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# Coupling Analysis of Fetal and Maternal Heart Rates via Transfer Entropy Using Magnetocardiography

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## Abstract

Recent studies have shown that occasional short term coupling between fetal and maternal cardiac systems occurs. Fetal magnetocardiography (fMCG) is a non-invasive technique that records the magnetic fields associated with the electrical activity of the fetal heart through sensors placed over the maternal abdomen. The fMCG allows accurate estimation of fetal heart rates (fHR) due to its high signal-to-noise ratio (SNR) and temporal resolution. In this study, we analyzed coupling between fHR and maternal heart rates (mHR) using Transfer Entropy (TE). TE determines coupling between two variables by quantifying the information transferred between them in both directions. In this work, we used 74 fMCG recordings to compute TE in both directions over 1-minute disjoint time windows (TW). We examined the effect of fetal movement (FM) as a factor of influence on the TE analysis. We identified 21 subjects with FM during the recording and separated them into two gestational age (GA) groups (GA1<32 and GA2≥32 weeks). Next, TE values were compared between TWs containing non-FM with TWs containing FM using Wilcoxon Signed-Rank test. In addition, we compared TE calculations for non-FM segments obtained from the 74 subjects using Rank-Sum test in the two GA groups. Our results showed that TE values from TWs containing FM are not significantly different than those computed for TWs of non-FM. In both directions, we found that TE values obtained from the 74 subjects did not show any significant difference between GA1 and GA2 which is consistent with previous studies. Our study suggests that FM does not affect the TE computations.

## I. Introduction

Evaluation of fetal well-being using fetal heart rate (fHR) has become an important feature in all pregnancies. With the advancements in biomagnetic technology and signal extraction methods it has been possible to non-invasively and simultaneously record an array of fetal parameters with a single device, such as the fetal magnetocardiography (fMCG). fMCG provides accurate estimation of the fHR due its high temporal resolution and therefore is very useful tool to investigate the underlying causes of the changes occurring in fHR. Changes in fHR can stem from various fetal-based conditions as well as external factors. Maternal psychological and physiological conditions such as maternal hormones transferred

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via the placenta, changes in the oxygen and nutrition supply for the fetus, maternal stress, and anxiety level may affect fHR [1], [2], [3]. Additionally, maternal relaxation has shown to be linked with decreased fHR and increased variability [4]. Furthermore, positive correlations between fHR and maternal heart rate (mHR) have been found over periods of 1 and 24 hours [5]. Also, it has been shown that fHR is highly correlated with maternal diurnal rhythm [6].

Several studies have investigated short-term interactions between fHR and mHR. Using phase synchronization analysis, studies have reported occasional beat-to-beat level coupling between fetal and maternal cardiac systems [7], [8]. A similar result was obtained by a model based method in [9] using an additive autoregressive processes with external contributing factors. Van Leeuwen et al. [10] investigated the influence of the maternal respiratory arrhythmia in the occurrence of the mHR and fHR short-term coupling. They reported that the fetal cardiac system seems to possess the capability to adjust its rate of activation in response to external stimulation. This stimulation can be associated with mechanical or auditory outcomes of the maternal heart rhythms.

The study of Marzbanrad et al. [11] uses Transfer Entropy (TE) computation introduced in [12] to quantify the mHR-fHR and fHR-mHR couplings using one-minute abdominal electrocardiography (ECG). They found that TE from mother to fetus increased in mid and late GA compared to early GA while TE in the other direction did not change significantly. Additionally, they found not significant effects of maternal respiratory rate on TE values in both directions. To our knowledge, TE has never been applied to fMCG signals. Thus, we calculated TE for mHR and fHR obtained from fMCG recordings to investigate their interactions at different GAs. In addition, fetal movement (FM) has been associated with fHR changes [13], [14] and the effect of FM on mHR-fHR interaction has not been studied. Therefore, we also examined the influence of FM on the TE analysis.

## II. Methods

### A. Data Collection and Preprocessing

For this study, we used 74 recordings obtained from a low-risk group of pregnant women between 28–38 weeks of GA. Data was collected from the 151 channel SARA (SQUID Array for Reproductive Assessment) system. Spontaneous data was recorded under the protocols approved by the Institutional Review Board with sampling rate of $sf = 312.5$ Hz. Recordings were filtered between 1 Hz and 50 Hz and maternal R peaks (iRm) were identified. To obtain fMCG, maternal MCG was removed using the Orthogonal Projection algorithm [15], [16] and R peaks of the fMCG data (iRf) were identified using an adaptive Hilbert transform approach [17], [18]. Fetal and maternal RR intervals (fRR and mRR) were calculated and smoothed using a moving window of 5 beats. Then, fRR and mRR were resampled to 4 Hz using cubic spline interpolation. In addition, the actogram was computed [19] to quantify FM. We defined a substantial FM when actogram values attained 0.12 cm above the baseline.

### B. Transfer Entropy

Transfer entropy (TE) between two time series $X = x_1, \ldots, x_N$ and $Y = y_1, \ldots, y_N$ is computed as

$$TE_{X \to Y} = H\left(y_i \middle| y_{i-\tau}^{l}\right) - H\left(p\left(y_i \middle| y_{i-\tau}^{l}, x_{i-\tau}^{k}\right)\right) = \sum_{y_i, y_i^l, x_{i-\tau}^k} p\left(y_i \middle| y_i^l, x_{i-\tau}^k\right) log \left(\frac{p\left(y_i \middle| y_{i-\tau}^{l}, x_{i-\tau}^{k}\right)}{p\left(y_i \middle| y_{i-\tau}^{l}\right)}\right), \quad (1)$$

where $i$ is a given time point, $\tau$ and $t$ are the time lags of X and Y, respectively, $k$ and $l$ are the lengths of the blocks containing the past values of $X$ and $Y$, respectively [12].

We computed TE for the mHR and fHR in two directions: maternal to fetal (M→F) and fetal to maternal (F→M). $X$ and $Y$ in Eq. (1) correspond to mRR and fRR intervals after re-sampling. In order to increase the robustness of measure against outliers and sparse regions of the distribution, the RR intervals were replaced by their integer ranks when sorted from the smallest to the largest. As suggested in [12], we assumed $k=l=t=1$ and computed TE for 40 time lags as $\tau$=0.25–10 sec in equal steps of 0.25 sec.

The fixed bin method by allocating the data points to equally-spaced bins was used to compute the conditional probabilities in Eq. (1). The same number of bins, i.e. $Q = 10$, were used in each dimension as in [11] which simplified the TE computation as follows:

$$TE_{X \to Y(\tau)} \approx \sum_{a=1, b=1, c=1}^{Q=10} \frac{m_{a,b,c}}{P} log \frac{m_{a,b,c} m_b}{m_{b,c} m_{a,b}}, \quad (2)$$

where $a$, $b$, and $c$ are the index of bins along $y_i$, $y_{i-1}$, and $x_{i-\tau}$ time series, respectively, and $P$ is the total number of triplets of $y_i$, $y_{i-1}$, and $x_{i-\tau}$. The number of data points in the intersection of the bins are denoted by $m_{a,b,c}$, $m_{a,b}$ and $m_{b,c}$ while $m_b$ is the number of data points at the $b$-th bin in $y_{i-1}$. More details on the computation of TE can be found in [12].

## III. Results

### A. The Effect of Fetal Movement

The recordings used in this study were in the range of 6 to 11 minutes duration. Therefore, we computed TE using 1-minute disjoint time windows (TW). We first analyzed the effect of FM on TE computation. After FM calculation, we identified TW that contains FM. We decided to label as a TW with FM when the 1-minute window contains ≥70% of FM. Fig. 1 displays TW together with FM intervals for a subject. As seen in the figure, TW4 and TW6 contain at least 70% of FM. Therefore, TEs obtained from TW4 and TW6 contribute to the FM group while all others contribute the non-FM group.

For each TW, we used the re-sampled mRR and fRR values within that specific TW and obtained 40 $TE_{(M \to F)}$ and 40 $TE_{(F \to M)}$ values corresponding to the 40 different time lags

ranking from 0.25 to 10 sec. Next, mean TE and maximum TE values for each TW were computed for further analysis.

Fig. 2 displays an example of TE computation for the first TW of a fMCG recording. In Fig. 2(a) SARA array is shown where two sensors are marked as the ones containing mMCG and fMCG traces (Fig. 2(b)). The corresponding RR and re-sampled RR intervals are shown in Fig. 2(c). Fig. 2(d) displays the $TE_{(M\rightarrow F)}$ (red) and $TE_{(F\rightarrow M)}$ (blue) values for TW1 corresponding to a non-FM window. In 2(e), we also display TE values for TW6 that represents a window with FM.

Out of 74 subjects, only 21 recordings have at least one TW with FM. Therefore, we have used those 21 subjects for comparing the TE values between non-FM and FM segments. The mean and maximum TE values of the TW with FM and non-FM were computed. Next, Wilcoxon signed-rank test ($\alpha$ = 0.01) was used for comparison between TE values obtained from TW with FM and non-FM. We performed the analysis in two GA groups: GA1 < 32 weeks ($n_1$=7) and GA2 ≥ 32 weeks ($n_2$=14).

Table I shows the median of mean and maximum TEs together with the $25^{th}$ and $75^{th}$ percentiles for both non-FM and FM segments. Table I also includes p-values obtained from the signed-rank test. Results show that mean and maximum $TE_{(M\rightarrow F)}$ and $TE_{(F\rightarrow M)}$ in both GA groups are not significantly different (p>0.01) between non-FM and FM segments. However, we found that the difference of the maximum $TE_{(F\rightarrow M)}$ between non-FM and FM segments at GA2 trends to be significant (p=0.030). Our results show a non-significant increase in the mean and max $TE_{(F\rightarrow M)}$ values for GA1 (i.e. mean from 1.24 to 1.27 and max from 1.49 to 1.57) showing a percentage difference around 5%. For mean and maximum $TE_{(M\rightarrow F)}$ values a non-significant decrease in GA1 and a non-significant increase at GA2 were found.

### B. Comparison Between Gestational Age Groups

We investigated GA effect over TE computation by comparing TE values of TW with non-FM between the two GA groups using all 74 subjects. There were 31 subjects in GA1 (<32 weeks) while GA2 (≥32 weeks) includes 43 subjects. We conducted Wilcoxon Rank-Sum test ($\alpha$ = 0.01) to compare mean and maximum TEs in both directions. Table II displays the median and the percentiles in both directions for the two GA groups. Neither mean nor maximum $TE_{(M\rightarrow F)}$ showed a significant difference between the two GA groups. On the other hand, mean and maximum $TE_{(F\rightarrow M)}$ showed a decrease from GA1 to GA2. Mean and maximum $TE_{(F\rightarrow M)}$ tend to significance (p=0.043 and p=0.055) between groups with percentage differences in the range of 5–6%.

## IV. Discussion

In this study, we applied TE technique using fMCG recordings to investigate the relationship between fHR and mHR in both directions for longer recordings in comparison with the work using ECG reported in [11]. The main advantage of fMCG over ECG is that electrical currents are significantly attenuated by the tissues surrounding the maternal abdomen [20], [21], which can drastically diminish the amplitude of the ECG signals. In addition, ECG

usually fails between 28 to 34 weeks of gestation because of the formation of vernix caseosa around the fetal body which acts as a strong electrical insulator [20], [22]. Because of these reasons, fMCG can reveal any interaction occuring between the fHR and mHR more accurately than ECG especially in the third trimester.

In comparison with the work reported in [11] using ECG, our work can reveal the possible influence of non-stationarity in fHR on TE analysis due to the high SNR and temporal resolution of fMCG recordings. fHR becomes a more non-stationary process in the late GA due to the increased number of FM. In general, our results are consistent with the ones reported in [11] in terms of TE and GA relation. They found no significant difference in the TE values between the mid and late GA groups which is consistent with our results. Their mean and maximum $TE_{(F\rightarrow M)}$ values also showed no significant change between mid and late GA which is as well consistent with our work. On the other hand, our mean and maximum $TE_{(F\rightarrow M)}$ values (see Table II) between GA groups trended towards significance.

FM has been associated with fHR changes [13], [14] and can be a possible fetal-based factor in fHR and mHR interactions. Therefore, we also investigated how FM affects the TE calculation of the fHR and mHR coupling. Our results show that $TE_{(M\rightarrow F)}$ and $TE_{(F\rightarrow M)}$ show no significant change during FM in both GA groups (see Table I). However, maximum $TE_{(F\rightarrow M)}$ is trend to be significant in GA2 suggesting a possible effect of FM on both fetal and maternal HR. This possible effect might be a result of maternal sensitivity to FM which needs to be confirmed with larger sample size recordings since there were only a few set of epochs containing FM. Based on our findings, we can conclude for this small number of subjects for the TE-FM analysis, that FM has no significant effect on TE computations especially in the direction from mother to fetus.

Previous studies [5], [6], [7], [8], [9] on the fetal–maternal HR synchronization by other methods demonstrated that occasional coupling between fetal and maternal heart rates occurs. However, the direction of the influence has been studied only in [11] using TE method. Identifying the directional influence can provide additional information about how the fetal cardiac activity is affected by the physiological and psychological maternal factors. In future, we will extend our study using other methods as well as TE to identify the possible influences of drugs like opioids used my mothers.

## V. Conclusion

This study reports the first findings of TE analysis on fMCG recordings. The interactions between mHR-fHR and fHR-mHR were quantified for 74 subjects. We identified that 21 subjects had FM intervals during the recording. For the analysis using the 74 subjects, we found no significant difference between GA1 (<32 weeks) and GA2 (≥ 32 weeks) consistent with previous study. For the 21 subjects with FM, when comparing TE values between non-FM segments and FM segments, our results showed no significant effect of FM in the TE computations.

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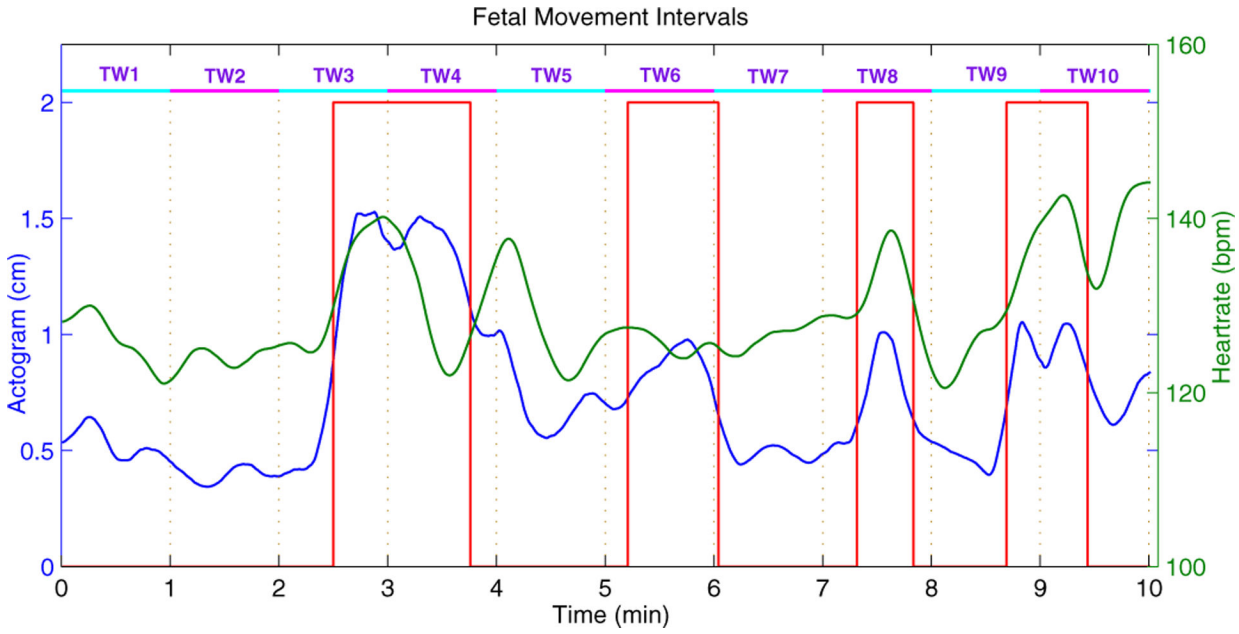


**Fig. 1.**

Fetal movement intervals are shown together with actogram (blue) and fetal heart rate (green) throughout the recording. Red lines indicate the movement intervals. 1-minute time windows are also marked by dashed-brown lines.

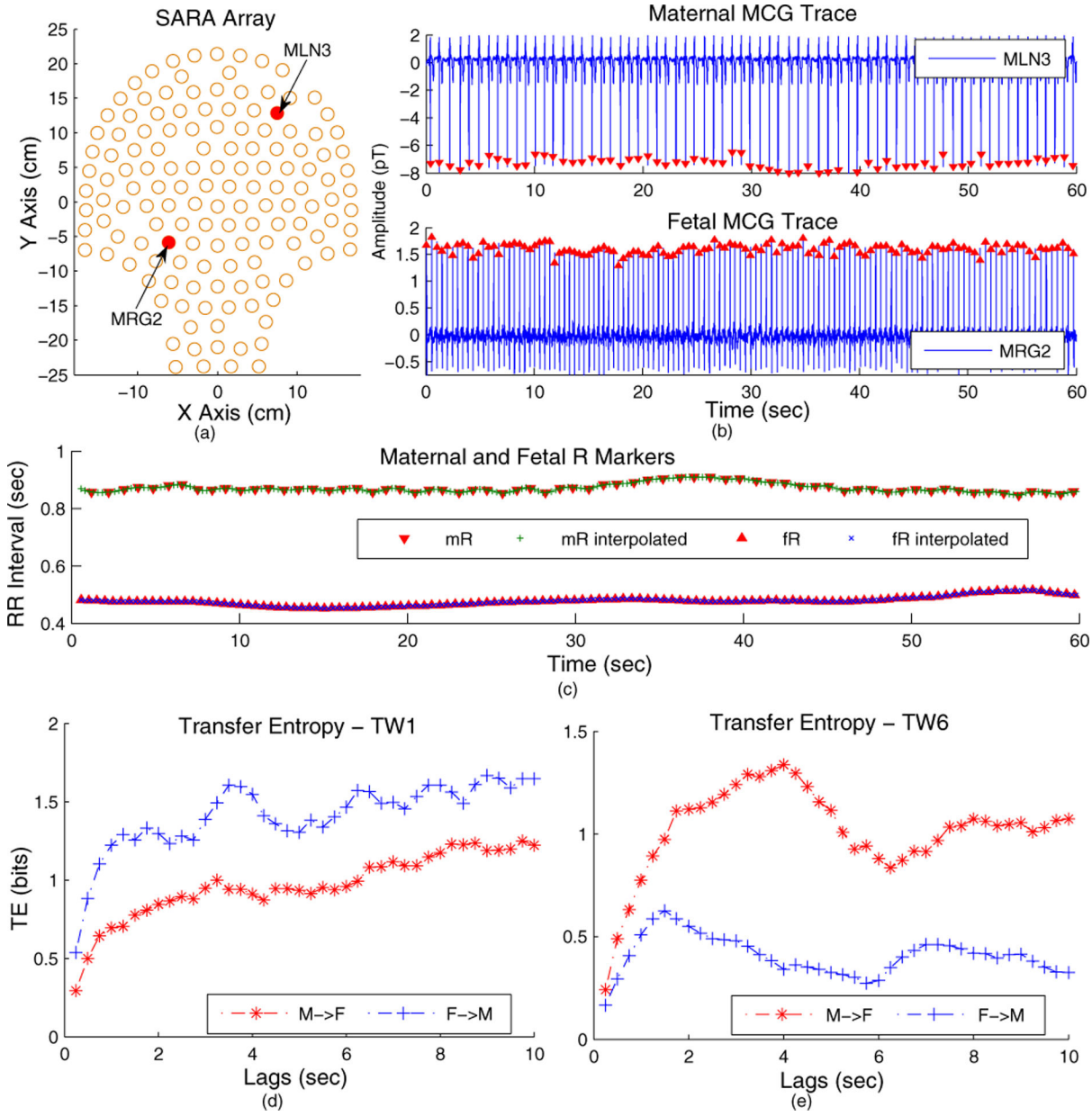


**Fig. 2.**

(a) SARA array where two sensors are highlighted that contain mMCG and fMCG data. (b) mMCG and fMCG traces recorded from two sensors for TW1. (c) mRR, fRR and re-sampled mRR and re-sampled fRR intervals within TW1. (d)-(e) $TE_{(M\rightarrow F)}$ and $TE_{(F\rightarrow M)}$ for TW1 and TW6, respectively.

**TABLE I**

Medians, $25^{th}$ and $75^{th}$ Percentiles of the TE values in the non-FM and FM Segments at two GA ranges. We only included subjects such as their recordings contain at least one FM segment. Statistical analysis was done using Wilcoxon Signed-Rank Test ($\alpha$ = 0.01).

| | GA1 < 32 weeks (n=7) | | | GA2 ≥ 32 weeks (n=14) | | |
|---|---|---|---|---|---|---|
| | **Non-FM** | **FM** | **p value** | **Non-FM** | **FM** | **p value** |
| Mean $TE_{(M\rightarrow F)}$ | 1.18 [1.06 1.25] | 1.03 [0.93 1.21] | 0.109 | 1.16 [1.10 1.23] | 1.21 [1.06 1.43] | 0.173 |
| Mean $TE_{(F\rightarrow M)}$ | 1.24 [1.17 1.27] | 1.27 [1.20 1.40] | 0.375 | 1.20 [1.14 1.28] | 1.20 [1.12 1.37] | 0.391 |
| Max $TE_{(M\rightarrow F)}$ | 1.47 [1.29 1.50] | 1.21 [1.08 1.46] | 0.109 | 1.40 [1.37 1.53] | 1.44 [1.28 1.60] | 0.358 |
| Max $TE_{(F\rightarrow M)}$ | 1.49 [1.41 1.51] | 1.54 [1.49 1.68] | 0.297 | 1.46 [1.38 1.52] | 1.53 [1.39 1.68] | 0.030 |

**TABLE II**

Medians, $25^{th}$ AND $75^{th}$ percentiles of the TE values in the two GA groups for all 74 subjects. Statistical analysis was performed using Wilcoxon Rank-Sum Test ($\alpha$= 0.01)

| | GA1 (n=31) | GA2 (n=43) | p value |
|---|---|---|---|
| Mean $TE_{(M\rightarrow F)}$ | 1.21 [1.17 1.25] | 1.20 [1.13 1.26] | 0.887 |
| Mean $TE_{(F\rightarrow M)}$ | 1.24 [1.17 1.27] | 1.17 [1.10 1.25] | 0.043 |
| Max $TE_{(M\rightarrow F)}$ | 1.48 [1.44 1.52] | 1.46 [1.40 1.53] | 0.726 |
| Max $TE_{(F\rightarrow M)}$ | 1.50 [1.42 1.52] | 1.43 [1.34 1.51] | 0.055 |