# Average, synchronize and analyze recurrent Bioelectrical Waves

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# Goal : Use formal approaches for very practical problems

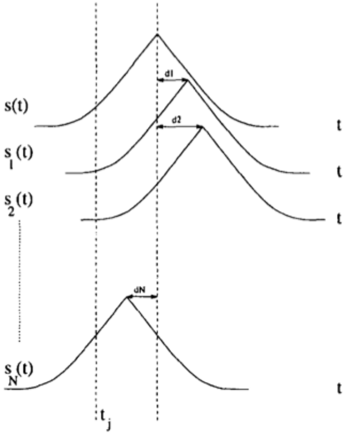
Bioelectrical signals are :

- repetitive (ECG, EMG, ...)
- spontaneously or evoked (ECG, EP, ...)
- with small variations and noisy

From the Signal Processing/Biological knowledge :

- How to get rid of the noise presence (s(t) ?)
- How to measure variability ?
- How to interpret results ?
- How to model the observations ?

$\Longrightarrow$ improve the Bio/DSP skills




+ NOISE

# Goal : characterize Waves or variabilities (simple model)

From the data set :

- delays ?
- amplitudes (small, large) ?

$\Longrightarrow$ averaging and synchronization

- estimation theory
- probabilistic approach

# Averaging

Let's assume the observation model (normal law $\mathcal{N}(0,\sigma)$ for the white noise) with unknown signal $s$

$$\boxed{x_i(n) = s(n) + w_i(n)} \quad \text{digital signal} \tag{1}$$

define the vector $\mathbf{x}_i = [x_i(0)\ x_i(1)\ \cdots\ x_i(N-1)]^T$, then the PDF of the observation is :

$$p(x_i(n);s(n)) = \frac{1}{\sqrt{2\pi\sigma^2}} e^{-\frac{1}{2\sigma^2}(x_i(n)-s(n))^2} \Rightarrow \tag{2}$$

$$p(\mathbf{x}_i;\mathbf{s}) = \prod_{n=0}^{N-1} p(x_i(n);s(n)) = \frac{1}{(2\pi\sigma^2)^{N/2}} e^{-\frac{1}{2\sigma^2}\sum_{n=0}^{N-1}(x_i(n)-s(n))^2} \tag{3}$$

$$p(\mathbf{x}_i;\mathbf{s}) = \frac{1}{(2\pi\sigma^2)^{N/2}} e^{-\frac{1}{2\sigma^2}(\mathbf{x}_i-\mathbf{s})^T(\mathbf{x}_i-\mathbf{s})} \tag{4}$$

If the observations are independent the global PDF is :

$$p(\mathbf{x}_1;\mathbf{x}_2;\cdots;\mathbf{x}_I;\mathbf{s}) = \prod_{i=1}^{I} p(\mathbf{x}_i;\mathbf{s}) = Me^{-\frac{1}{2\sigma^2}\sum_{i=1}^{I}(\mathbf{x}_i-\mathbf{s})^T(\mathbf{x}_i-\mathbf{s})} \tag{5}$$

This PDF can be viewed as a Likelihood function $\Rightarrow$ MLE

# Averaging

An estimation $\hat{\mathbf{s}}$ of $\mathbf{s}$ can be computed from the minimization (see MLE Theory)

$$\hat{\mathbf{s}} = \arg\min_{\mathbf{s}} \sum_{i=1}^{I} (\mathbf{x}_i - \mathbf{s})^T (\mathbf{x}_i - \mathbf{s}) = \arg\min_{\mathbf{s}} \sum_{i=1}^{I} (\mathbf{x}_i^T \mathbf{x}_i - 2\mathbf{x}_i^T \mathbf{s} + \mathbf{s}^T \mathbf{s}) = \arg\min_{\mathbf{s}} J \tag{6}$$

Equivalent to :

$$\frac{\partial J}{\partial \mathbf{s}} = 0 \Leftrightarrow -2\sum_{i=1}^{I} \mathbf{x}_i + 2\sum_{i=1}^{I} \mathbf{s} = 0 \Rightarrow \hat{\mathbf{s}} = \frac{1}{I} \sum_{i=1}^{I} \mathbf{x}_i \tag{7}$$

That is simply the sample mean (approximated mathematical expectation) ! ! !

What happens with this estimation if a **magnitude factor** is present (physiological variability) ?

# Weighted Averaging

Let's assume the observation model (normal law $\mathcal{N}(0,\sigma)$ for the white noise) with unknown signal $s$ and $a_i$'s :

$$x_i(n) = a_i s(n) + w_i(n) \tag{8}$$

define the vector $\mathbf{x}_i = [x_i(0)\; x_i(1)\; \cdots\; x_i(N-1)]^T$ and $\mathbf{w}_i$, the observation is replaced by :

$$\mathbf{x}_i = a_i \mathbf{s} + \mathbf{w}_i \tag{9}$$

Then the criteria $J$ to be minimized is :

$$\hat{\mathbf{s}}, \hat{\mathbf{a}} = \arg\min_{\mathbf{s},\mathbf{a}} \sum_{i=1}^{I} (\mathbf{x}_i - a_i\mathbf{s})^T (\mathbf{x}_i - a_i\mathbf{s}) = \arg\min_{\mathbf{s},\mathbf{a}} \sum_{i=1}^{I} \|\mathbf{x}_i - a_i\mathbf{s}\|_2^2 \tag{10}$$

$$\hat{\mathbf{s}}, \hat{\mathbf{a}} = \arg\min_{\mathbf{s},\mathbf{a}} \|\mathbf{X} - \mathbf{s}\mathbf{a}^T\|_F^2 \tag{11}$$

with $\mathbf{X}$ the matrix formed by the $\mathbf{x}_i$'s, and $\|.\|_F^2$ the squared Frobenius norm.
The solution of this minimization is obtained by using two partial derivatives $\frac{\partial J}{\partial \mathbf{s}}$ and $\frac{\partial J}{\partial \mathbf{a}}$.

$$\frac{\partial J}{\partial \mathbf{s}} = \frac{\partial}{\partial \mathbf{s}} \frac{1}{I} \sum_{i=1}^{I} (\mathbf{x}_i^T\mathbf{x}_i - 2a_i\mathbf{x}_i^T\mathbf{s} + a_i^2\mathbf{s}^T\mathbf{s}) = \sum_{i=1}^{I} (-2a_i\mathbf{x}_i + 2a_i^2\mathbf{s}) \tag{12}$$

$$\frac{\partial J}{\partial \mathbf{s}} = 0 \Rightarrow \hat{\mathbf{s}} = \frac{1}{\sum_i a_i^2} \sum_{i=1}^{I} a_i\mathbf{x}_i = \textit{weighted averaging} \tag{13}$$

but $\mathbf{x}_i = a_i\mathbf{s} = \frac{a_i}{\alpha}\mathbf{s}\alpha = \tilde{a}_i\tilde{\mathbf{s}}$, not unique solution ! $\Rightarrow$ impose $\sum a_i^2 = \mathbf{a}^T\mathbf{a} = 1$ (good for Lagrange multiplier)

# Weighted Averaging

But $a_i$'s are unknown ...
Let's compute the second partial derivative (turns out to be several derivatives regards $a_i$'s) :

$$\frac{\partial J}{\partial a_i} = \frac{\partial}{\partial a_i}\frac{1}{I}\sum_{i=1}^{I}(\mathbf{x}_i^T\mathbf{x}_i - 2a_i\mathbf{x}_i^T\mathbf{s} + a_i^2\mathbf{s}^T\mathbf{s}) = \sum_{i=1}^{I}(-2\mathbf{x}_i^T\mathbf{s} + 2a_i\mathbf{s}^T\mathbf{s}) \tag{14}$$

$$\frac{\partial J}{\partial a_i} = 0 \Rightarrow \hat{a}_i = \frac{\mathbf{x}_i^T\mathbf{s}}{\mathbf{s}^T\mathbf{s}} \tag{15}$$

In fact, since **s** and **a** are unknown results (13) and (15) cannot be computed. To perform the global minimization result (13) should be replaced in (9) and the partial derivatives with respect to the $a_i$'s computed to get the estimations of the magnitude factors $\Rightarrow$ highly non linear ... instead use an Alternated Least Square algo :

INIT

$$(1)\ \mathbf{s} = \frac{1}{\mathtt{I}}\sum_{\mathtt{i}=1}^{\mathtt{I}}\mathbf{x}_{\mathtt{i}}\ ;\ (2)\ \mathtt{a}_{\mathtt{i}} = \frac{\mathbf{x}_{\mathtt{i}}^T\mathbf{s}}{\mathbf{s}^T\mathbf{s}}\ \mathtt{for}\ \mathtt{i} = 1 \ldots \mathtt{I} \tag{16}$$

$$\mathtt{normalize}\ \mathtt{a}_{\mathtt{i}}'\mathtt{s}\ \mathtt{by}\ \sqrt{\sum \mathtt{a}_{\mathtt{i}}^2} \tag{17}$$

DO

$$(1)\ \mathbf{s} = \frac{1}{\sum_{\mathtt{i}}\mathtt{a}_{\mathtt{i}}^2}\sum_{\mathtt{i}=1}^{\mathtt{I}}\mathtt{a}_{\mathtt{i}}\mathbf{x}_{\mathtt{i}}\ ;\ (2)\ \mathtt{a}_{\mathtt{i}} = \frac{\mathbf{x}_{\mathtt{i}}^T\mathbf{s}}{\mathbf{s}^T\mathbf{s}}\ \mathtt{for}\ \mathtt{i} = 1 \ldots \mathtt{I} \tag{18}$$

$$\mathtt{normalize}\ \mathtt{a}_{\mathtt{i}}'\mathtt{s}\ \mathtt{by}\ \sqrt{\sum \mathtt{a}_{\mathtt{i}}^2} \tag{19}$$

WHILE CONVERGENCE (e.g. Frobenius norm)

# Weighted Averaging-PCA

If we impose the solution $\mathbf{s} = \mathbf{X}\mathbf{m}$ (weighted averaging of the observations or linear combination) and maximize its energy $C = \mathbf{s}^T\mathbf{s}$ ($\approx E[s^2]$) subject to the constraint $\mathbf{m}^T\mathbf{m} = 1$. Then,

$$C = \mathbf{m}^T\mathbf{X}^T\mathbf{X}\mathbf{m} = \mathbf{m}^T\mathbf{R}_x\mathbf{m} \tag{20}$$

Where $\mathbf{R}_x$ is the approximated Covariance matrix of the observations ($\mathbf{R}_x = E[\mathbf{x}\mathbf{x}^T]$)
Maximization of $C$ can be accomplished by means of the Lagrange's multiplier technique by defining the new criterion :

$$J = J(\mathbf{m}) = \mathbf{m}^T\mathbf{R}_x\mathbf{m} - \lambda(\mathbf{m}^T\mathbf{m} - 1) \tag{21}$$

Then the derivation of $J$ with respect to $\mathbf{m}$ is :

$$\frac{\partial J}{\partial \mathbf{m}} = 2\mathbf{R}_x\mathbf{m} - 2\lambda\mathbf{m} = \mathbf{0} \Rightarrow \mathbf{R}\mathbf{m} = \lambda\mathbf{m} \tag{22}$$

This corresponds to a eigenvalues/eigenvectors decomposition of the matrix $\mathbf{R}_x$, where $\mathbf{m}$ is an eigenvector and $\lambda$ the respective eigenvalue. How to select the correct eigenvalue/eigenvector ?
Replace $\mathbf{m}$ by an eigenvector $\mathbf{v}$ of $\mathbf{R}_x$ in $J$, it gives $J = \lambda$. Then $J$ is max when choosing $\mathbf{m} = \mathbf{v}$ the eigenvector corresponding to the largest $\lambda$.

# Weighted Averaging-Generalization

How to relate this estimation to the solution of the eigenvalue/eigenvector decomposition ?
The criteria to be minimized is in fact :

$$J = \|\mathbf{X} - \mathbf{s}\mathbf{a}^T\|_F^2 = tr(\mathbf{X} - \mathbf{s}\mathbf{a}^T)^T(\mathbf{X} - \mathbf{s}\mathbf{a}^T) = tr(\mathbf{X}^T\mathbf{X} - \mathbf{X}^T\mathbf{s}\mathbf{a}^T - \mathbf{a}\mathbf{s}^T\mathbf{X} + \mathbf{a}\mathbf{s}^T\mathbf{s}\mathbf{a}^T) \tag{23}$$

$$J = tr(\mathbf{R}) - tr(\mathbf{X}^T\mathbf{s}\mathbf{a}^T) - tr(\mathbf{a}\mathbf{s}^T\mathbf{X}) + tr(\mathbf{a}\mathbf{s}^T\mathbf{s}\mathbf{a}^T) = tr(\mathbf{R}) - 2tr(\mathbf{X}^T\mathbf{s}\mathbf{a}^T) + tr(\mathbf{a}\mathbf{s}^T\mathbf{s}\mathbf{a}^T) \geqslant 0 \tag{24}$$

Where $\mathbf{R}_x$ is the approximated Covariance matrix of the observations ($\mathbf{R}_x = E[\mathbf{x}\mathbf{x}^T]$).
We aim to minimize $J$ ($\geqslant 0$), since $tr(\mathbf{R}) \geqslant 0$ then this minimization is equivalent to :

$$\max_{\mathbf{s},\mathbf{a}}\{2tr(\mathbf{X}^T\mathbf{s}\mathbf{a}^T) - tr(\mathbf{a}\mathbf{s}^T\mathbf{s}\mathbf{a}^T)\} = \max_{\mathbf{s},\mathbf{a}} J' \tag{25}$$

Imposing the solution $\mathbf{s} = \mathbf{X}\mathbf{m}$ ($\mathbf{s}$ is a linear combination of the observations, see before), then we get :

$$\max_{\mathbf{s},\mathbf{a}}\{2tr(\mathbf{X}^T\mathbf{X}\mathbf{m}\mathbf{a}^T) - tr(\mathbf{a}\mathbf{m}^T\mathbf{X}^T\mathbf{X}\mathbf{m}\mathbf{a}^T)\} = \max_{\mathbf{s},\mathbf{a}}\{2tr(\mathbf{R}\mathbf{m}\mathbf{a}^T) - tr(\mathbf{a}\mathbf{m}^T\mathbf{R}\mathbf{m}\mathbf{a}^T)\} \tag{26}$$

# Weighted Averaging-Generalization

The derivation with respect to **a** gives :

$$\frac{\partial J'}{\partial \mathbf{a}} = 2\mathbf{Rm} - 2\mathbf{m}^T\mathbf{Rma} = \mathbf{0} \Rightarrow \mathbf{Rm} = \mathbf{m}^T\mathbf{Rma} \tag{27}$$

If **m** is selected as an eigenvector **v** of **R** (constant with respect to the maximization), then (27) turns out to be $\lambda\mathbf{v} = \mathbf{v}^T\lambda\mathbf{va} = \lambda\mathbf{a}$, then $\mathbf{a} = \mathbf{v}$. This solution is valid because it has been seen that the optimal **s** is $\mathbf{s} = \frac{\mathbf{Xa}}{\mathbf{a}^T\mathbf{a}}$, corresponding to the form $\mathbf{s} = \mathbf{Xm}$.
Which eigenvector should be choosen ($J'$ has to be maximized) ?
Replace theses solutions in $J'$ we get :

$$J' = 2tr(\mathbf{Rvv}^T) - tr(\mathbf{vv}^T\mathbf{Rvv}^T) = 2tr(\lambda\mathbf{vv}^T) - tr(\lambda\mathbf{vv}^T\mathbf{vv}^T) = \lambda tr(\mathbf{vv}^T) = \lambda\mathbf{v}^T\mathbf{v} = \lambda \tag{28}$$

Then it is maximized when choosing the eigenvector $\mathbf{v}_{max}$ corresponding to the largest eigenvalue $\lambda_{max}$ !
The optimal solution consists in selecting $\mathbf{s} = \mathbf{Xv}_{max}$.

With respect to eigenvalue decomposition, it can be interpreted as the maximized weighted averaging $\mathbf{s} = \mathbf{Xm}$ subject to $\mathbf{m}^T\mathbf{m} = 1$ .

# Averaging

The model can be extended to :

$$x_i(n) = s(n - d_i) + w_i(n) \tag{29}$$

The ensemble mean is expressed as :

$$\hat{s}(n) = \frac{1}{I}\sum_{i=1}^{I} x_i(n) \tag{30}$$

when the number of observed signals is large enough and that the variable $d$ is random, this relation can be expressed as :

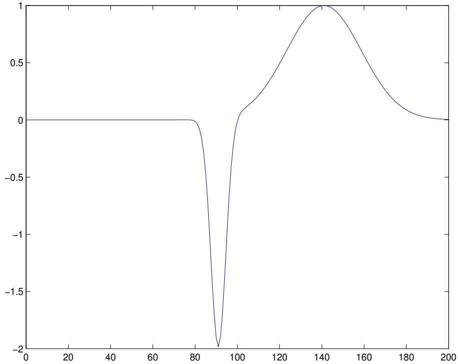
$$\boxed{\hat{s}(n) = \int s(t-a)p_D(a)da} \tag{31}$$

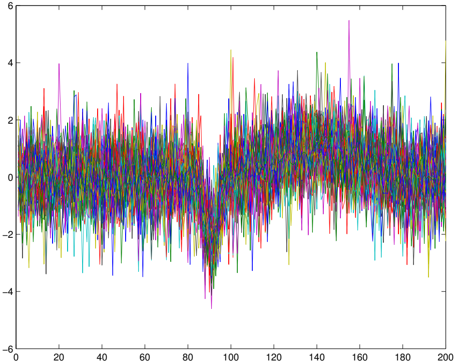
with $p_D(a)$ the probability densities of the delays.Then, the mean is the convolution of the pdf and the signal $s$

- If the pdf is a gaussian, $s$ is low pass filtered
- What happens if the noise is not gaussian (laplacian ?) $\Rightarrow$ the median replace the mean
- However, this quantity may be use to address the quality of a synchronization procedure.

# Simulations

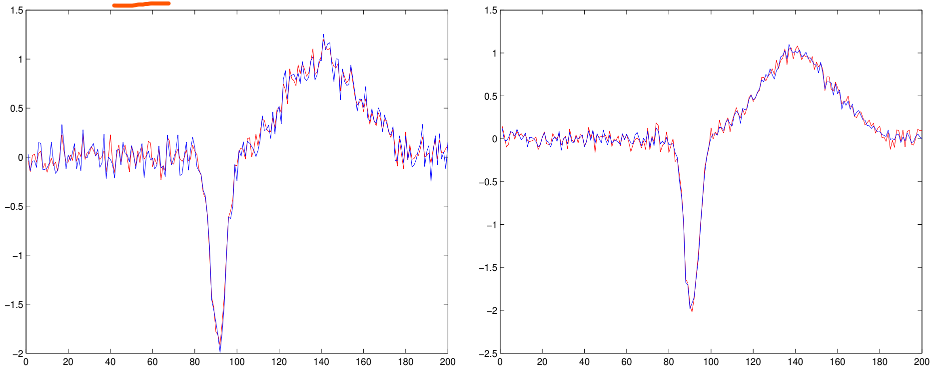
One pure observation, 100 noisy sweeps



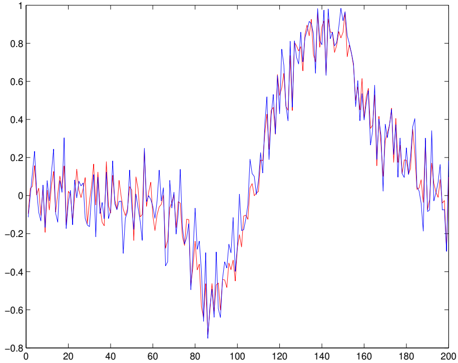
# Simulations

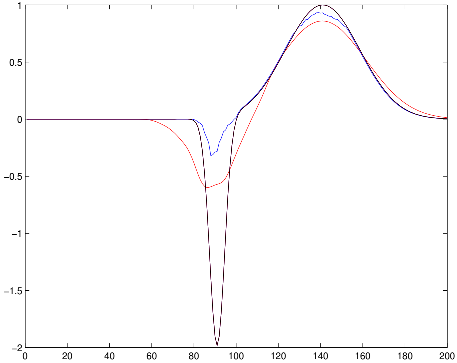
Gaussian noise (Left ) and Laplacian noise (Right)
Mean and Median



# Simulations

Delayed signal ($\sigma_d = 10$) with and without noise
Mean, Median and Original





# Alignment quality

Assuming that delayed signals are observed as following :

$$x_i(t) = w_i s(t - d_i) + n_i(t) \tag{32}$$

The ensemble mean is expressed as :

$$m_1(t) = \frac{1}{K} \sum_{i=1}^{K} x_i(t) \tag{33}$$

when the number of observed signal is large enough and that the random variables $w$ and $d$ are independant, this relation can be expressed as :

$$m_1(t) = \int \int w s(t-a) p_D(a) p_W(w) da dw \tag{34}$$

with $p_D(a)$ and $p_W(w)$ the probability densities of the delays and the weighting factor. Then, the mean is :

$$m_1(t) = \bar{w} \int s(t-a) p_D(a) da \tag{35}$$

# Alignment quality

When calculating the energy of the mean signal $V$ as :

$$V = \int m_1^2(t)dt \tag{36}$$

and assuming that in each observation $x_i$ the signal $s(t)$ is completely observed, the integral is :

$$V = \bar{w}^2 \int \int p_D(a)p_D(b)R_{ss}(a-b)dadb \tag{37}$$

where $R_{ss}(\tau)$ is the temporal cross-correlation function defined as :

$$R_{ss}(\tau) = \int s(t)s(t+\tau)dt \tag{38}$$

Using the definition of the characteristic function $\phi_D(u)$ such as :

$$p_D(a) = \int e^{-jua}\phi_D(u)du \tag{39}$$

and $\hat{R}_{ss}(u)$ the Fourier transform of $R_{ss}(t)$, it can be shown that (37) is :

$$\bar{w}^2 \int \int p_D(b)\phi_D(v)\hat{R}_{ss}(v)e^{-jvb}dvdb \tag{40}$$

which can be reduced to :

$$\bar{w}^2 \int \phi_D(v)\phi_D(-v)\hat{R}_{ss}(v)dv \tag{41}$$

# Alignment quality

The probability density being real, the property $\phi_D^*(u) = \phi_D(-u)$ is verified, giving :

$$V = \bar{w}^2 \int |\phi_D(u)|^2 \hat{R}_{ss}(v)dv \tag{42}$$

The cross-correlation being semi-definite positive, its Fourier transform $\hat{R}_{ss}(u)$ is then non negative and even. This implies that :

$$V = 2\bar{w}^2 \int_0^\infty |\phi_D(v)|^2 \hat{R}_{ss}(v)dv \geq 0 \tag{43}$$

Assuming the normal law $\mathcal{N}(m,\sigma)$ for $p_D(a)$, its characteristic function is :

$$\phi_D(v) = e^{jmv-(1/2)\sigma^2 v^2} \tag{44}$$

which implies for $V$ :

$$V = 2\bar{w}^2 \int_0^\infty e^{-\sigma^2 v^2} \hat{R}_{ss}(v)dv \tag{45}$$

# Alignment quality

The derivative of $V$ regards to $\sigma$ gives :

$$\frac{d}{d\sigma}V = -4\bar{w}^2\sigma \int_0^\infty v^2 e^{-\sigma^2 v^2} \hat{R}_{ss}(v)dv \quad \leq 0 \tag{46}$$

Then if the jitter variance decreases the criteria $V$ increases. Considering that after the alignment process the probability density of the residual delays could change its shape, if the function $|\phi_D(v)|^2$ can be approximated by a gaussian law such that :

$$|\phi_D(v)|^2 \approx e^{-\sigma^2 v^2} \quad pour \ \ v \in \Omega \tag{47}$$

with $\Omega$ the support of $\hat{R}_{ss}(v)$, then when $V$ increases it means that the variance, i.e. the alignment error, has been reduced.

# Goal : Use formal approaches for very practical problems

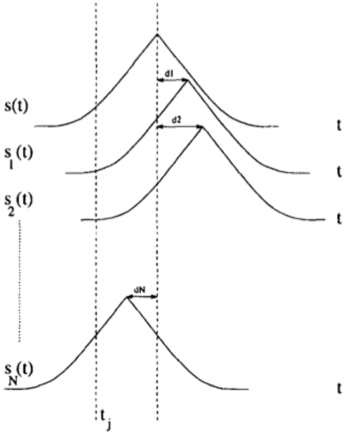
Bioelectrical signals are :

- repetitive (ECG, EMG, ...)
- spontaneously or evoked (ECG, EP, ...)
- with small variations and noisy

From the Signal Processing/Biological knowledge :

- How to get rid of the noise presence : average
- How to measure variability ($d_i$'s) ?
- How to interpret results ?
- How to model the observations ?

$\Longrightarrow$




+ NOISE

# Mean -> Variance

- the delays are artifacts and need to be canceled ?
- the delays convey physiological informations ?

$\Rightarrow$ Each individual delay is estimated (TDE) or its statistics (Variance) ?
Define the simple model :

$$x_i(t) = s(t-d_i) + n_i(t) \tag{48}$$

The variance is defined by (without noise) :

$$V_1(t) = \int s^2(t-a)p_D(a)da - m^2(t) \tag{49}$$

Assuming that delays are small (versus the derivatives of $s$), we have the Taylor expansion :

$$s(t-a) \approx s(t) - as'(t) \tag{50}$$

Then,

$$\begin{aligned} V_1(t) &= \int (s^2(t) + a^2 s'^2(t) - 2s(t)s'(t))p_D(a)da - m^2(t) && (51) \\ &= s^2(t) + s'^2(t)\int a^2 p_D(a) - 2s(t)s'(t)\int a p_D(a) - m^2(t) && (52) \end{aligned}$$

# Mean -> Variance

Assuming that $\bar{a}=0$, $m(t)=\int s(t-a)p_D(a)da=\int(s(t)-as'(t))p_D(a)da=s(t)\int p_D(a)da-s'(t).0=s(t)$
Then,

$$V_1(t)=\sigma_d^2 s'^2(t) \tag{53}$$

Introducing the noise and a random magnitude $w$ with a unit mean, corresponding to the model :

$$x_i(t)=w_i s(t-d_i)+n_i(t) \tag{54}$$

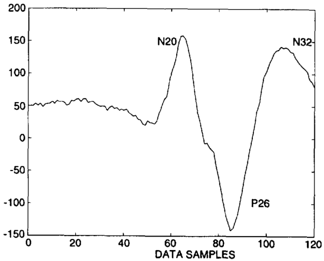
It can be shown that similarly we finaly get :

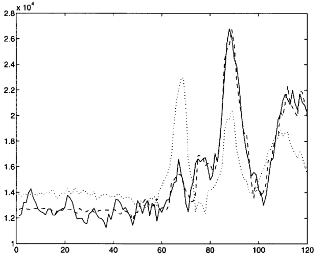
$$V_1(t)=s^2(t)\sigma_w^2+s'^2(t)\sigma_d^2(1+\sigma_w^2)+\sigma_n^2(t) \tag{55}$$

Then, the variance of the observations is function of the second order statistics of the magnitude, the delay and the noise.

If s(t) is known (or approximated), the quantities can be estimated (Least squares)

# A real example : EP



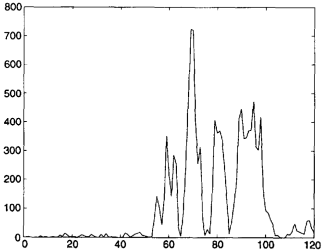




Table 1
Characteristics of the three waves

| Wave | N20 | P26 | N32 |
|---|---|---|---|
| $\hat{\sigma}_d$ (ms) | 0.17 | 2.06 | 2.16 |
| $\hat{\sigma}_p$ | 0.17 | 0.49 | 0.00 |

# Time Delay Estimation

Using the simple model :

$$x_i(n) = s(n - d_i) + w_i(n) \tag{56}$$

and using the MLE (see previous development), the delays $\mathbf{d}$ are estimated by maximizing the criteria :

$$\hat{\mathbf{d}} = \arg\max_{\mathbf{d}} \sum_n \sum_i \sum_{k>i} x_k(n + d_k) x_i(n + d_i) \tag{57}$$

Not proven to be the best estimator. It is if it attains the Cramer-Rao Lower Bound (CRLB).
Assuming this model and gaussian noise, the CRLB is :

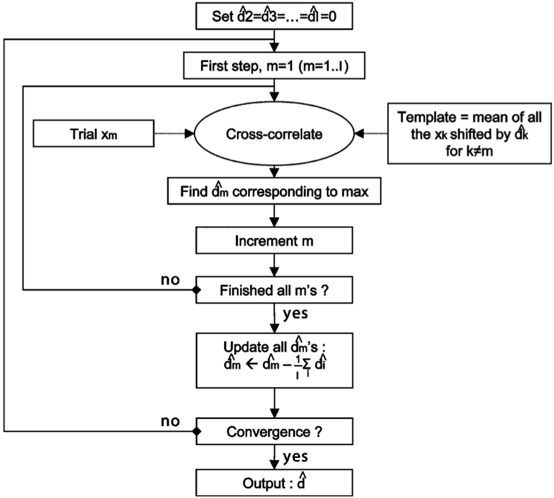
$$var(\hat{d}_i) \geqslant \frac{2\sigma_w^2}{\mathbf{s}'^T \mathbf{s}'} \tag{58}$$

Rem : if $\mathbf{s}$ is known $var(\hat{d}_i) \geqslant \frac{\sigma_w^2}{\mathbf{s}'^T \mathbf{s}'}$

Use an iterative (delays estimated iteratively) scheme instead of brute force optimization

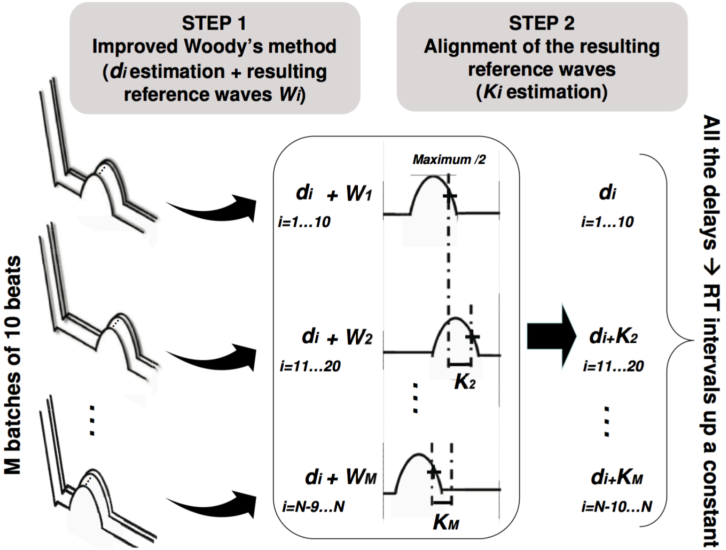
Application to ECG intervals modeling (QT/RR)

# Flowchart



Set $\hat{d}_2=\hat{d}_3=\ldots=\hat{d}_I=0$
First step, m=1 (m=1..I)
Trial $x_m$
Cross-correlate
Template = mean of all the $x_k$ shifted by $\hat{d}_k$ for $k\neq m$
Find $\hat{d}_m$ corresponding to max
Increment m
no
Finished all m's ?
yes
Update all $\hat{d}_m$'s : $\hat{d}_m \leftarrow \hat{d}_m - \frac{1}{I}\sum_i \hat{d}_i$
no
Convergence ?
yes
Output : $\hat{d}$

# Batch TDE


STEP 1
Improved Woody's method
(di estimation + resulting reference waves Wi)
STEP 2
Alignment of the resulting reference waves
(Ki estimation)
M batches of 10 beats
Maximum /2
di + W1
i=1...10
di + W2
i=11...20
K2
di + WM
i=N-9...N
KM
di
i=1...10
di+K2
i=11...20
di+KM
i=N-10...N
All the delays → RT intervals up a constant

# Goal : characterize Waves variations (complex model)

From the data set :

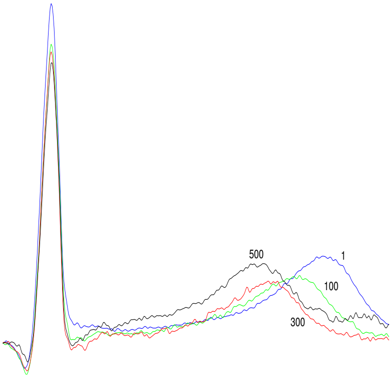
- delays ? $\Rightarrow$ change of the conduction velocity
- amplitudes ? $\Rightarrow$ change of the number of depolarized cells
- $x_i(t) = k_i s(\Phi(t)) + n_i(t)$
- scales (narrow, wide) ? $\Rightarrow$ change of the synchronization of the cells Repol./Depolarization
- mean shape ($\Rightarrow$ notion of shape distance) ?

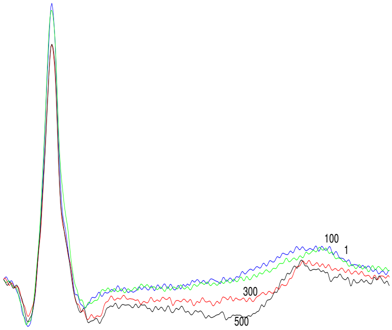
$\Longrightarrow$ unique framework

# An example : characterize T Waves variations

One healthy and one ischemic subjects during exercise test. *ECG LEAD V5*

- Constant cycling speed with 50W increased by 25W every 2 minutes
- Healthy : RR 950ms (1) - RR 575 ms (500)
- Ischemic : RR 750ms (1) - RR 570 ms (500)



## Model and properties

- based on the simple observation model (slightly different than befor)

$$x_i(t) = k_i s(\frac{t-d_i}{\alpha_i}) + n_i(t) \;\; with \;\; \alpha_i > 0; k_i > 0$$

$k_i$, $\alpha_i$, $d_i$ : amplitude coefficient, scaling factor, delay

- the normalized integrals are defined as (assuming positivity)

$$S(t) = \left(\int_0^t s(u)du\right) / \left(\int_0^T s(u)du\right)$$

$$X_i(t) = \left(\int_0^t x_i(u)du\right) / \left(\int_0^T x_i(u)du\right)$$

- for any value of t we get (increasing functions)

$$y = S(t) = X_i(t_i) \Leftrightarrow t = S^{-1}(y) \;\; \text{with} \;\; t_i = \psi_i(t)$$

- providing the key relation

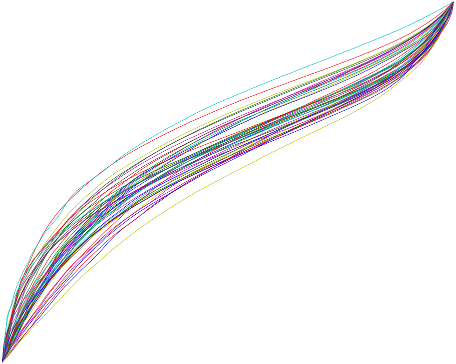
$$t_i = \alpha_i S^{-1}(y) + d_i$$

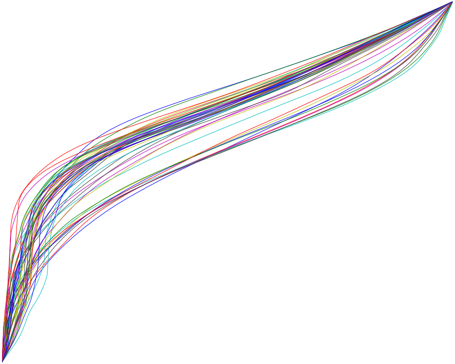
# Model and properties

- in the discrete case $\mathbf{t}_i = [X_i^{-1}(0)\; X_i^{-1}(\delta_y) \cdots X_i^{-1}(1)]$
- the key relation is

$$\mathbf{t}_i = \alpha_i \mathbf{t} + d_i \mathbb{1} \tag{59}$$

- $\Longrightarrow$ linear function of the parameters (not the case in time)
- example on 50 ($i = 1:10:500$) roughly segmented T waves ($\mathbf{t}_i$'s)





# Model and properties

- in the discrete case $\mathbf{t}_i = [X_i^{-1}(0)\, X_i^{-1}(\delta_y) \cdots X_i^{-1}(1)]$
- the key relation is
$$\mathbf{t}_i = \alpha_i \mathbf{t} + d_i \mathbb{1}$$
- $\Longrightarrow$ linear function of the parameters (not the case in time)

$\alpha_i$'s, $d_i$'s, $\mathbf{t}$ are estimated by computing $\mathbf{T} = [\mathbf{t}_1 \cdots \mathbf{t}_N] = \mathbf{V\Sigma U}'$ (SVD)

$k_i$'s are then calculated by using the expression $\int_0^T x_i(u)du/\alpha_i$

# Parameters estimation

- $\alpha_i$, $d_i$, $\mathbf{t}$ are of interest
- two stages estimation ($\mathbf{t}$) & ($\alpha_i$, $d_i$) by zeroing the mean of each $\mathbf{t}_i$
- first estimation solve

$$\check{\mathbf{t}} = arg\ \min_{\mathbf{t}}(\sum_i \|\mathbf{t}_i - \alpha_i \mathbf{t}\|^2)\ \ subj\ \ \mathbf{t}^T\mathbf{t} = 1 \tag{60}$$

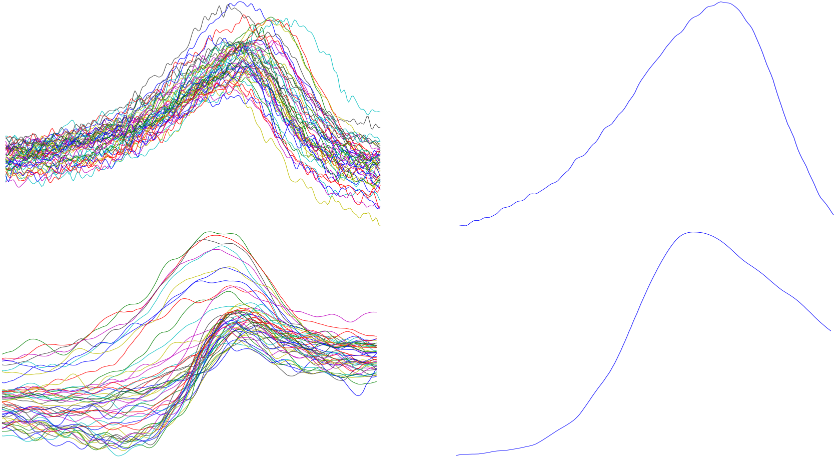
equivalent to

$$\check{\mathbf{t}} = arg\ \max_{\mathbf{t}} \mathbf{t}^T\mathbf{R}\mathbf{t} \tag{61}$$

where $\mathbf{R}$ stands for the correlation matrix of the observations $\mathbf{t}_i$'s.
$\check{\mathbf{t}}$ is then the first column of $\mathbf{V}$ such that $\mathbf{T} = [\mathbf{t}_1 \cdots \mathbf{t}_N] = \mathbf{V}\Sigma\mathbf{U}'$ (SVD)
The $\alpha_i$'s are computed from the SVD decomposition.
The mean $m_i$ of each $\mathbf{t}_i$ is in fact the center of gravity of $x_i(t)$ and is related to $m_1$ by $m_i = \alpha_i m + d_i$

# Parameters estimation

- $\check{\mathbf{t}}$ plays the role of the "mean shape" (scale and shift invariant)
- $\check{\mathbf{t}}$ is in fact a weighted ($> 0$) average of increasing functions
  - qualified as inverse normalized integral
  - its derivative provides the positive temporal mean shape



# Model and properties

- The first observation $x_1$ is taken as the reference $\Longrightarrow$ correction of the parameters

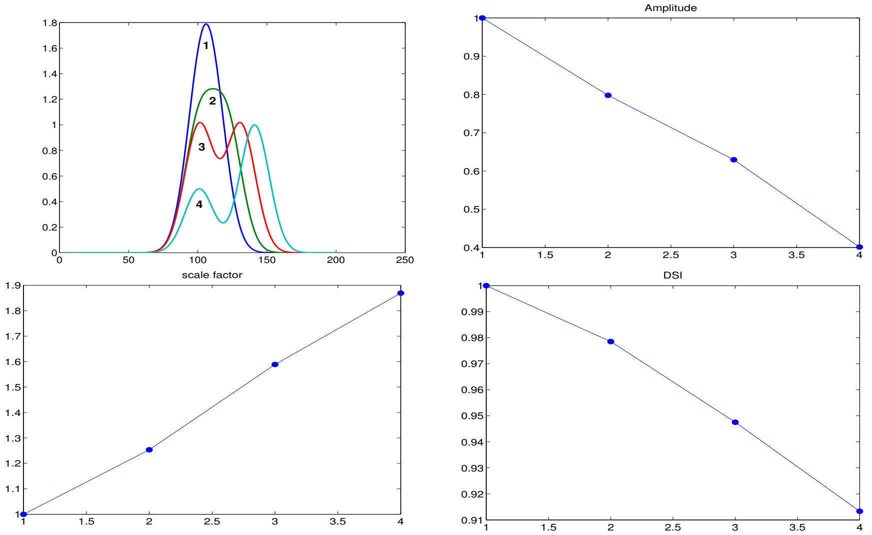
$$\alpha_i/\alpha_1,\ k_i/k_1,\ d_i - d_1$$

- Difference Shape Index (DSI) is performed on each couple of observations $(((1;2),(1;3),\ldots)$ by using previous SVD decomposition on 2xN $\mathbf{T}_i$ matrices.

  For each matrix $\mathbf{T}_i$ the 2 singular values $\lambda_{1,i}$ and $\lambda_{2,i}$ (with $\lambda_{1,i} > \lambda_{2,i}$) allows :

$$0.5 < DSI_i = \frac{\lambda_{1,i}}{\lambda_{1,i} + \lambda_{2,i}} < 1$$

# Simulation : different shapes

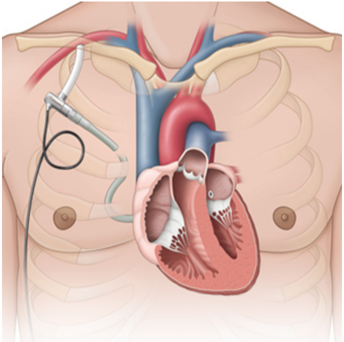


## Goal and tools

Develop non invasive new strategies for ventricular continuous monitoring during continuous-flow Left Ventricular Assist Device (LVAD) therapy by exploring possible relationship between the ventricular volume and the electrical myocardial activity.

## Assumption

LVAD $\Longrightarrow$ mechanical unloading of LV $\Longrightarrow$ changes of ventricular electrical activity



Changes of the ventricle blood volume $\Rightarrow$ Influence on ECG :

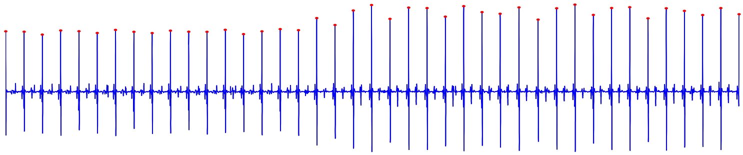
- Position of the heart in the chest
- Brody effect
- Change in thickness of the ventricular muscle wall
- Effect of stretch of the muscle fibers on the AP (depolarization) [Franz]

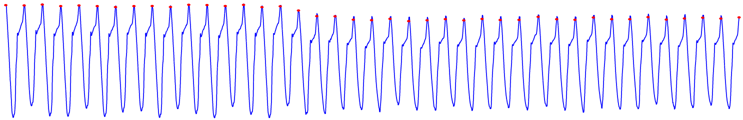
## Initial Approach

R wave peak (RWP) values are compared to the corresponding (in time) Left Ventricular Volume (LVV) during pump speed changes.

## Other ECG features

For each QRS : Amplitude, Difference Shape Index, scale factor, delay ?





Pump OFF Pump ON

# Experimental data collection

- 6 Pigs underwent LVAD implantation : (1-5) Gyro Centrifugal Pump 2 and (6) Circulite Synergy Micropump
- (1-5) 2 females and 3 males 47$\pm$8 Kg, (6) male 80 Kg.
- For Gyro 1300-1700 rpm and for Circulite 12000-18000 rpm
- ECG (DIII), systemic arterial pressure and left ventricular volume and pressure (transducer catheter) were recorded

- The R wave peak magnitude (RWP) and QRS complex extracted from each cycle.
- $\text{LVV}_{RWP}$, measured at the time of RWP.
- To reduce the effect of ventilation (pigs ventilated), 20 consecutive RWP and $\text{LVV}_{RWP}$ are averaged over time : $\text{RWP}_p$ and $\text{LVV}_{RWP_p}$

# All Pigs

Correlation coefficients between left ventricular volume $LVV_{RWPp}$ and :

- R wave peak $RWP_p$
- Difference Shape Index (DSI)
- amplitude coefficient (AMP)
- Scale factor (SF) for the 6 pigs.
- p-value $\dagger < 0.001$, $\S NS$

| $LVV_{RWPp}$ *vs* | 1 | 2 | 3 | 4 | 5 | 6 |
|---|---|---|---|---|---|---|
| $RWP_p$ | $-0.94^{\dagger}$ | $-0.96^{\dagger}$ | $-0.86^{\dagger}$ | $-0.84^{\dagger}$ | $-0.86^{\dagger}$ | $-0.84^{\dagger}$ |
| DSI | $-0.02^{\S}$ | $0.05^{\S}$ | $0.43^{\dagger}$ | $0.01^{\S}$ | $-0.09^{\S}$ | $-0.27^{\S}$ |
| AMP | $-0.54^{\dagger}$ | $-0.89^{\dagger}$ | $0.71^{\dagger}$ | $-0.48^{\dagger}$ | $-0.46^{\dagger}$ | $-0.89^{\dagger}$ |
| SF | $0.03^{\S}$ | $0.44^{\dagger}$ | $-0.83^{\dagger}$ | $-0.12^{\S}$ | $0.08^{\S}$ | $-0.29^{\S}$ |

# Pig (6)

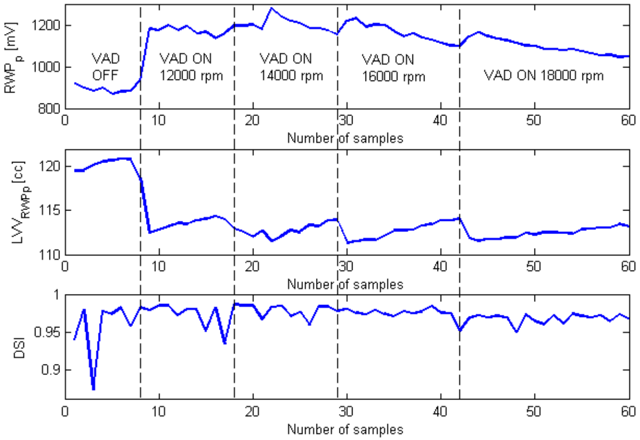



Figure – RWP$_p$, LVV$_{RWPp}$ and DSI profiles for pig (6) before VAD activation and during VAD speed change.

## Conclusion

- Only RWP is consistently correlated with LVV
- Results are in agreement with Franz's work
- Relationship with other LVV features ?
- Possible non-invasive monitoring of the LVV
  $\Longrightarrow$ setting of the pump speed and prevent suction

# Summary

- T or R waves analysis can be addressed as a shape analysis
- Delays, scales, mean shape estimated in the inverse normalized integrals domain
- Dynamic Time Warping as an alternative to find $\Phi(t)$