DETECTION OF AUTOREGULATION IN THE BRAIN OF PREMATURE INFANTS

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Problem Statement

Problem : defective cerebrovascular autoregulation : ΔCBF (Cerebral Blood Flow) $\Longrightarrow$ brain injuries.
Premature infants have a propensity for such troubles because :

- $\Delta MABP$ (Mean Arterial Blood Pressure) frequent
- $\Delta MABP \Longrightarrow \Delta CBF$ in some infants

1st means to detect defective autoregulation : $\Delta MABP \Longleftrightarrow \Delta CBF$
But, if ΔSaO_2 (arterial Oxygen Saturation) $\rightarrow 0$, then $\Delta HbD \Longleftrightarrow \Delta CBF$ (hypothesis)
2nd means to detect defective autoregulation : $\Delta MAP \Longleftrightarrow \Delta HbD$ when $\Delta SaO_2 \rightarrow 0$
Solution : apply mathematical methods to quantitate the concordance between HbD and $MABP$, which reflects impaired autoregulation, with to hope to allow physicians to administrate medicines to sick infants such that $\Delta CBF \rightarrow 0$.

Methods

Correlation

Description : concordance between two signals in the time domain

$$COR = \frac{\sum_{t=1}^{N}(x(t)-\bar{x})(y(t)-\bar{y})}{\sqrt{\sum_{t=1}^{N}(x(t)-\bar{x})^2 \sum_{t=1}^{N}(y(t)-\bar{y})^2}} \tag{1}$$

with N the number of samples considered and $\bar{x}$, $\bar{y}$ stands for the mean of $x(t)$, respectively $y(t)$.

Coherence

Description : concordance between two signals in the frequency domain

$$COH_{xy}(f) = \frac{|P_{xy}(f)|^2}{P_{xx}(f)P_{yy}(f)} \tag{2}$$

with $P_{xy}(f)$ the crosspower spectral density (CSD) of $x(t)$ and $y(t)$ at a given frequency f, and $P_{xx}(f)$, $P_{yy}(f)$ the power spectral densities (PSD) of $x(t)$, respectively $y(t)$. The spectral density functions are estimated using Welch's method.

Partial Coherence and Principal Power Spectral Density

Let us start from $x_1(t)$, $x_2(t)$, $x_3(t)$ (time domain).
Step 1 : compute Fourier transform : $X_1(f)$, $X_2(f)$, $X_3(f)$ (freq. domain)
Step 2 : expression of the linear dependence between signals (*black-box model*)

$$X_3^1 = X_3 - \frac{P_{13}}{P_{11}}X_1 \tag{3}$$

where P_{13} is the CSD between x_1 and x_3, P_{11} is the PSD of x_1 ($\approx$ energy of x_1), X_3 is dependent on X_1 and X_2, and X_3^1 is dependent on X_2 (+ generalization to X_2^1, X_1^3, ... and X_3^{12}, X_2^{13}, ...
Step 3 : calculation of the partial coherence (PCOH)

$$COH_{23}^1 = \frac{|P_{23}^1|^2}{P_{22}^1 P_{33}^1} \tag{4}$$

+ generalization. PCOH is a measures of the concordance between two signals in the frequency domain computed without the influence of some other signals.
Step 4 : calculation of the principal power spectral density (pPSD). Same steps as for PCOH, but uses linearly independent vectors computed by means of an eigenvalue decomposition of the initial autopower matrix :

$$X_1(f), X_2(f), X_3(f) \longrightarrow X_1'(f), X_2'(f), X_3'(f) \tag{5}$$

After the calculation of $(COH')_{23}^1$, calculation of :

$$(P')_{33}^{12} = (P')_{33}^{1}(1 - (COH')_{23}^{1}) \tag{6}$$

+ generalization. pPSD is a measure of the independence level of one signal compared to the others.

Subspace-based Methods

Description : quantify and extract the common information present in several signals in the case where the channels are contaminated by different undesired harmonics.
The signals $x(t)$ and $y(t)$ are set in matrices, and the common subspace is determined :

$$H_x = \begin{pmatrix} x_0(t) & x_1(t) & \cdots & x_{N-m+1}(t) \\ x_1(t) & x_2(t) & \cdots & x_{N-m+2}(t) \\ \vdots & \vdots & \ddots & \vdots \\ x_{m-1}(t) & x_m(t) & \cdots & x_{N-1}(t) \end{pmatrix}$$

$$H_y = \begin{pmatrix} y_0(t) & y_1(t) & \cdots & y_{N-m+1}(t) \\ y_1(t) & y_2(t) & \cdots & y_{N-m+2}(t) \\ \vdots & \vdots & \ddots & \vdots \\ y_{m-1}(t) & y_m(t) & \cdots & y_{N-1}(t) \end{pmatrix}$$

FIGURE 1: A schematic way to understand the subspace-based methods : the yellow parts in the matrices correspond to the common part to signals $x(t)$ and $y(t)$

HTLS − SEP : allows two input signals, fit a linear model to the signals.
MUSCLE : allows two or more input signals, uses unitary matrices for determining a set of linearly independent vectors spanning the common subspace.
Definition : EDS model (Exponentially Damped Sinusoid)

$$x(t) = \sum_{k=1}^{K} c_k^x z_k^t + n_x(t), \quad t = 0, 1, \ldots, N-1 \tag{7}$$

with $n_x(t)$ representing the noise, K the signal order and z_k, $k = 1, \ldots, K$ the so-called signal poles :

$$z_k = e^{(j2\pi f_k - d_k)T} \tag{8}$$

with f_k, $k = 1, \ldots, K$ represent the frequencies, d_k, $k = 1, \ldots, K$ the dampings, and T the constant sampling interval. Furthermore, c_k^x, $k = 1, \ldots, K$ represent the so-called complex amplitudes associated with $x(t)$:

$$c_k^x = a_k^x e^{j\phi_k^x} \tag{9}$$

with a_k^x, $k = 1, \ldots, K$ stands for the amplitude and ϕ_k^x, $k = 1, \ldots, K$ for the phase.
Definition : CPC : importance of the common part $\hat{x}_c(t)$ of original signal $x(t)$

$$CPC_x = \frac{\sum_{t=0}^{N-1}(\hat{x}_c(t))^2}{\sum_{t=0}^{N-1}(\hat{x}_c(t))^2 + \sum_{t=0}^{N-1}(x(t) - \hat{x}_c(t))^2} \tag{10}$$

Problem : determine the EDS form of the common part to the signals
Step 1 : apply HTLS-SEP or MUSCLE : determine the common subspace to the signals
Step 2 : apply SAMOS, ESTER or iterative method : order of the common part
Step 3 : apply HTLS : determine common poles (f_k and d_k)
Step 4 : apply LS : determine complex amplitudes (a_k and ϕ_k)
Step 5 : build EDS model of common part
Step 6 : compute CPC

Experimental Results

Experimental conditions

- MAP, SaO_2 and HbD were measured simultaneously and continuously (55 babies aged from 24 to 31.6 weeks, with a weight ranging from 570 to $1470g$, for a recording time ranging from 1h30 to 23h35). HbD was assessed by near-infrared spectroscopy (NIRS), and MABP by intravascular catheterisation.
- a sliding window approach was used because the concordance between the signals might vary as a function of time. The presented measures were calculated over 30-minute recordings.
- HbD is the signal having been considered to compute the CPC's. In the case of the 3-input MUSCLE, the third signal considered is SaO_2.
- all signals were filtered to keep only the recording intervals during which the variation of SaO_2 around its mean does not exceed 5%

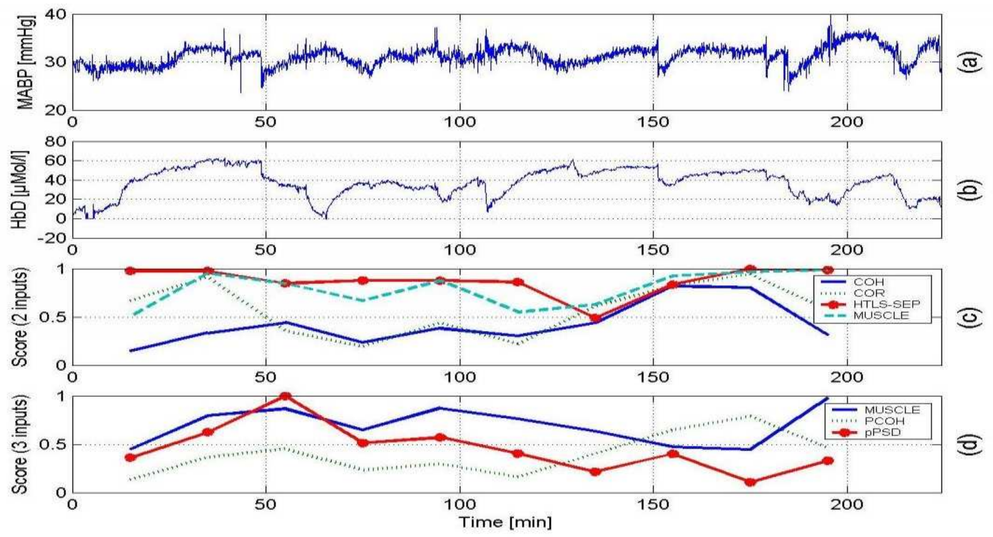


FIGURE 2: Simultaneous changes in MABP (a) and HbD (b) in a premature infant, with corresponding measures for two (c) and three (d) input signals

Analyses

- first two hours of the recording : fluctuations in MABP seem at first sight not to be associated with parallel changes in HbD
- last two hours : fluctuations in MABP are associated with parallel changes in HbD (case of impaired autoregulation)
- last 45 minutes : HbD presents still parallel changes with the ones of MABP, even if slightly delayed. The CPC values are more sensitive to detect an impaired autoregulation.

Conclusion

- the hypothesis of linearity of PCOH and pPSD gives acceptable results
- HTLS-SEP and MUSCLE are more sensitive
- MUSCLE can be generalized to study more than two signals
- a larger follow-up study is needed to confirm the performance of the methods, and to evaluate statistically the predictive measure values with respect to possible brain damage.