Mutual Information Estimates of CTG Synchronization

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Abstract

We examined the use of mutual information (MI) and the instantaneous phase of the analytic signal to address synchronization of uterine pressure (UP) and fetal heart rate (FHR). MI was used to assess the UP-FHR coupling because it is suitable for non-linear systems with non-Gaussian noise. Estimating degree of synchronicity and UP-FHR delay length is useful since they are physiological correlates to fetal hypoxia. Mutual information of the UP/FHR discriminated N and MA fetuses more often (9 of 18 epochs) and earlier (100 min) than conventional cross-correlation.

1. Introduction

Labour and delivery is routinely monitored electronically with sensors that measure and record maternal uterine pressure (UP) and fetal heart rate (FHR), a procedure referred to as cardiotocography (CTG). The objective of this monitoring is to detect the fetus at substantial risk of hypoxic injury so that intervention can prevent its occurrence.

Clinicians' interpretation of intra-partum CTG signals relies on the temporary decreases in FHR (FHR *decelerations*) in response to uterine contractions. FHR decelerations are due mainly to two contraction-induced events: 1) umbilical-cord compression and 2) a decrease in oxygen delivery through an impaired utero-placental unit. There is general consensus that deceleration depth, frequency and timing with respect to contractions are indicators of both the insult and the ability of the fetus to withstand it.

Assessing synchronization of the cardiotocography (CTG) signals uterine pressure (UP) and fetal heart rate (FHR) is a challenge both because of noise (signal discontinuities) and non-stationarity. As labour progress the maternal and fetal states evolve: contractions get more frequent and the cumulative effect of reduced oxygen transfer means that the fetus can experience increasing levels of hypoxia, progressing from respiratory to metabolic acidosis and finally to direct myocardial depression. Measurements under these conditions show that pH levels lower and base deficit increases: the buffer stores of the fetus which allow it to combat the increased acidosis become depleted [1]. Under such conditions, the state of the fetus as indicated by the FHR is quite non-stationary during labour and delivery.

We have characterized the stimulus-response system of UP and FHR using system identification (SI) [2]. However, obtaining delay estimates from SI involved lengthy and iterative modelling with a sweep of candidate delays. It would be helpful to have a better mechanism to estimate the delay before estimating the SI models.

It would also be helpful to compare SI models with other synchronization estimates. In this study we used mutual information to estimate synchronization and delays using both FHR and UP signals as well as the instantaneous phase of these two signals, estimate from the analytic signal produced via the Hilbert Transform. Phase MI has been used with other biological signals in [3].

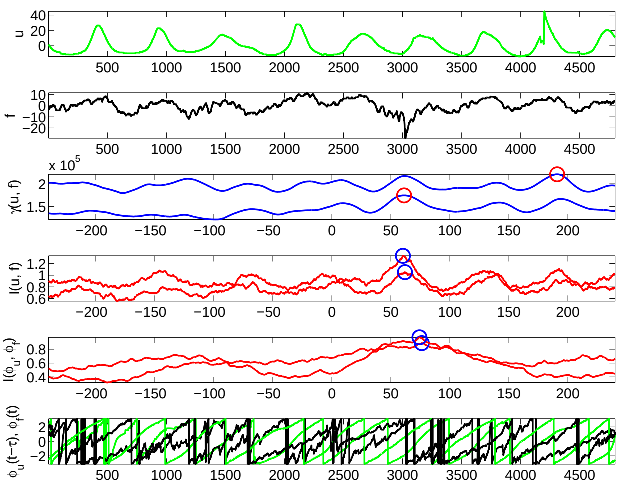
2. Data

We used CTG from singleton, term pregnancies having no known congenital malformations, with $\geq$3 hours of tracing just prior to delivery. The CTG records for this study consisted of 40 pathological (P), 103 metabolic acidotic (MA) and 105 normal (N) fetuses. The metabolic acidotic fetuses were defined by base deficit $\geq$12, $Apgar_5$ $\leq$8 and with no apparent neurological injury. It would be advantageous to identify these MA fetuses because they can be considered "close calls", where appropriate intervention can occur to prior to the onset of injury.

3. Methods

3.1. Preprocessing

The CTG data was recorded in a clinical setting, so it was subject to specific types of noise. The loss of sensor contact can temporarily interrupt the UP or FHR signals, and interference from the (much lower) maternal heart rate can corrupt the FHR. These both appeared in the signal as a sharp drop to much lower amplitude followed by a sharp (a)Epoch 1,2



(b)Epoch 1,. . .,21

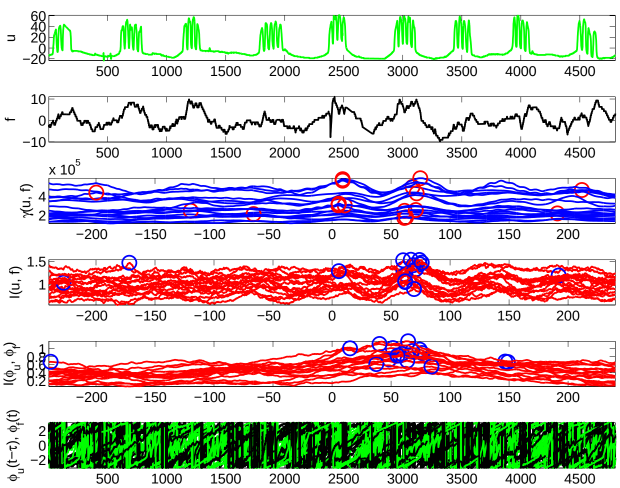


Figure 1. Typical epochs of a single case for a) Epoch 1 and 2 and b) Epoch 1,. . .,21 showing (from top to bottom) UP $u(t)$, FHR $f(t)$, cross correlation $\gamma(u, f)$, mutual information $I(u, f)$, phase mutual information I_{ϕ_u,ϕ_f}, and phases ϕ_u and ϕ_f. The lower 4 panels of a) show the overlaid results from epochs 1 and 2 while b) overlays all 21 epochs.

signal restoration. As described in [4], we preprocessed the data to bridge interruptions with linear interpolation.

We detrended the signals by a high-pass filter selected to pass a long contraction or deceleration without incurring excessive filter delay. We chose a filter with a cutoff frequency of $\frac{1}{220s} = 4.5 \times 10^{-3}$ Hz as a compromise between these competing demands.

To address the issue of non-stationarity we extracted 20-min epochs with 10-min overlap between successive epochs. This epoch length typically spanned several UP contraction-FHR deceleration pairs. Epochs with insufficient valid signal were discarded.

3.2. Instantaneous Phase

The Hilbert transform $\hat{s}(t)$ of signal $s(t)$ is defined as:

$$\hat{s}(t) = \frac{1}{\pi}\text{pv}\int_{\infty}^{\infty} \frac{s(\tau)}{t-\tau} d\tau \qquad (1)$$

where pv is the Cauchy principal value. The complex analytic signal is defined as:

$$\Psi(t) = s(t) + j\hat{s}(t) = A(t) \cdot e^{j\phi(t)} \qquad (2)$$

where $A(t)$ and $\phi(t) = \arctan(\frac{\hat{s}(t)}{s(t)})$ are defined as the instantaneous amplitude and phase, respectively. For the preprocessed UP and FHR signals $u(t)$ and $f(t)$, we calculated corresponding instantaneous phases $\phi_u(t)$ and $\phi_f(t)$.

Because the Hilbert Transform is a filtering operation typically implemented with an fast Fourier transform (FFT), it is subject to edge effects. To reduce this, we calculated the HT from the entire signal length rather than per-epoch.

3.3. Mutual Information

The mutual information $I(X;Y)$ of variables X and Y is defined as

$$\begin{aligned} I(X;Y) &= H(X) - H(X|Y) \\ &= \sum_x \sum_y p(x,y) \frac{\log p(x,y)}{p(x)p(y)}. \end{aligned}$$

where $H(X)$ is the entropy of X and $H(X|Y) = H(X,Y) - H(Y)$ is the conditional entropy of X given Y. Mutual information is therefore the amount of uncertainty (i.e., entropy) about X that is resolved by observing Y. Reduction of uncertainty is equivalent to information [5]. Mutual information is symmetrical: $I(X;Y) = I(Y;X)$.

We calculated MI for both the preprocessed UP and FHR signal pair $u(t)$ and $f(t)$ as well as their instantaneous phases $\phi_u(t)$ and $\phi_f(t)$. Binning was used for the probability densities $p(u)$, $p(f)$ and $p(u, f)$ required for MI calculation. We also tried on other density estimation methods including one based on nearest neighbours. These are known to generate less biased estimates than binning, although we found that for this study, any introduced bias from binning did not present a obstacle to finding a trustworthy maximal MI.

We observed the time lag and value of the maximum MI over a range of possible UP-FHR lags (± 240 min) for each

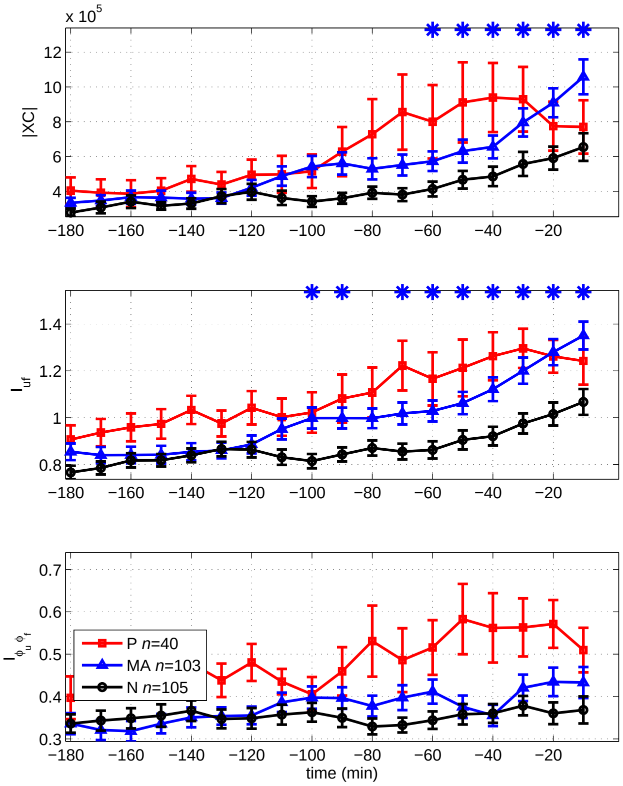


Figure 2. Group mean± standard error of UP-FHR synchronization in the last 3 hours of labour and delivery using cross-correlation (top), mutual information (middle) and phase mutual information (bottom). The horizontal time scale is in units of minutes.

20 min epoch and compared these with cross-correlation (XC) estimates. Surrogate UP-FHR pairs generated by the amplitude-adjusted Fourier Transform technique were used to test MI significance.

4. Results

Figure 1 show the results for a single fetus case. Figure 1a) shows the tendency of XC to find false peak lags in two adjacent epochs. In Figure 1b), the dispersion of the peak cross-correlation over all epochs compared to the much tighter clustering for the two maximum mutual information measures is apparent.

Figure 2 shows that in the final three hours of labour and delivery, MI I_{uf} for the raw UP/FHR values discriminated N and MA fetuses more often (9 of 18 epochs) and earlier (100 min) than XC or phase MI $I_{\phi_u \phi_f}$. Phase MI I_{ϕ_u, ϕ_f} was higher in the MA and P groups, although did it not reach statistical significance. Statistically significant differences are indicated by asterisks. Phase MI delay estimates (not shown) had much less variance than either of the other techniques, although it did not discriminate N and MA.

5. Conclusions

These results are in line with clinical expectations. With such a changing environment of increasing hypoxia during labour and delivery, the stimulus-response characteristic between UP and FHR changes accordingly: the degree of synchronization, and the delay and recovery time to deceleration all tend to increase.

We have also shown that MI provides more discriminative estimates of UP-FHR synchrony earlier in labour compared to conventional linear cross-correlation. This may indicate that the MA approach better accounts for nonlinearities in the UP-FHR system and the non-Gaussian noise (e.g., signal dropouts) present the CTG signals.

While MI estimates reached statistically significant levels of difference, the phase MI estimates did not. The linear interpolation approach that we used to address missing data (interruptions) can significantly corrupt the phase. We anticipate that better handling of missing data will lead to better phase MI estimates.

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