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Multi-Channel Electrohysterography Enabled Uterine Contraction Characterization and Its Effect in Delivery Assessment^{*,**}

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ABSTRACT

Uterine contractions are routinely monitored by tocodynamometer (TOCO) at late stage of pregnancy to predict the onset of labor. However, TOCO reveals no information on the synchrony and coherence of contractions, which are important contributors to a successful delivery. The electrohysterography (EHG) is a recording of the electrical activities that trigger the local muscles to contract. The spatial-temporal information embedded in multiple channel EHG signals make them ideal for characterizing the synchrony and coherence of uterine contraction. To proceed, contractile time-windows are identified from TOCO signals and are then used to segment out the simultaneously recorded EHG signals of different channels. We construct sample entropy SamEn and Concordance Correlation based feature ψ from these EHG segments to quantify the synchrony and coherence of contraction. To test the effectiveness of the proposed method, 122 EHG recordings in the Icelandic EHG database were divided into two groups according to the time difference between the gestational ages at recording and at delivery (TTD). Both SamEn and ψ show clear difference in the two groups ($p < 10^{-5}$) even when measurements were made 120 h before delivery. Receiver operating characteristic curve analysis of these two features gave AUC values of 0.834 and 0.726 for discriminating imminent labor defined with $TTD \leq 24$ h. The SamEn was significantly smaller in women (0.1433) of imminent labor group than in women (0.3774) of the pregnancy group. Using an optimal cutoff value of SamEn to identify imminent labor gives sensitivity, specificity, and accuracy as high as 0.909, 0.712 and 0.743, respectively. These results demonstrate superiority in comparing to the existing SOTA methods. This study is the first research work focusing on characterizing the synchrony property of contractions from the electrohysterography signals. Despite the very limited dataset used in the validation process, the promising results open a new direction to the use of electrohysterography in obstetrics.

1. Introduction

Uterus is a unique organ, which is of clear biological functionality within only a short period of time, i.e., at early stage of pregnancy, it provides a stable and quiescent environment for the development of fetus; close to delivery, it generates forceful contractions to expel fetus out. When the change from quiescence to forceful contractions happens too quickly, fetus might be expelled out from the uterus before mature, resulting in preterm birth (less than 37 weeks of gestation). According to the World Health Organization, preterm birth happens about every 10 babies, and this gives rise to about 15 million preterm babies each year worldwide [1, 2]. Preterm birth is the leading cause of neonatal mortality and morbidity. Up to 85% of the 1-million children deaths under the age of 5 are directly or indirectly related to preterm birth. For the lucky survivors, they are still more likely to have long-life health complications[3].

For this reason, uterine contractions are one of the most common reasons for obstetrical visits throughout pregnancy. To prevent any possibility of bad complication happening, the detection of uterine contraction becomes a necessity for

the visit of prenatal care. Although the intrauterine pressure catheter (IUPC) is considered as the gold-standard for uterine activity (contraction) monitoring, it is restrictedly used in obstetrics, due to the inherent risks of infection [4]. A practical alternative is the tocodynamometer (TOCO): a strain gauge positioned on the abdomen of pregnant women. When tension builds up in the uterus due to the appearance of contractions, it is captured by the pressure sensor with an increase of output signal. Ideally, this device is capable of identifying the frequency, duration and the power of contractions. Despite its lower precision in comparing with IUPC, the non-invasive nature makes TOCO a standard way for contraction monitoring [5].

Although, contractions are fundamental requirement for a successful delivery, the wide use of TOCO in uterine contraction detection does not guarantee enough competence in obstetrical practice. As the TOCO is attached to woman abdomen by an elastic belt, the nature of the pressure sensor implies that the output signal is sensitive to the tightness of the fasten belt. Together with the different attenuation caused by the difference in fat thickness of patients, the TOCO signal might not be able to detect contractions effectively, especially in the patients of obese [6].

The relationship between uterine contractions and the underlying electrical activities in terms of action potentials

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in the uterine myometrium provides an alternative way of contractions detection. Physiological experiments have shown that the contraction strength, duration and frequency are fully related to the bursting activity of electrical signals[7]. Placing electrodes on the abdomen of pregnant women, the electrical activities of the myometrium underneath the electrodes can be collected, forming electrohysterography (EHG). Euliano *et al* compared the effectiveness of EHG signals in detecting uterine activity with that of the TOCO signal, and showed that the EHG-based method was superior[4]. This work has been inspiring great research efforts in developing algorithms to extract and reconstruct uterine contractions using EHG signals. Noticing the higher amplitude of the EHG signals during contraction, Horoba *et al* calculated the moving average of the root mean square (RMS) of the EHG under a sliding window of 60 s, and marked segments with RMS values higher than a threshold as the contraction episodes [8]. Inspired by the propagation of the contractions throughout the uterine wall, Hassan *et al* proposed to identify contractile episodes by high values of nonlinear correlation coefficient between signals recorded by different electrodes [9]. Tylcz *et al* moved forward by applying the nonlinear correlation analysis to a selected component of the discrete wavelets transform of the original EHG signal [10]. Song *et al* adopted a new approach, i.e., calculating the zero-crossing rate of the EHG signals [11]. More detailed informations on EHG based uterine contraction identification methods can be found in the recently published review paper [12].

Indeed, the EHG based methods have shown a relatively high successive rate in identifying real contractions. However, it is typically accompanied by high false detection rate. For example, the non-linear correlation analysis based method proposed by Tylcz *et al* was capable of identifying 83.5% of the real contractions. However, this high rate on true contraction detection was accompanied by a false detection rate of 68.2% [10]. When using these automatically identified contractile segments in classifying imminent labor and pregnancy patients, no clear improvement in classification precision was observed [10]. In contrast, TOCO is less likely to miss-label dummy intervals as contraction, and might be more powerful in preterm prediction. For this reason, several publicly-available EHG databases provide the simultaneously recorded TOCO signals [13, 14]. Empowered by the TOCO signals, the contractile EHG segments could be effectively identified, from which features that characterize term/preterm or labor/pregnancy would be extracted to classify patients of risk. Despite the high performance scores reported in the literatures [14, 15, 16], the real benefits it could bring in practical application were still questioned [17].

Both theoretical and clinical studies have all confirmed the key function of uterine contraction to a successful delivery of fetus [18, 19]. However, the generation of contraction alone is not sufficient. To expel the fetus out, contractions should appear not only synchronously but also globally, i.e., the contractions start near the fundus of uterus and propagate downward. The signals revealed by the strain gauge in-

side the tocodynamometry is a macro effect of contractions. Suffered from interferences from maternal movements and other technical limitations, the TOCO limits its power in detecting contraction duration and frequency. Consequently, the TOCO alone has a very limited usage in the diagnosis of dystocia, even without any external interference [20].

The fundamental roles of electrical activities in triggering muscle contractions inspire researchers to explore new methods for predicting preterm birth [21, 22] and imminent labor [10]. Most of these works emphasize on extracting the embedded information in the noisy time series of EHG to separate term/preterm patients in a machine-learning way [23]. The frequently used features include RMS, entropy, frequency, etc., among which the entropy features such as sample entropy and approximate entropy are proven to have superiority over the others [24, 25], thanks to their strong power in characterizing irregularity[26]. Combining these features, some of the machine-learning based models demonstrate strong power in prediction preterm birth [21]. However, this end-to-end fashion prevents its usage in real practice due to the lack of reasonable explanation. Research works that attempt to integrate the contractile information in preterm or imminent labor prediction were carried out simply by extracting same types of features only from the contractile EHG segments identified from TOCO or other methods [14], rather than characterizing contraction itself, such as synchrony and coherence. In addition, as the features were extracted from specific channels (time series), they are lack of the power in revealing spatial pattern of electrical activity. Recently, some explorative works have been carried out to characterize the temporal-spatial irregularity of the uterine electrical activities by constructing the entropy quantities from multiple channels EHG recordings [27]. However, due to the lack of information on the contraction, these multi-channel EHG based entropies features are still lack of efficiency. In addition, research works that focus on characterizing the propagation of contractions throughout the whole uterus did not bring much benefits to practical diagnosis [28, 29].

Targeting the real clinical demands in uterine contraction monitoring, this paper aims to provide a way for quantifying the synchrony and coherence of contractions and to verify their abilities in detecting imminent labor from normal pregnancies. To proceed, contractile time windows identified from the TOCO signals are used to segment out EHG fragments from all channels of electrodes. As these electrical segments are direct manifestations of contractile activities at different locations, we establish quantitative representations of synchrony and coherence of contractions from these segments. The effectiveness of the quantities in detecting imminent labor are then tested on public available database.

2. Materials and Methods

2.1. Overview of the proposed method

Keeping in mind the essential roles of synchronized and coherent uterine contractions, we focus on characterizing the spatial regularity and synchrony of the contractile activity of

the uterine wall, by extracting the spatial-temporal information embedded in the EHG segments from multiple channels. To the end, as illustrated in Fig. 1, the proposed method takes both the simultaneously recorded multiple-channel EHG signals and the TOCO signal as inputs. The raws EHG signals are first preprocessed by a Butterworth filter and downsampled, while the TOCO signals are used to identify the contractile time-windows. Both the preprocessed raw EHG signals and the contractile time-windows are used in the EHG segmentation stage, where EHG segments of all channels under each of the contractile time windows are selected out and used to construct quantities that describe the spatial regularity and synchrony of that contraction. Finally, obtained quantitative descriptions of synchrony and spatial regularity of uterine contractions are used to classify imminent labor patients. In the following, we detail each of the stages.

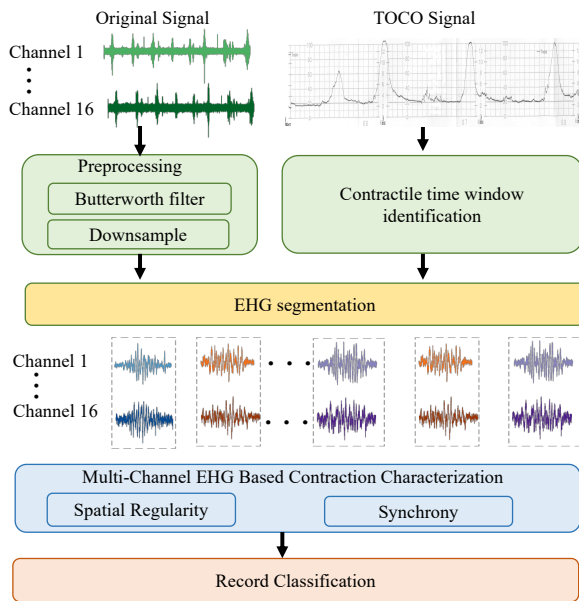


Figure 1: Workflow of the proposed method.

2.2. Data Materials and Preprocessing

2.2.1. dataset description

As stated in the previous section, this paper focuses on characterizing the properties of uterine contractions of interest to obstetricians' clinical practice in predicting the onset of real labor. Information on uterine contractions is the pre-requirements. Although, there are several datasets with TOCO signals available [13, 14], we used the Icelandic 16-electrode Electrohysterogram Database from PhysioNet in the present study [13], taking into account data accessibility and better characterization of the coherence and synchrony of contractions. This database, established by a collaboration between groups in France and Iceland, contains 122 EHG recordings collected at Landspítali University Hospital, Akureyri Hospital and the Akureyri Primary Health Care Centre using 4×4 electrodes configuration. In contrast to the commonly used TPEHG and TPEHGT databases, whose

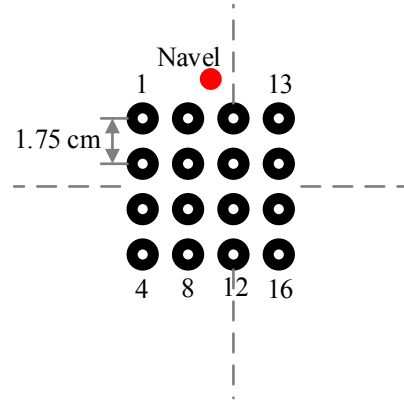


Figure 2: Data acquisition protocol used by the Icelandic EHG database. 16 electrodes are aligned into a square-shape, with the four corner ones labeled with indices 1, 4,13 and 16, respectively[13].

signals were recorded in a bipolar way with a sampling frequency of 20 Hz, the Icelandic 16-electrode signals were monopolar and recorded with a sampling frequency of 200 Hz, for a duration of 16-30 minutes. In addition, the uterine contractile activities were simultaneously recorded by the tocography(TOCO) and included in the database.

Aside from the difference in recording protocol, most of the participants contributed multiple EHG recordings in the database, and the total 122 EHG records were from 45 participants. Recall the aim of the current study, i.e., to predicting whether imminent labor would happen according to these multiple EHG monitoring, these 122 records are independent samples. To this purpose, these signals are typically categorized into labor and pregnancy groups, with the labor group defined as the recordings performed on participants who gave birth within 24 hours, and the pregnancy group are recordings performed on patients at a time-to-delivery (TTD) larger than 24 hours. However, participants in two groups did not show any difference in their physical examinations (see Table 1). The high p -values obtained from the Wilcoxon rank-sum tests on the measurements reveal that the these examinations have little ability in distinguishing pregnancy and labor patients. Same observations hold even when we categorize the recordings according to the criteria of different TTDs ($> 72h$, $>120h$).

2.2.2. preprocessing method

The EHG signals typically consists of long recordings (~ 30 minutes) of the electrical activity of the uterine myometrium. Combined with a sampling frequency up to 200 Hz, processing these signals may require enormous computational resources and may be affected by the interferences of different noise sources. Considering the fact that the main components of uterine electrical activities, i.e., the fast and slow waves, are of the frequency 0.03 to 1.0 Hz and 0.3 to 1.0 Hz, respectively [30], the raw EHG signals were first preprocessed by a Butterworth low-pass filter of 4th order with a cut-off frequency of 3 Hz and then downsampled with

Table 1
Physical information of patients included in the study

Groups	Pregestational BMI			BMI at Recording			Maternal age(years)			Gravidity		
	Average	SD	p-value	Average	SD	p-value	Average	SD	p-value	Average	SD	p-value
≤24h (n=14)	26.23	5.89	0.73	30.95	4.94	0.27	30.45	5.61	0.69	3.27	1.91	0.23
>24h (n=108)	25.22	4.30		29.19	3.87		29.68	6.46		2.46	1.34	
≤72h (n=19)	26.10	5.65	0.72	30.91	4.73	0.20	30.08	5.51	0.83	3.33	1.84	0.14
>72h (n=103)	25.23	4.34		29.17	3.90		29.74	6.50		2.43	1.34	
≤120h (n=99)	26.49	5.24	0.38	30.69	4.27	0.16	30.27	5.30	0.77	3.00	1.83	0.42
>120h (n=23)	25.07	4.36		29.14	4.00		29.67	6.59		2.47	1.35	

a moving-average of 200 ms-window. The time-windows where contractions can be detected from the simultaneously recorded TOCO signal are then used to segment out the contractile fragments from each channels. The following subsection details the procedures of identifying contractile EHG segments.

2.3. Methods

2.3.1. Uterine Contraction Identification

Correct detection of contractions is of essential importance in obstetric practices. Although contractile information might be retrieved directly from the EHG signal itself [11, 10], its practical usage might be severely limited by the relatively high rate of mis-labelling non-contractile segments as uterine contractions[10]. In addition, using EHG signals to determine contractile segments explicitly excludes time synchrony between contractions from different channels, which is the basis for quantitating synchrony of contractions. In contrast, TOCO might not record every contraction, but the identified contractile segments are typically direct manifestation of the contractile activities on the uterine wall[4]. To this end, two clinical experts (J. Shen and L. Mu) identified contractions (contractile time windows δt_i) from the Tocodynamometer signals based on the following criteria:

1. A significant increase of abdominal pressure, manifested by a TOCO signal larger than 30,
2. The TOCO segment has a rough Gaussian shape without sharp edges within a time interval,
3. The duration must be larger than 10 seconds.

These criteria helps us determining the time window of each contraction $\delta t_i = [t_i^s, t_i^e]$, i.e., the starting t_i^s and ending points t_i^e of each contraction i . Since the TOCO and EHG signals were recorded simultaneously, the identified time windows δt_i are then used to segment out fragments \mathbf{x}_i^p from each EHG recording of different channel p . As the electrical signals \mathbf{x}_i^p are direct manifestation of contractile activities of different locations on the uterine wall, their temporal-spatial relations are ideal for characterizing the synchrony and coherence of contractions.

Fig.3 shows one of the TOCO signals (ID: ice045) included in the Icelandic EHG database, where 4 contractions (δt_1 to δt_4) can be identified (marked with the dashed lines). Under each of the contractile time-window, for example, the

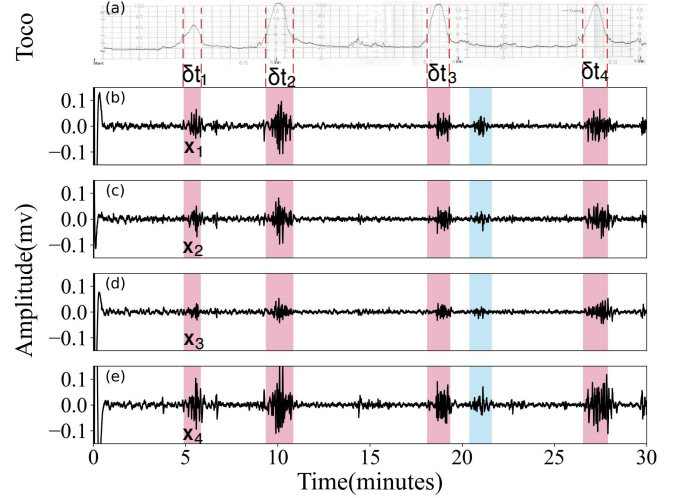


Figure 3: Contractile EHG segmentation method. (a) TOCO signals with contractile segments identified by clinical experts. (b-e) The simultaneously recorded EHG signals from different electrodes. Shaped areas mark the time-windows where contractions were detected from the corresponding TOCO signal shown in (a).

δt_1 , EHG segments \mathbf{x}_p are sliced out from all the N_c channels of the recordings (for illustrative purpose, only 4 channels are displayed in panels (b) to (d)). Clearly, there is a strong correspondence between the electrical activity and uterine contraction, as suggested in[31]. However, this correspondence might not be the same among channels. As can be seen from the figure, segment \mathbf{x}_3 shows very weak burst activity under the first contractile time window. A reasonable explanation to this inconsistency would be the absence of contraction underneath that specific electrode. Diving a little deeper, we would also notice that there is a time difference in the onset of the burst activities $\mathbf{x}_1, \mathbf{x}_2$ and \mathbf{x}_4 recorded at different positions. These spatial-temporal relations embedded in these EHG segments are indeed what the obstetricians are interested in. In addition, not all the bursting activity in EHG results in a detectable mechanical contraction (the blue shaped area). These bursts might be some artifacts from other organs, and contribute nothing to real contractions. With no doubt that treating these segments as contractions would lead to poor performance in real practice.

The above observations motivate us developing quanti-

Table 2

Identified contractile segments in EHG recordings from different patient groups.

Group	Contractions	Patients
Pregnancy	293	61
Labor	81	9
Total	374	70

tative descriptions to the uterine contraction using the multiple channel EHG segments under each contractile time-window. To this end, we applied contraction detection criteria to TOCO signals included in the Icelandic EHG database, where identified 293 contractions for the 61 patients in the pregnancy group and 81 contractions for the 9 patients in the labor group (see Table II). In the following subsection, we present how these EHG segments are used.

2.3.2. Multi-Channel EHG Based Contraction Characterization

Many obstetricians have found that the contractions detected from the TOCO signals provide little information about the synchrony and coherence of contractions, which are believed to be important for a successful expulsion of the fetus[32]. The EHG signals collected from electrodes are localized electrical activities of the underlying muscle cells. They could be useful in characterizing the contraction properties of interest to clinicians. As shown in Fig.3, under the same contractile time-window, the EHG segments of different channels show differences in strength, timing and duration. These differences could be a direct consequence of the very localized and clustered contractions on the uterine wall[33]. Since synchronized contractions are the most important key contributor to the propelling force, we focus on quantitating the spatial-temporal regularity of the contractile EHG segments, like in many other existing works[34, 27, 35]. In the following, we introduce the spatial sample Entropy and concordance correlation coefficient to quantitate the spatial regularity and synchrony of contractions throughout the uterus.

Sample Entropy Based Spatial Regularity Characterization For each record in the Icelandic EHG database, we identify all n contractile time-windows $\{\delta t_1, \delta t_2, \dots, \delta t_n\}$, where δt_i is the 2-element tuple describing the starting and ending point of the i^{th} contraction. Denoting by $N(i)$ the number of points recorded from each of the N_c channels under the contractile time window δt_i , we concatenate all the contractile segments $\mathbf{x}_p = [x_1, x_2, \dots, x_N]$ to form a long sequence $\mathbf{X} = [\mathbf{x}_1, \mathbf{x}_2, \dots, \mathbf{x}_{N_c}]$, with $p (= [1, 2, \dots, N_c])$ the channel index. Apparently, there are $L = N \cdot N_c$ data points within \mathbf{X} . The relationship between uterine muscle cell mechanical activity and the underlying electrical activity suggests the spatial-temporal correlations embedded in \mathbf{X} being suitable candidates to the characterization of the properties of uterine contractions. For this reason, we first introduce the sample entropy to quantitate the regularity of \mathbf{X} .

To this end, the spatial sequence \mathbf{X} are subdivided into $L - m + 1$ small segments $X_m[u]$ of length m , where $u (= 1, 2, \dots, L - m + 1)$ indicates the u^{th} segment (u is the first index of the sequence of m consecutive indices). For each u , we calculate the number of occurrence B_u that the distance between $X_m(u)$ and other segments $X_m(u')$ with $u \neq u'$ is within a tolerance of r . We used here the classical Euclidean distance. This yields an estimate of the empirical probability $C_u^m(r)$ as:

$$C_u^m(r) = \frac{B_u}{L - m + 1} \quad (1)$$

Here, $C_u^m(r)$ characterizes the probability of the existence of any periodic pattern of length m in the sequence of \mathbf{X} . If this sequence \mathbf{X} is regular, we would expect the existence of other longer periodic patterns. Introducing the average over all small segments $\Phi_{av}^m(r)$ defined as:

$$\Phi_{av}^m(r) = \frac{\sum_{u=1}^{L-m+1} C_u^m(r)}{L - m + 1} \quad (2)$$

we come up with the SamEn defined as

$$\text{SamEn}(m, r, L) = -\ln \frac{\Phi_{av}^{m+1}(r)}{\Phi_{av}^m(r)} \quad (3)$$

to describe the spatial regularity of the contractile EHG segments collected from different locations on the uterine wall. Apparently, according to this definition, regular (period) time sequence gives an Sample entropy value close to 0, while chaotic time series give very large positive sample entropy values.

Concordance Correlation based Synchrony Characterization Concordance correlation was first introduced by L.I. Lin to evaluate the agreement between two independent measurements [36]. Due to its robustness, the concordance correlation coefficient (CCC) is widely used in various fields[37, 38, 39]. Here, we adopt the CCC to describe the synchrony between two localized contractile segments \mathbf{x}_p and \mathbf{x}_q as

$$\text{CCC}_{p,q} = \frac{2\sigma_{x_p, x_q}}{\sigma_{x_p}^2 + \sigma_{x_q}^2 + (\bar{x}_q - \bar{x}_p)^2} \quad (4)$$

where σ_x is the variance of the time series x , $\sigma_{x,y}$ is the covariance of x and y , and \bar{x} represents the mean of x . With N_c channels of EHG segments collected simultaneously, the synchrony of contractions over the entire uterus can then be represented as

$$\psi = \frac{N_c^2}{2} \cdot \sum_{p=1}^{N_c} \sum_{q=p+1}^{N_c} \text{CCC}_{p,q} \quad (5)$$

Clearly, a perfectly synchronized contraction across the uterus will result in a value of $\psi = 1.0$, whereas localized, random contraction, without any synchrony, will lead to a value of ψ close to zeros.

2.3.3. Statistical Methods

The obtained characteristics of contractions identified from different patient groups (labor/pregnancy or later introduced categories based on time-to-delivery) are presented with descriptive statistics, including average, 95% confidence interval (CI), and standard deviations. A Wilcoxon rank-sum test is performed to examine whether there is a significant difference between patient groups, classified by different criteria values of the TTD introduced earlier. Through out this work, a p value < 0.05 is considered as statistically significant. Using these statistically significant quantities, we construct a receiver operating characteristic (ROC) curve by introducing different cut-off values to the patients. The area under curve (AUC) is further determined to quantify the ability of these quantities to discriminate between different types of patients.

3. Results

We divided the records in the Icelandic EHG database into different categories. In particular, we varied the critical time T_c used to delineate the time to delivery (TTD), according $TTD \geq T_c$ and $TTD < T_c$. With the two features introduced to describe the properties of contraction, namely the SamEn and ψ , we show in Fig.4 a direct comparison of the patients in the two groups determined by the criteria $T_c = 24$ h. As expected, the entropy values (SamEn) are getting smaller, and the ψ are getting larger, as a pregnancy evolves toward delivery, contractions become more regular and synchronized. More importantly, both of the two features show a clear separation between the pregnancy ($TTD \geq 24$) and labor ($TTD < 24$) groups. This ability in discrimination is confirmed by the tiny p values obtained from a Wilcoxon rank-sum test (see Table 3). In addition, despite a gradual decrease in the abilities of these features in separating different groups with increasing TTD, a p value as small as 10^{-10} suggests its power in predicting imminent labor 120 hours in advance (see Table 3 for detailed information).

The statistical difference between the groups shown in Table 3 suggests that a threshold value c can be set to detect

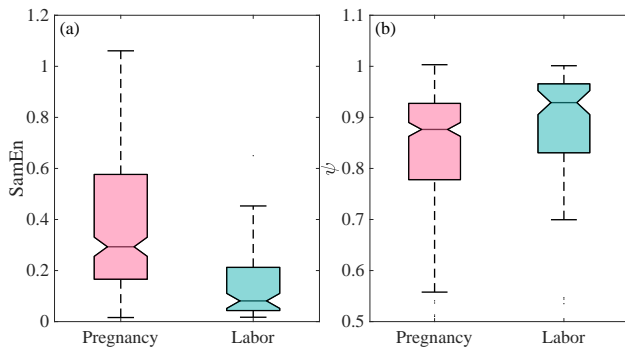


Figure 4: Distribution of the SamEn (a) and ψ (b) features of contractions identified from EHG signals recorded from the patients in the pregnancy ($TTD > 24h$) and labor ($TTD \leq 24h$) groups .

Table 3

Statistical comparison of features between groups determined by different TOD.

groups	SamEn(CI)	p	ψ (CI)	p
$>24h$ (11)	0.377(0.349-0.406)	6.45E-19	0.836(0.823-0.850)	2.60E-08
$\leq 24h$ (59)	0.143(0.119-0.168)		0.900(0.881-0.920)	
$>72h$ (12)	0.370(0.341-0.399)	1.02E-13	0.838(0.824-0.852)	4.78E-06
$\leq 72h$ (58)	0.184(0.149-0.220)		0.891(0.872-0.909)	
$>120h$ (15)	0.365(0.336-0.394)	1.69E-10	0.837(0.822-0.851)	4.92E-05
$\leq 120h$ (55)	0.214(0.176-0.253)		0.887(0.870-0.904)	

imminent labor, i.e., samples with $SamEn \leq c$ (or $\phi \geq c$) are imminent labor patients, who are likely to give birth within a period no longer than T_c . Applying this idea to the data in the Icelandic database, those who do give birth within T_c same as the model predicts are termed as true positive (TP) samples, while those who contradict the model's prediction as imminent labor are termed as false positive (FP). Under the same scenario, a sample is termed as true negative (TN) when the model's prediction as a pregnant patient matches the final outcome of that patient, otherwise it is termed as false negative(FN). These quantities enable the construction of two frequently used metrics in evaluating classification performance, i.e., sensitivity, specificity and accuracy, defined as:

$$\begin{aligned} \text{sensitivity} &= \text{TPR} = \frac{\text{TP}}{\text{TP} + \text{FN}} \\ \text{specificity} &= \text{TNR} = \frac{\text{TN}}{\text{TN} + \text{FP}} \\ \text{accuracy} &= \frac{\text{TN} + \text{TP}}{\text{TP} + \text{FP} + \text{TN} + \text{FN}} \end{aligned} \quad (6)$$

Further more, when a set of different threshold values c are used to discriminate pregnancy and labor groups, a Receiver Operating Curve (ROC) can be plotted. In Fig.5, we show the obtained ROC curve of the SamEn feature in classifying labor ($TTD \leq T_c$) and pregnancy ($TTD > T_c$) groups using different T_c .

The ROC is a fundamental tool for assessing the discriminative power of features, as the Area Under Curve (AUC) quantifies the power of features to distinguish different groups. In general, a higher AUC value indicates better classification performance. In our case, the entropy based feature SampEn has an AUC value of 0.834, indicating its high power in predicting imminent delivery within 24 h[40]. Although, the concordance correlation based feature ψ does not have the same classification strength, the value of the AUC of 0.7 suggests its potential application in determining imminent delivery. More importantly, the proposed features retain their discriminatory power even when the EHG signals were measured 120 hours before delivery (AUC=0.698 and 0.650).

In Table 4, we show the performance of the proposed features SamEn and ψ in classifying the imminent labor patients under the condition of their optimal threshold values c_o . Both the two quantities demonstrate high power, especially in detecting patients who would give birth within 24 hours. The sample entropy based feature SamEn gives the

Table 4
Comparison of Classification Performance of the proposed method with the SOTA ones

Reference	Features	T_c	c	AUC	Sensitivity	Specificity	Accuracy
Our study	SamEn	24 h	0.22	0.834	0.909	0.712	0.743
		72 h	0.22	0.773	0.833	0.707	0.729
		120h	0.22	0.698	0.733	0.709	0.714
	ψ	24 h	0.91	0.726	0.727	0.695	0.700
		72 h	0.91	0.688	0.667	0.690	0.686
		120h	0.91	0.650	0.533	0.673	0.643
[10]	Detrended fluctuation analysis, mean powerfrequency, nonlinear correlation analysis, sampleentropy variance, modified approximate entropy	1week	–	–	0.807	0.763	0.762
[42]	ApEn	–	–	0.696	0.540	0.770	0.590
	Modified ApEn	–	–	0.621	0.560	0.650	0.600
	SamEn	1week	–	0.696	0.630	0.570	0.630
	Modified SamEn	–	–	0.635	0.560	0.560	0.570
	Time Reversibility	–	–	0.540	0.480	0.350	0.460
[43]	MSamEn	–	0.460	–	0.730	0.600	–
	GSC	–	0.790	–	0.600	0.600	–
	Combined index	–	0.540	–	0.500	0.870	–

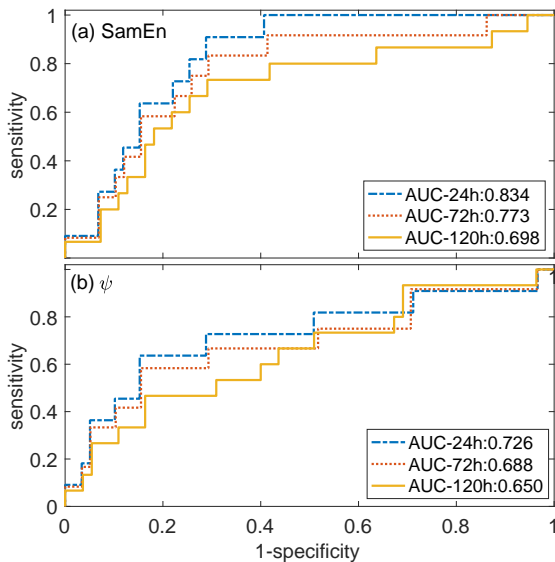


Figure 5: The Receiver Operator Characteristic curves of the sample-based feature SamEn (a) and the concordance correlation based feature (b) in discriminating imminent labor defined by different T_c .

sensitivity, specificity and overall accuracy as high as **0.909**, **0.712**, and **0.743**, respectively. Comparing to most of the SOTA methods reported in literature, the proposed one gives higher performance scores in terms of AUC, sensitivity, specificity and accuracy, except the one proposed by Tylcz et al., where a sensitivity, specificity and accuracy of 0.807, 0.763 and 0.762 are reported in detecting imminent labor one week before [10]. However, caution should be paid when interpreting these results, as the performance results were obtained using synthetic training and testing samples generated by the oversampling synthetic algorithm SMOTE, resulting in overly optimistic classification results [41].

This strong discriminatory power results from the ability

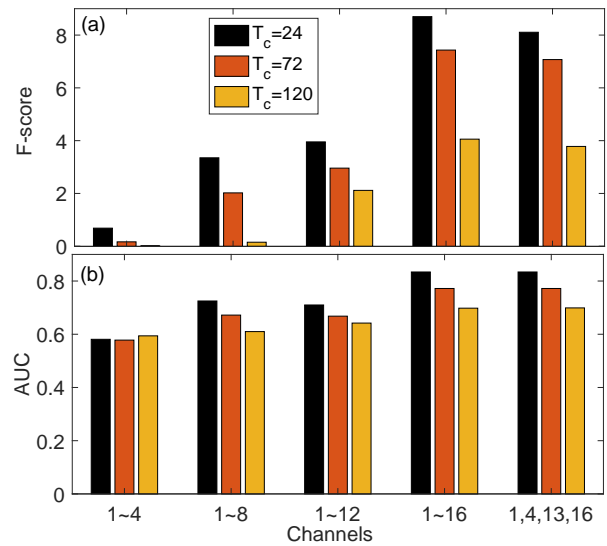


Figure 6: The discriminatory power of the SamEn feature constructed from different channels of EHG signals. (a) Discriminatory power characterized by feature score F-score. (b) Discriminatory power represented by the AUC values in predicting imminent labor patients.

of the proposed features in characterizing the synchrony and coherence of uterine contractions. Since the EHG signals recorded by electrodes are the direct manifestation of muscle activity underneath the electrodes, the more channels of EHG are used in constructing the SamEn feature, the more local information are taken into account. Consequently, the feature is more efficient in describing synchrony, and eventually contributes to strong discriminatory power. We demonstrate this by constructing both the entropy and the concurrence correlation based features from different EHG signals of different channels. We quantify these features' effectiveness in classifying imminent labor by introducing the feature score F-score defined in [44] and their AUC values obtained

in discriminatory tasks. Fig.6 shows how the SamEn's discriminatory power varies with the number of channels used in calculating SamEn of patients. The same feature (SamEn), when is calculated using the EHG signals from channel 1~4 (see Fig.2 for the real locations of these electrodes), its power in discriminating imminent labor patients is much weaker comparing to that calculated by using the EHG of all channels (channels 1~16). In general, including more channels of EHG signal in constructing these features typically improves feature's classification ability. However, when the 4 outmost channels (channels 1, 4, 13 and 16 in Fig.2) are used to calculate the entropy feature, SamEn has the same predictive power in detecting imminent labor as the entropy feature obtained by using all the channels (see the most right two branches of bars in Fig.6). This phenomena would be interpreted as an implicit evidence for the propagation of contractions demonstrated in vitro experiments[45].

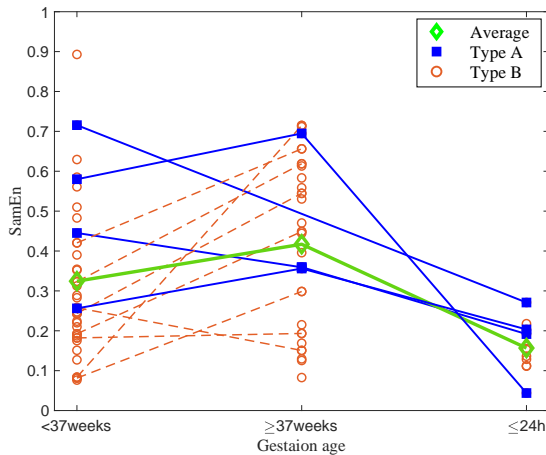


Figure 7: Evolution of uterine contractions throughout the whole pregnancy in terms of SamEn. The whole period of pregnancy was represented by three gestational ages < 37 and ≤ 37 weeks, and < 24 h before delivery according to the data available in the database. Individuals who have recordings at pregnancy and labor stages (Type A) are marked as blue filled squares. Individuals who only have the labor records or don't have the labor records (Type B) are marked by open orange circles.

The statistical analysis shown above strongly suggests that the contractions become more synchronized and coherent toward final delivery, a condition required to expel the fetus out[18]. Physicians are interested in individual's evolution pattern throughout the whole pregnancy. In Fig.7, we plot the synchrony property (characterized by the proposed SamEn feature) of uterine contractions of patients enrolled in the Icelandic database at three different presentative stages, i.e., < 37 weeks, ≥ 37 weeks, and < 24 hours to delivery. Although most of patients (Type B) included in the database do not have EHG records at the labor stage (≤ 24 hour to delivery), those who provided EHG signals both at pregnancy stages (< 37 weeks, ≥ 37 weeks) and labor stage (Type A) show a similar evolution trends as that of the collective be-

havior (Average), suggesting its great clinical potential in determining immediate delivery by setting an optimal cut-off value.

4. Discussion

Uterine contractions are the direct force to the delivery of babies. Although, contractions are routinely monitored and measured in regular prenatal care during the last stage of pregnancy, anxiety is still very common among pregnant women. There is very little information on the timing of birth that can be given based on the TOCO signals. As a results, pregnant women with contractions detected at early stage are likely to be hospitalized, in order to prevent any unexpected risks. The fact is, more than 50% of these patients don't have any risk of preterm birth but are receiving unnecessary treatment[46]. On the other side, 20% of those who are not hospitalized suffer from emergent labor[47]. It has long been noticed that the generation of contraction alone is not sufficient to propel the fetus[32]. Synchronized contractions throughout the whole uterus are also very important [18]. In this study, we proposed a method that quantifies the synchrony and coherence of uterine contractions. Statistical Analysis carried out the patients included in the Icelandic EHG database reveals their clinical applications in predicting imminent labors.

Although, the electrohysterography has long been known of great potentials in obstetric applications, the existing explorative works mainly focus on mapping the electrical signals to the pregnancy outputs (preterm or normal term) by extracting information on contraction intensity, duration and interval [4, 48, 49, 5]. Despite the claimed high precision in identifying preterm pregnancies, there still does not exist any matured clinical practice. To promote clinical use of EHG, research works should focus on exploring ways to meet the requirements of obstetric practice. Recently, a clinical trial has been carried out by Qian et al. [50] to grade oxytocin augmentation by characterizing contraction intensity using features extracted from the measured EHG signals.

Besides the intensity, revealing the propagation pattern of contractions is also important in clinical practice [32]. To propel the fetus out, contractions must initiate at the fundal and propagate throughout the whole uterus in a synchronized way[51]. Multiple-channel EHG signals are ideal to characterize the propagation pattern of contractions[52, 10, 27, 29], as the EHG signals of each channel are direct manifestation of the muscle activity underneath the electrode. However, contractions are rare before the onset of labor. Using the entire EHG recordings to characterize the contractile events will be severely interfered by non-contractile segments. To tackle this, we take the full advantages of tocodynamometer in detecting uterine contractions. Since the contractile windows identified by TOCO signals are seldom mis-labeled dummy intervals, the multiple-channel EHG segments under these windows provide ideal media to the characterization of the spatial-temporal behavior of the contractions.

The study has also several limitations. First, this study did not distinguish spontaneous and induced labor. There is

no information on whether the deliveries are natural or induced by medical treatment. The time difference between the gestational ages at signal recording and final delivery is the only indicator for this study. The small sample size is the second limitation. The entire database contains 122 pregnant samples, only 14 of which gives births with 24 hours. This small size will make the obtained performance scores of step-wise shape and of big fluctuations.

5. Conclusions

The contractile activity on the uterine wall is routinely monitored by tocodynamometer to guide active management of labor and delivery. Localized electrohysterography signals under the contractile windows identified from the TOCO provide effective ways to describe the synchrony and regularity of uterine contractions, which have never been quantitated but are believed to play an important role in the delivery of fetus. In this paper, we proposed a method that combines the advantages of tocodynamometer and multiple channels EHG signals to characterize the synchrony of contractions. Applying this method to analyze data samples in the Icelandic EHG database, the obtained quantitative description of the synchrony of contractions in terms of sample entropy SamEn and concordance correlation coefficient ψ show a great power (AUC:0.834, $p : 0.6 \times 10^{-19}$) in discriminating imminent labors (< 24 hours). Moreover, the discriminatory power persists (AUC: 0.698, $p : 1.69 \times 10^{-10}$) even when diagnosis was made 120 hours before real delivery. However, the synchrony and coherence properties of uterine contractions cannot be easily revealed by the currently available monitoring devices such as tocodynamometer. Clinicians have to use their hands to feel the contractions. The results represented in this study suggest better way in evaluating uterine contractions, i.e., simultaneously recording the uterine muscle electrical activities and uterine contractions. However, as the validation was carried out on a small dataset in which there are only 81 patients and 9 giving births within 24 hours, clinical trials including more sampling patients are encouraged.

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