woman, two different signal time segments, each containing a propagating (i.e., it shows a delay between consecutive channels) surface AP, were visually selected on the preprocessed signal and used as reference for validation by mean square estimation of the model parameters.

Since possible artifacts, such as those due to ECG and movements, do not propagate along the electrode grid, the surface APs in the different channels represent the same AP propagating below the electrodes. We assume that the conduction wave can be approximated by a planar wave. Due to the planar wave assumption, the spatiotemporal information of the surface AP recorded by one column and one row of the electrode grid is representative of the AP propagation. The best row and column are then selected using the similarity among the recorded signals as quality index. A high interchannel signal similarity, in fact, provides a first evidence that the selected electrodes are recording APs originating from a single source. Furthermore, as we assume that the AP propagates either vertically or horizontally [13], we single out the line (either the column or the raw) that is parallel to the AP direction of propagation, estimated by analysis of the AP conduction velocity. In fact, no spatial information could be derived from the electrodes that are aligned orthogonally to the AP propagation direction. Note that, due to the preliminary line selection based on the interchannel signal similarity, the conduction velocity estimates in the selected line are more reliable [33].

Possible indexes of the shape similarity between two signals are the correlation coefficient and the coherence spectrum [34]. Differently from the correlation coefficient, the similarity index provided by the coherence spectrum, which is the frequency equivalent of the correlation coefficient, is independent of the signal phase, and therefore, does not require preliminary signal alignment. The coherence spectrum is therefore calculated for all the couples of signals in a line and the median value considered as line signal quality index.

For assessing the surface AP conduction velocity between two electrodes, the phase-difference method is employed [35]. The conduction velocity is calculated between all the possible couples of channels in the considered lines. A more robust estimation of the delay can then be obtained by exploiting the redundancy of this information and taking the median value of the delay estimates.

Once a channel line is identified on the basis of coherence and propagation, the eight-channel-surface APs in the time domain are used for identification of the model parameters in the space domain. However, due to the wavelength of the uterine AP and the spatial low-pass filtering effect of the biological tissues interposed between the myometrium and the skin, the signal simultaneously recorded by the eight electrodes may not provide enough spatial information for reconstructing a complete surface AP in the space domain. After calculation of the surface AP conduction velocity, assumed to be constant, time information is used to recover the missing spatial information. Eventually, the surface AP, SAP(z), is represented by 16 spatial samples (see Fig. 8).

The parameters of the model in (8) and (11) are identified on simulated and real signals by minimization of the mean error $e$, which is given by

$$ e = \frac{1}{N} \sum_{z=1}^{N} (\text{SAP}(z) - \text{SAP}_M(z))^2 $$

between the measured (simulated) reference signal SAP(z) and the modeled potential $\text{SAP}_M(z) = \mathbf{\tilde{h}}^{-1} \{ \phi_v(k_z) \}$. The Nelder–Mead simplex search method is used for the minimization of $e$, which is given for $\text{SAP}_M = \text{SAP}_M$ [36]. For the minimization of $e$, the values of the abdominal fat and muscle thickness are initialized at 19 and 12 mm, respectively; for the considered abdominal tissues, these are the mean values reported in the literature for young women [37].

III. RESULTS

A. Simulation Results

Simulated surface APs were obtained for all the possible combinations of realistic values of $\Delta h_b$ and $\Delta h_{c}$, and for a fixed set of source parameters. Ten values of abdominal muscle thickness, $\Delta h_b$, and fat tissue thickness, $\Delta h_{c}$, between 1 and
16 mm and between 1 and 30 mm, respectively, were considered for the simulations [37]. Gaussian white noise was added to each of the simulated surface AP. The noise power was estimated as the mean squared error between SAP and \(\hat{S}_\text{AP}\) obtained by the model identification on the real signals. Each noisy simulated surface AP was used as reference to obtain an estimate of the fat thickness, \(\hat{\Delta}h_c\), and the abdominal muscle thickness, \(\hat{\Delta}h_b\), as described in Section II-D.

The standard deviation, \(SD_b\), of the abdominal muscle thickness estimates and the standard deviation, \(SD_c\), of the fat tissue thickness estimates were calculated over 50 noise sequences. The standard deviation of the fat and abdominal muscle thickness estimates in Fig. 5(a) and (b) refers to the worst case SNR, i.e., SNR = 12 dB. In these simulations, vertical propagation was assumed, i.e., the abdominal muscle conductivity in the \(z\)-direction \(\sigma_{zb}\) is the longitudinal conductivity and \(\sigma_{xb}\) is the transversal one. The estimates are unbiased. Fig. 5(a) shows that for \(\Delta h_b > 1\) mm, \(SD_c < 1.5\) mm. As for the standard deviation of the abdominal muscle estimates, see Fig. 5(b), for \(\Delta h_b > 1\) mm, \(SD_b < 4\) mm. In the simulations reported in Fig. 5(a) and (b), the standard deviation of the abdominal muscle thickness estimates is, in general, higher than the fat thickness. For a simulated vertical propagation, this tendency is also present when higher values of SNR are considered, and it is due to the convexity of the error function, which is slightly higher in the direction of \(\Delta h_c\) than in the direction of \(\Delta h_b\). When horizontal propagation is simulated, the surface AP is more sensitive to variations of the abdominal muscle thickness and the estimation of \(\Delta h_b\) becomes more accurate than \(\Delta h_c\).

### B. Measurement Results

For each patient, the abdominal muscle and the fat layer thickness were measured by echography by two independent observers and the model parameters identified on two different time segments of the EHG signal. The values of tissue thickness recorded by echography and those estimated from the EHG signal using the volume conductor model are shown in Fig. 6 for each analyzed patient. In Fig. 6, the echographic measurements refer to the contraction period and are reported in terms of inter-observer mean and standard deviation. The difference between the values of tissue thickness recorded by echography during the quiescent period and contraction (not reported in the figure) was \(0.11 \pm 0.67\) mm for the fat tissue and \(-0.23 \pm 0.34\) mm for the abdominal muscle. For comparison, Fig. 6 also shows the mean and standard deviation of the parameters estimated from the surface APs.

As from the table in Fig. 6, the mean values of thickness measured echographically by the two observers were \(\Delta h_c = 11.32 \pm 6.17\) mm and \(\Delta h_b = 9.36 \pm 3.63\) mm, respectively. The mean difference between the echographic and the electrophysiological estimates was \(\Delta_c = 0.97 \pm 1.99\) mm for the fat and \(\Delta_b = -1.02 \pm 1.21\) mm for the abdominal muscle. The mean total difference between the echographic and the EHG...
estimates, i.e., with no distinction between the two different tissues, was $0.02 \pm 1.9$ mm.

The variability between the two types of measurements was comparable, with a mean interobserver variability of 1.1 mm by echography and a mean difference between the tissue thickness estimated by the two surface APs of 1.2 mm.

In Fig. 7, the estimated values of tissue thicknesses are plotted against the values measured by echography. By operating a linear regression of the data with the hypothesis of zero intercept, we obtained correlation coefficients $R = 0.9458 (p < 0.05)$ and $R = 0.9342 (p < 0.05)$ for the fat tissue and the abdominal muscle tissue, respectively. The angular coefficient of the regression lines is 1.03 and 0.89 for the fat tissue and the abdominal muscle tissue, respectively. The good agreement between the measured and estimated parameters was also confirmed by their high correlation ($R = 0.9458$ and $R = 0.9342$).

The tissue thickness was measured twice in the same location: during contraction and during the quiescent period. For the validation of the model, the reference values were those obtained during contraction since APs are present only during the contraction period. According to our echographic measurements, a decrease in the fat tissue and an increase in the abdominal muscle tissue thickness is observed when a contraction occurs. However, the small mean difference measured in our experiments (0.11 mm for the fat and 0.23 mm for the abdominal muscle) is not statistically significant ($p > 0.5$), leading to the conclusion that the thickness of these tissues is approximately constant independently on the contraction of the uterine muscle.

In general, the values of fat and abdominal muscle thicknesses of our experiments are lower than those reported in the literature for nonpregnant women in the same age range. During pregnancy, in fact, due to the expansion of the uterus, the subcutaneous tissues tend to stretch, especially in the region surrounding the umbilicus.

In conclusion, our results show that the proposed mathematical model of the conduction of EHG signals from the myometrium to the skin surface. The shape of the cellular AP is modeled by a Gamma probability density function. Based on physiological and experimental observations, the number of model parameters can be reduced. The model is then identified from the EHG signal recorded on women in labor by surface electrodes. Of the five estimated parameters, two can also be measured by echography. The model can therefore be reliably validated by comparison with the echographic measurements [38].

The model was tested on ten segments of EHG signals recorded on five women in labor. On average, the parameters estimated using the model differed from the ones measured by echography by less than 1 mm for the fat tissue and 1.2 mm for the abdominal muscle tissue. The good agreement between the measured and estimated parameters was also confirmed by their high correlation ($R = 0.9458$ and $R = 0.9342$).

On simulated signals, the error between the measured and estimated surface APs resulted more sensitive to the abdominal muscle or the fat tissue thickness error, depending on the considered direction of propagation (vertical or horizontal). This dependency between the estimate accuracy and the AP direction of propagation is likely to be related to the anisotropy of the abdominal muscle. The comparable parameter errors obtained on real data for the two different biological tissues can therefore be explained by the comparable number of selected surface AP propagating horizontally (four) with respect to those propagating vertically (six).

For each woman, the tissue thickness was echographically measured by two observers and estimated on two different segments of the EHG signal. The interobserver variability of the echographic measurements was comparable to the variability of the tissue values estimated by analysis of two surface APs: both variabilities resulted to be slightly higher than the mean difference between the two methods. In general, our simulations show that even considering the worst realistic value of SNR, the standard deviation of the parameter estimates is modest for any realistic values of tissue thickness.

The variability between the two types of measurements was comparable, with a mean interobserver variability of 1.1 mm by echography and a mean difference between the tissue thickness estimated by the two surface APs of 1.2 mm.
that the myometrial tissue is isotropic and the hypothesis that APs propagate exclusively either along the longitudinal or the circumferential axis of the uterus. Therefore, in the future, the role played by the complex 3-D geometrical and anatomical structures of the myometrium in the conduction of electrical activity needs to be understood and possibly integrated in the source model. Nevertheless, on the basis of our results, the proposed mathematical model for the potential source leads to an accurate description of the data with a limited number of parameters. Therefore, it is suitable to support future studies on the mechanism of AP propagation in humans, and ultimately sustain the development of accurate noninvasive techniques for uterine contraction monitoring and preterm labor prediction.

REFERENCES


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