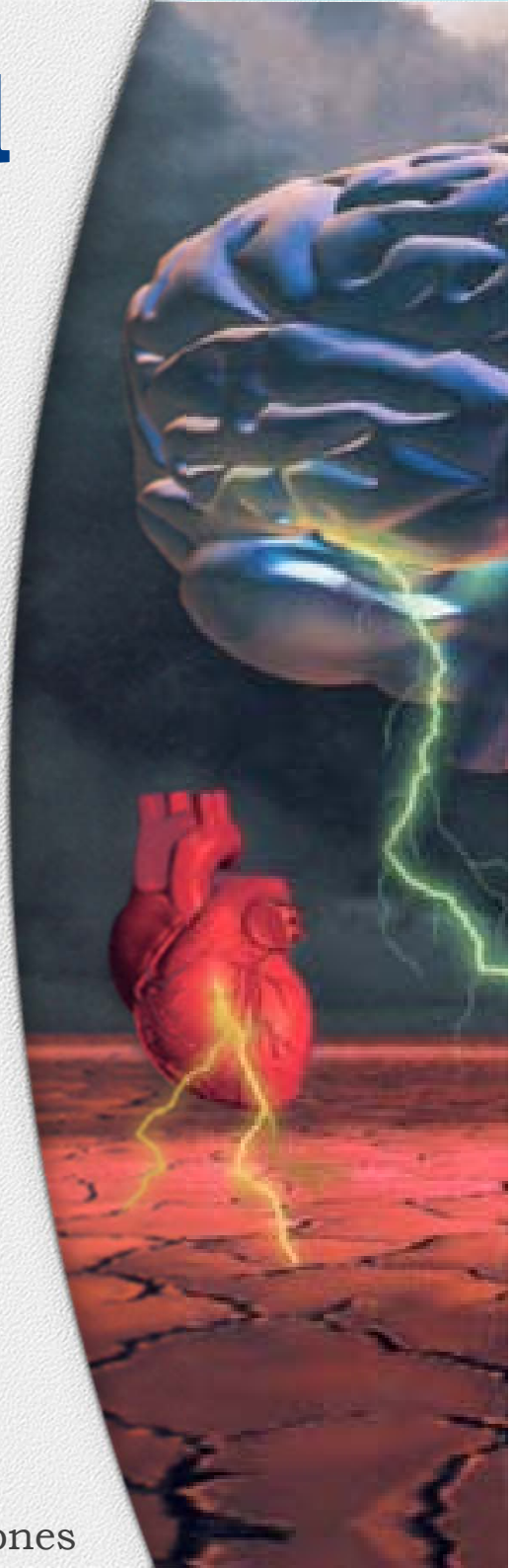
Signal processing guided by physiology:

Making the most of cardiorespiratory signals

Pablo Laguna



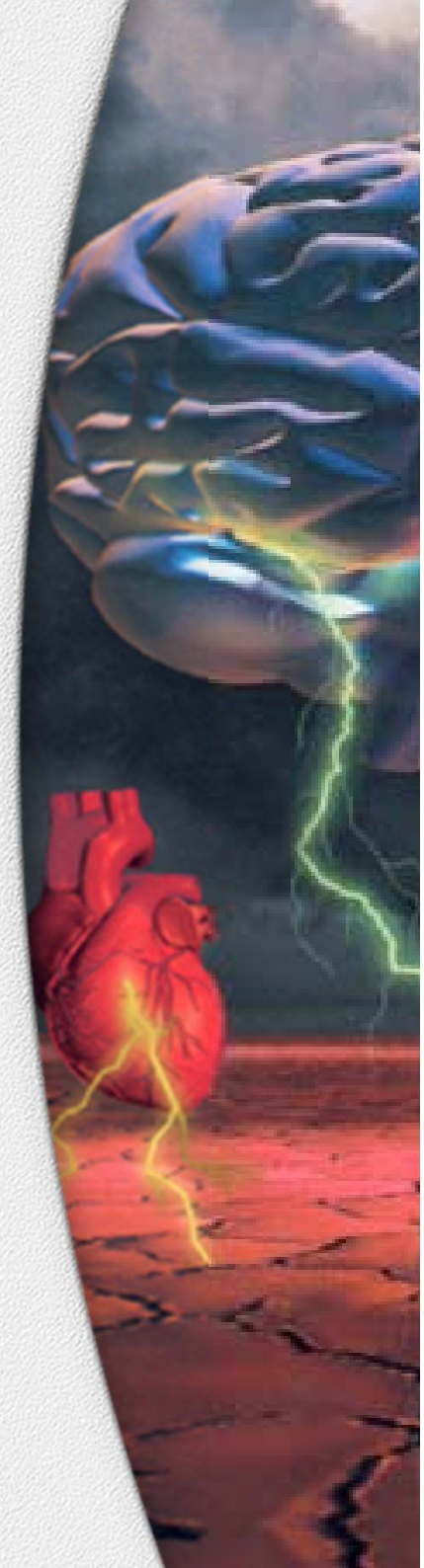
Universidad Zaragoza
1542

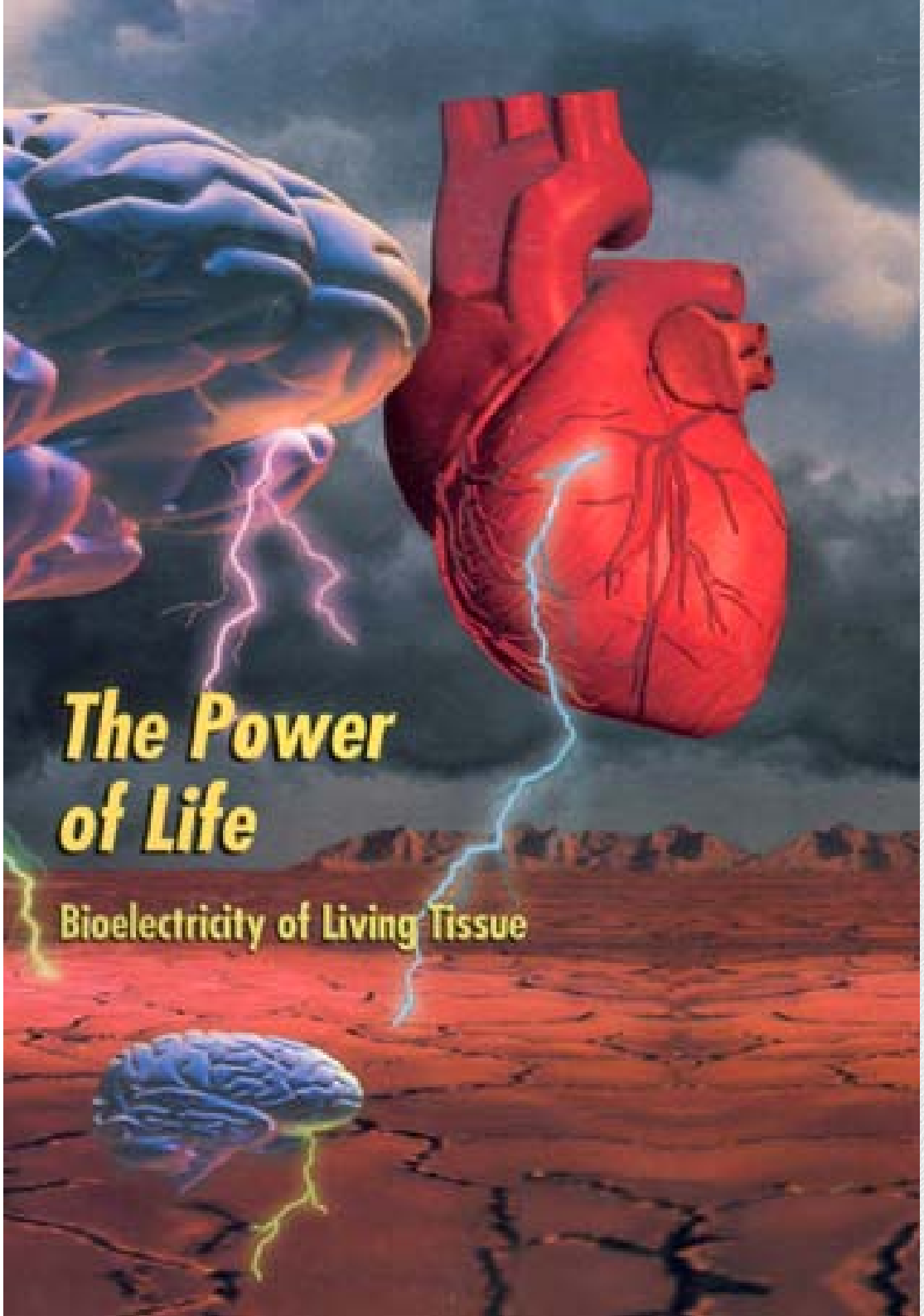
ciber-bbn
Centro Investigación Biomédica en Red
Bioingeniería, Biomateriales y Nanomedicina

Santiago 2013. Master en Tecnologías de la Información y las Comunicaciones

Bioelectrical signals convey info from biological systems:

- **Muscle**
- **Neuronal**
- **Heart**
- **-----**





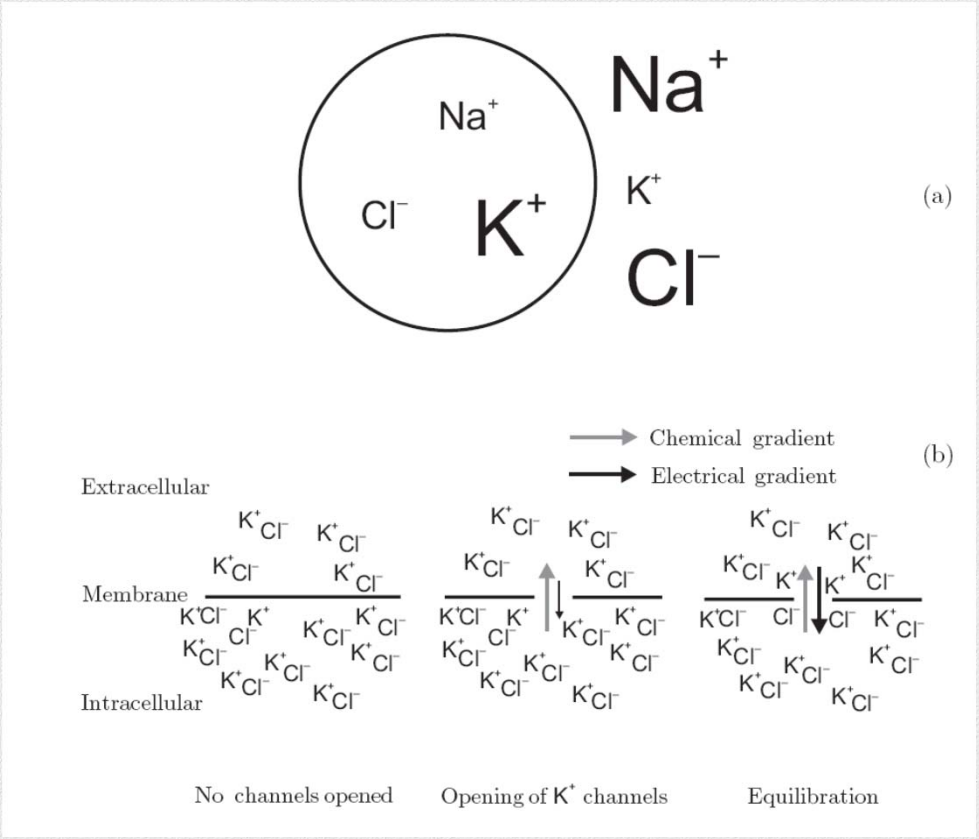
- Bioelectric signal **contain relevant information** about the underlying biological system

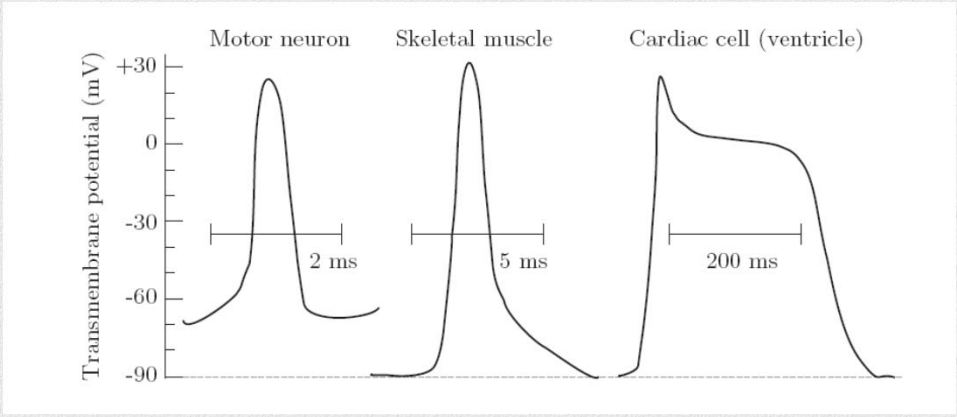
- Their **decoding** has allow to identify and clarify a large number of pathological conditions

Info within the biomedical signal

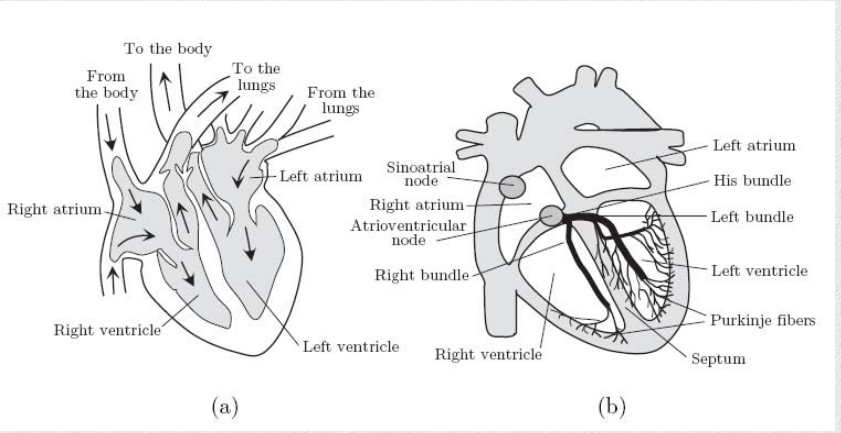
- May not be apparent in the signal
  - Measurement noise
  - Other interacting signals
  - Not visible to the human eye
- Signal processing usually required
  - Extract the useful info
  - Covert to meaningful and interpretable data
- Not optimum to deep into the system/organ,
  - but, usually inexpensive and suitable for massive scrutiny making still wise to **go for the most**

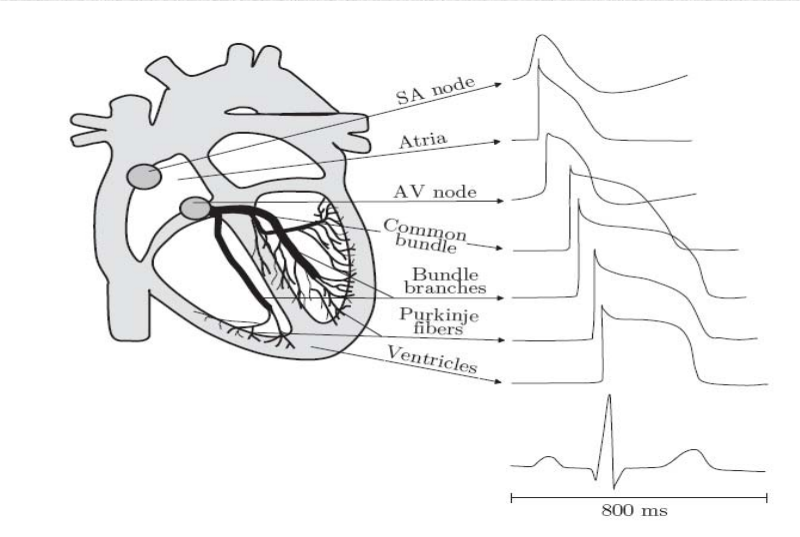
bioelectric signal origin





ECG signal origin





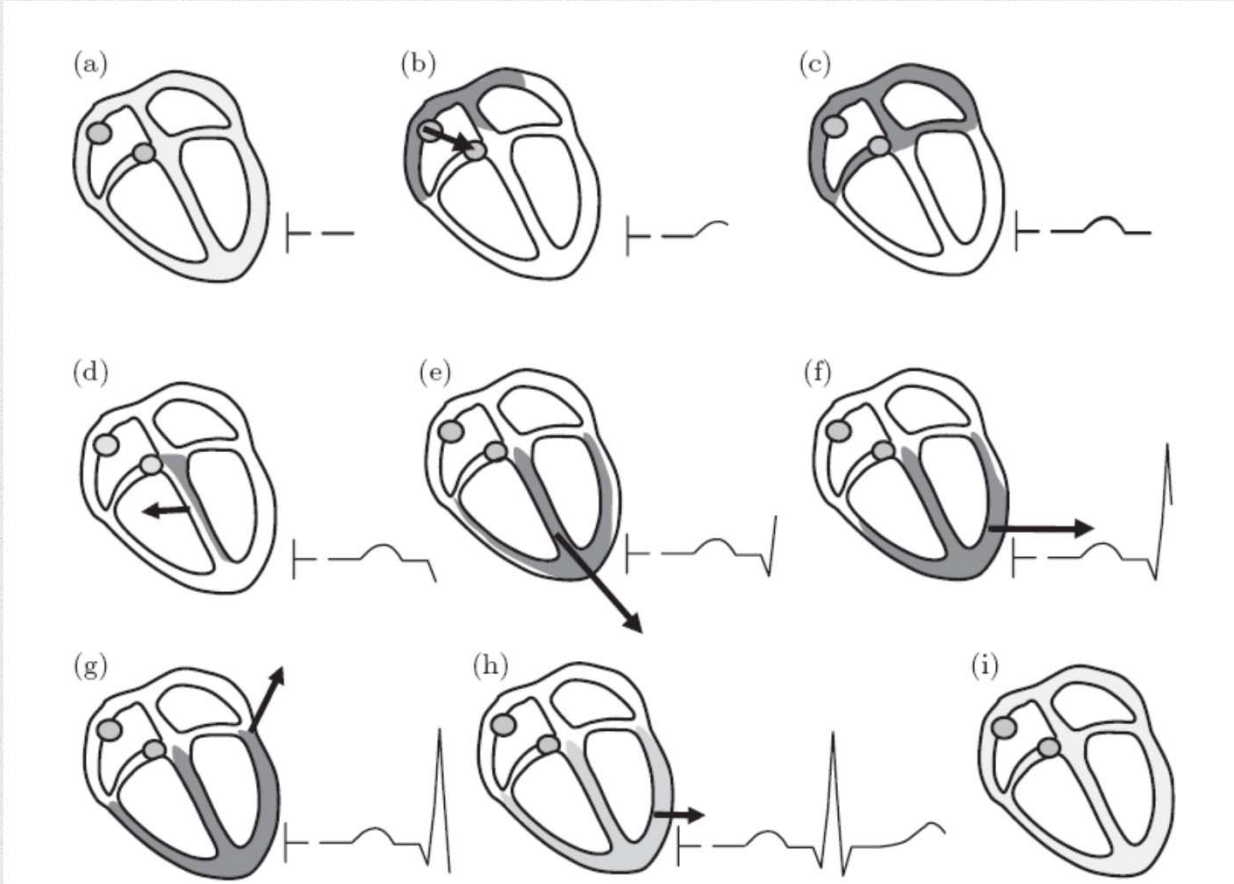
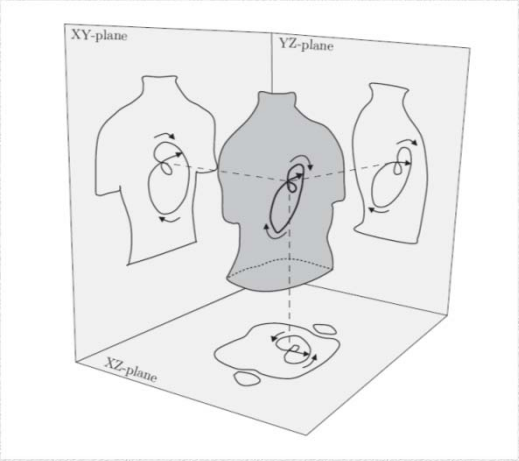
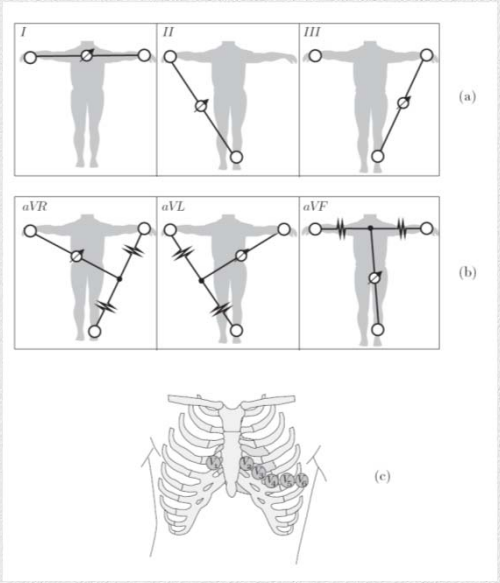
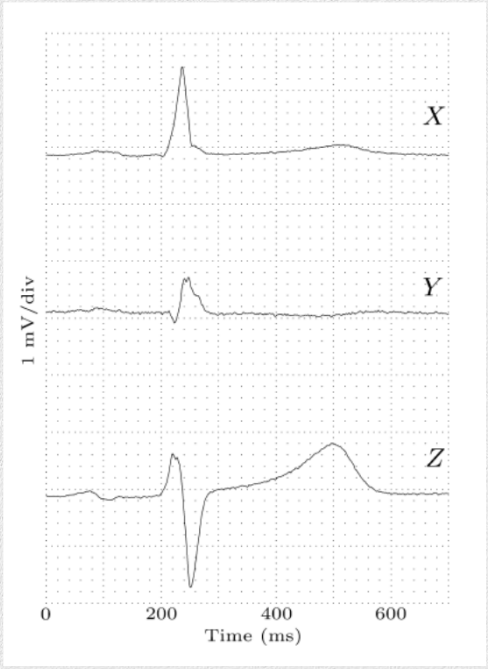


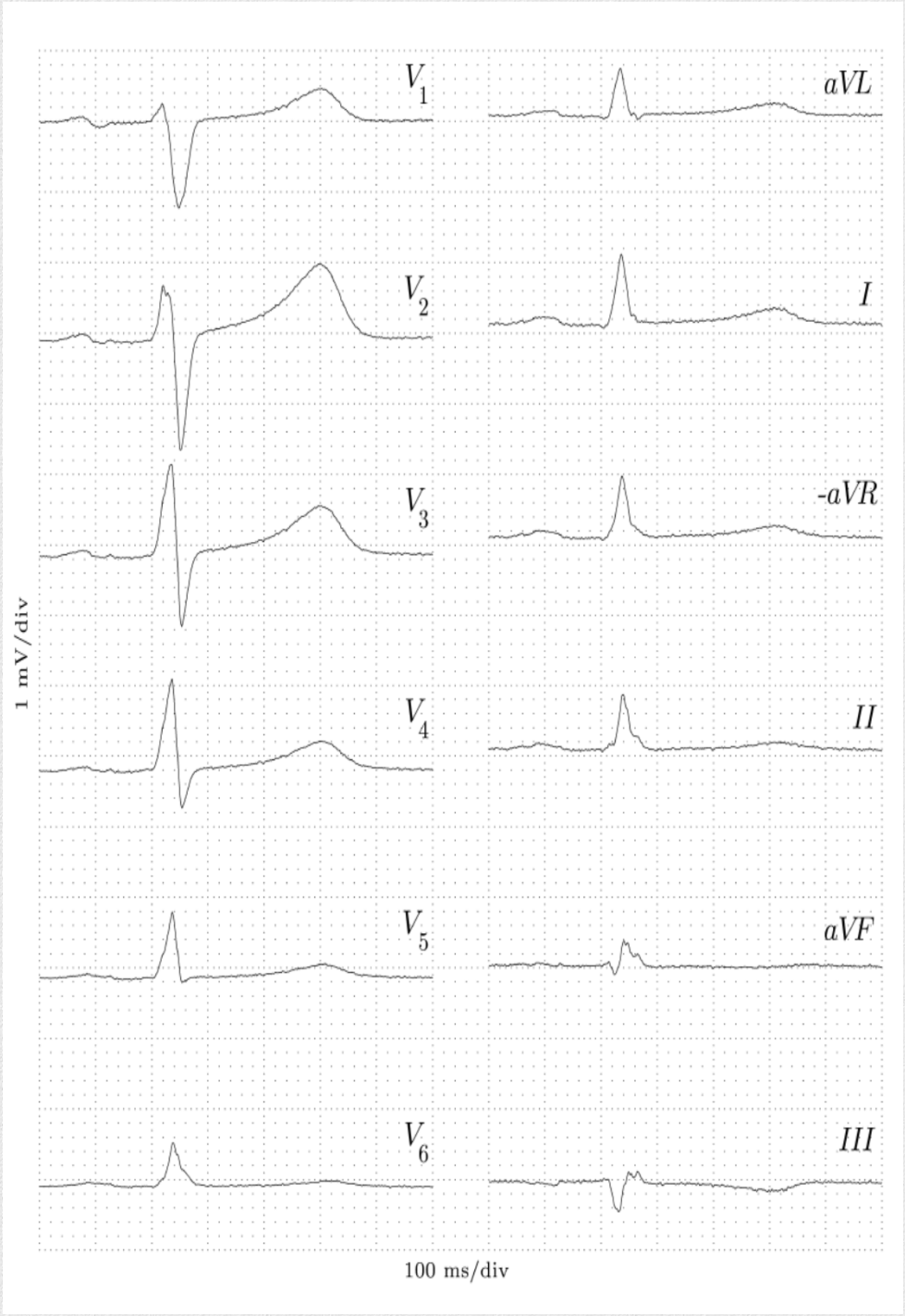
Figure 6.4: The ECG recorded in by an electrode positioned at the location of the symbol ⊢. (a) All cardiac cells at rest, (b) atrial depolarization, (c) the electrical impulse passing through the AV node, (d)–(g) ventricular depolarization, (h) ventricular repolarization, and (i) all cardiac cells again at rest.



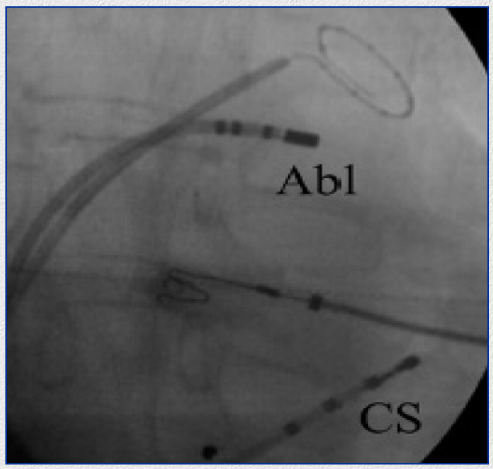


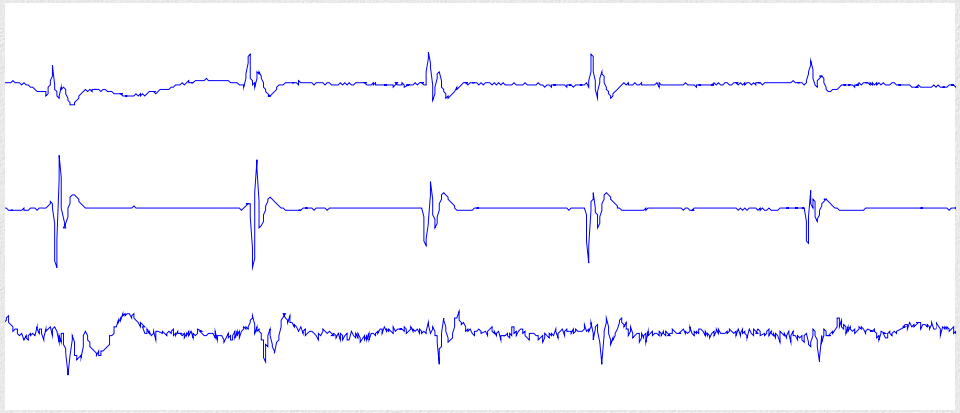


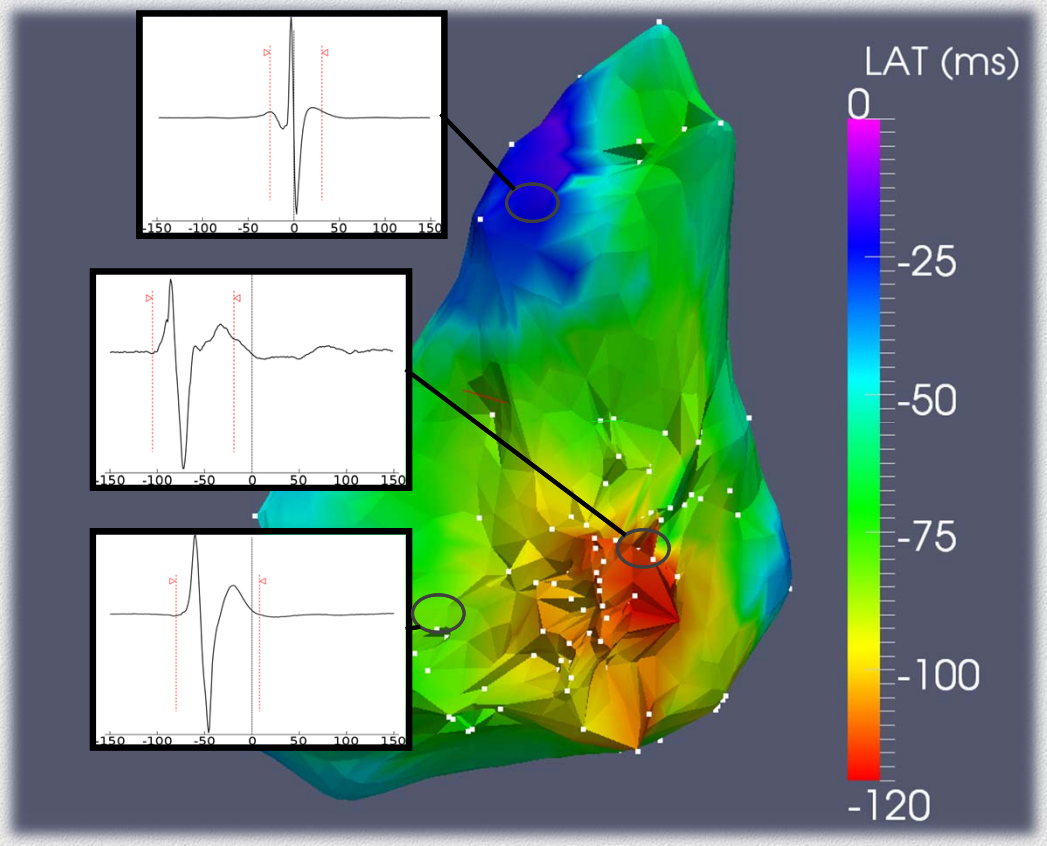
ECG Recording



EGM signal origin

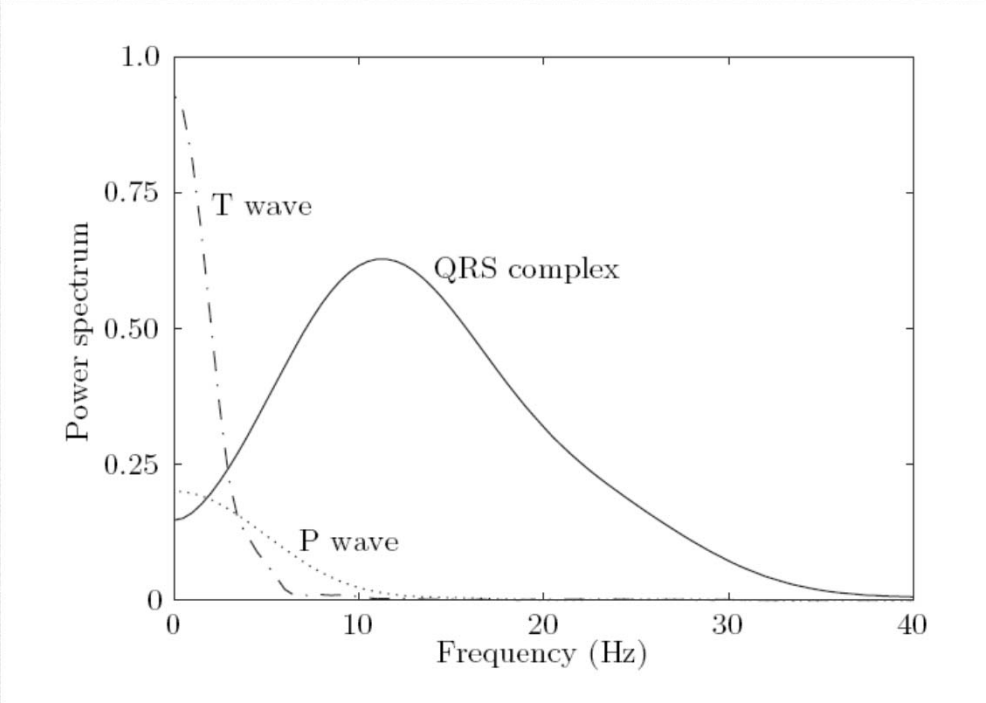






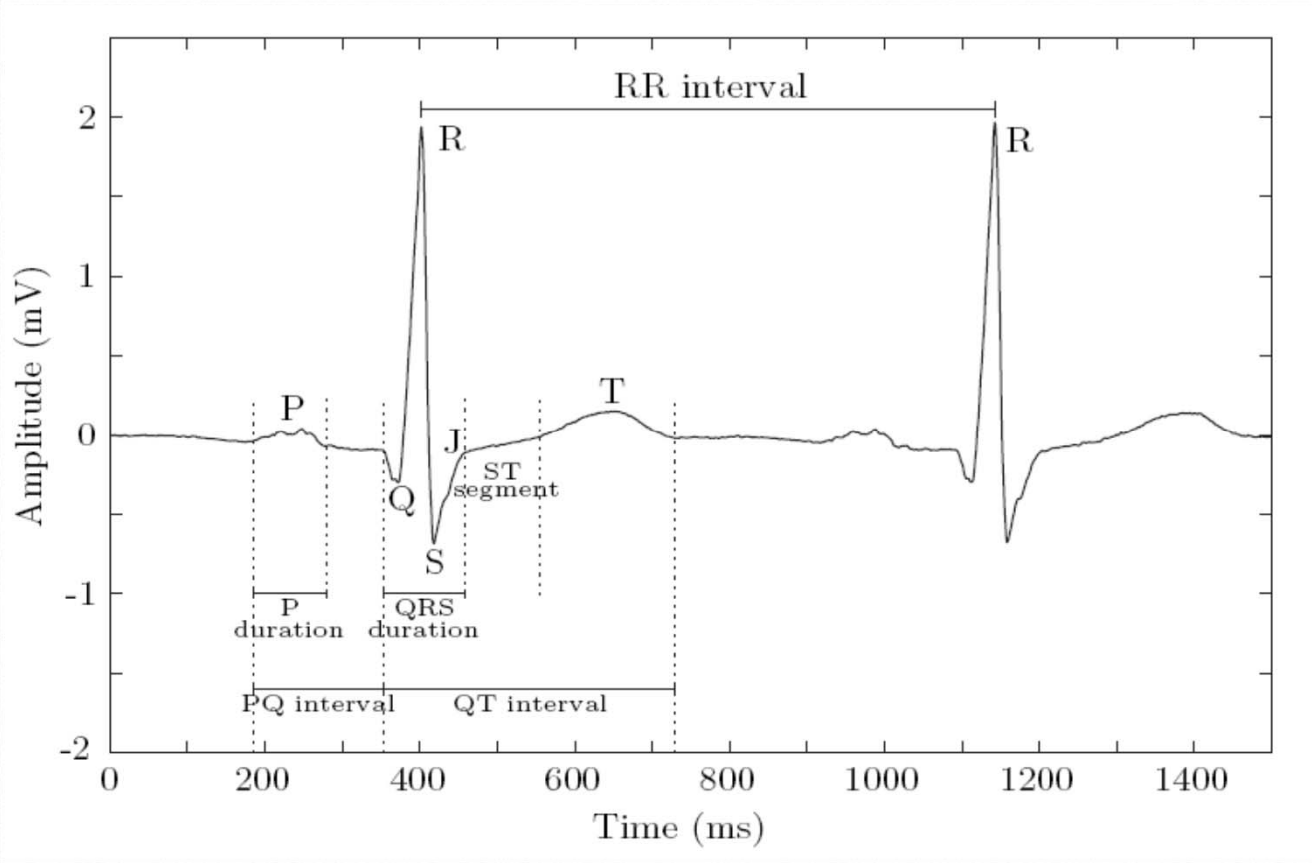
ECG signal Characteristics

- Pseudo periodic
- Transitory
- Non stationary



Clinically relevant information

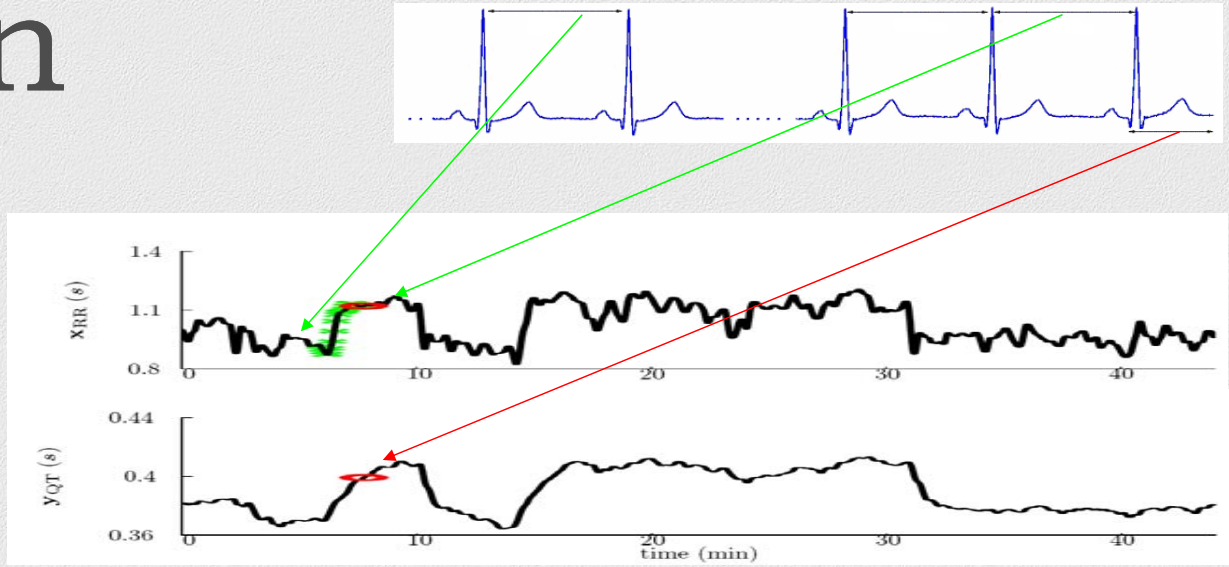
Static

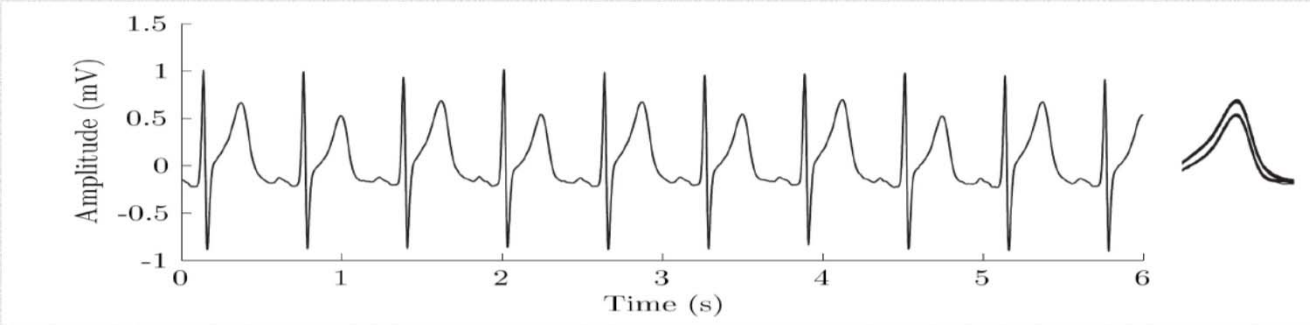


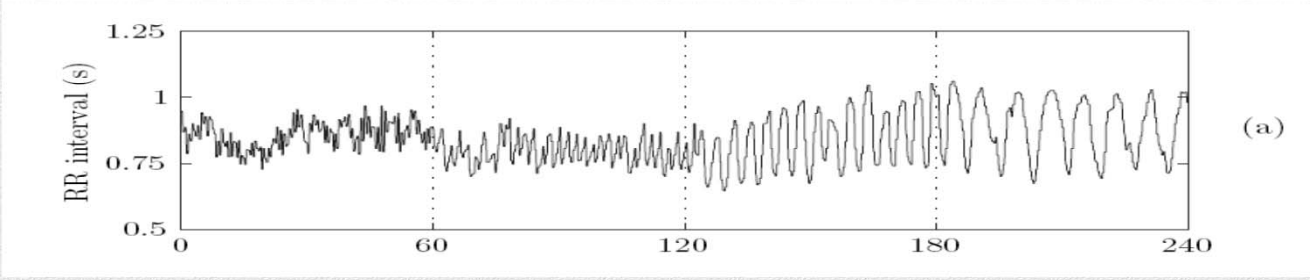
Clinically relevant information

Dynamic

- QT/RR
- Alternans
- Heart Rate Variability







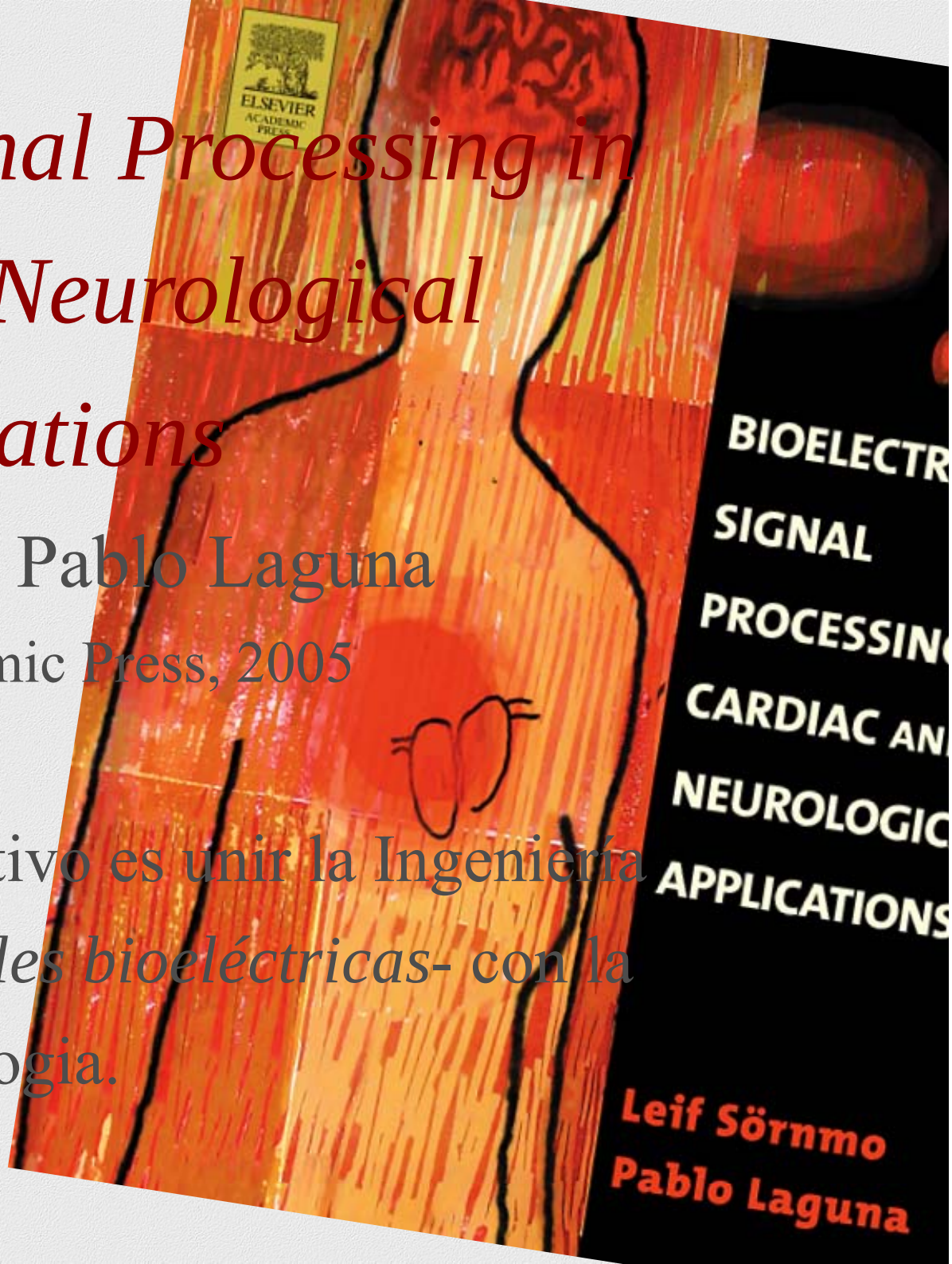
Biomedical signal processing: Objectives

- Reduce the subjectivity of manual measures
- Noise Reduction
- Extract new information
- Equipment and new functionalities
- Signal modeling
- Event visualization

Bioelectrical Signal Processing in Cardiac and Neurological Applications

Leif Sörnmo & Pablo Laguna

Elsevier/Academic Press, 2005



Libro de texto cuyo objetivo es unir la Ingeniería *-tratamiento de las señales bioeléctricas-* con la fisiologia.

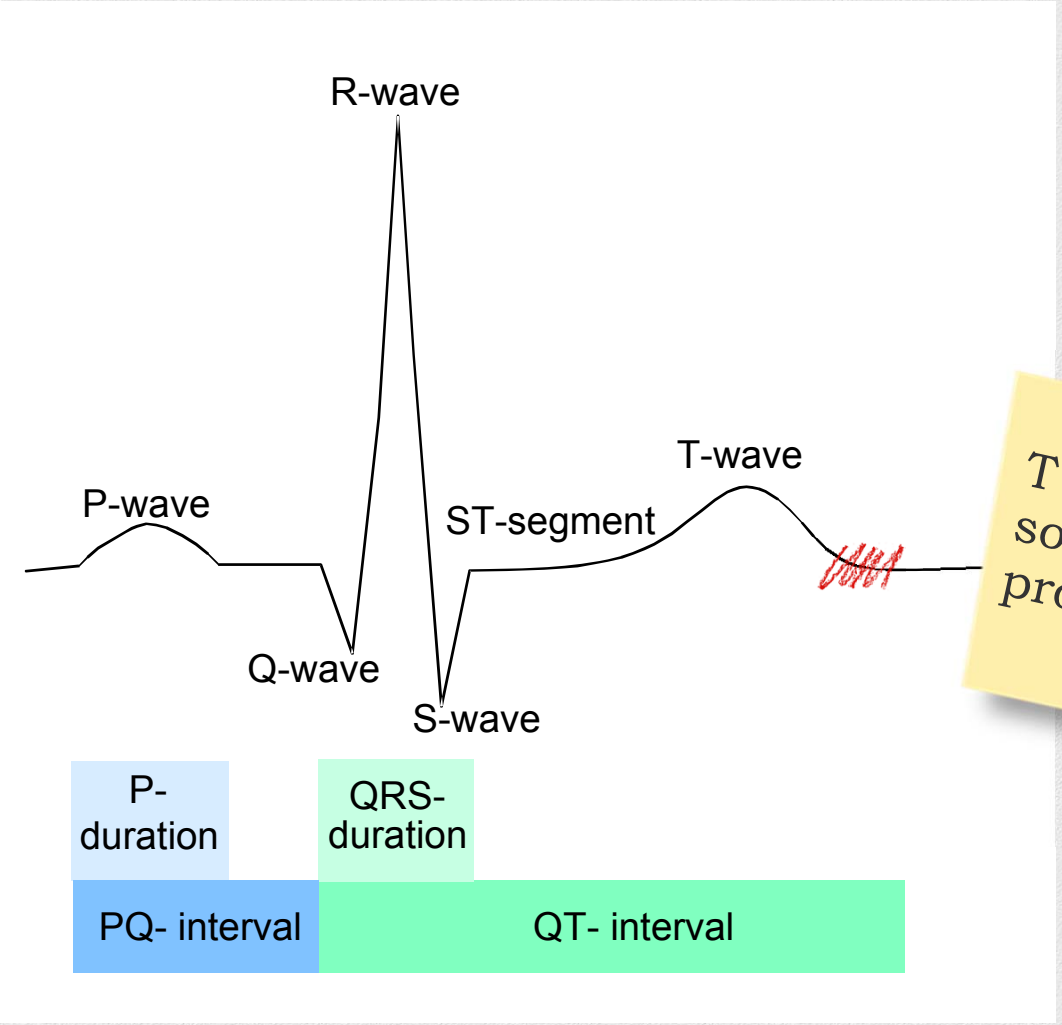
Biomedical signal processing difficulties

As opposite to other signal processing application:

- Biomedical signal originate at the inner human body
  →
  Their informative content is known just partially.
- The "truth" is rarely at our disposal to validate the tools.

Reducing subjectivity at manual measures

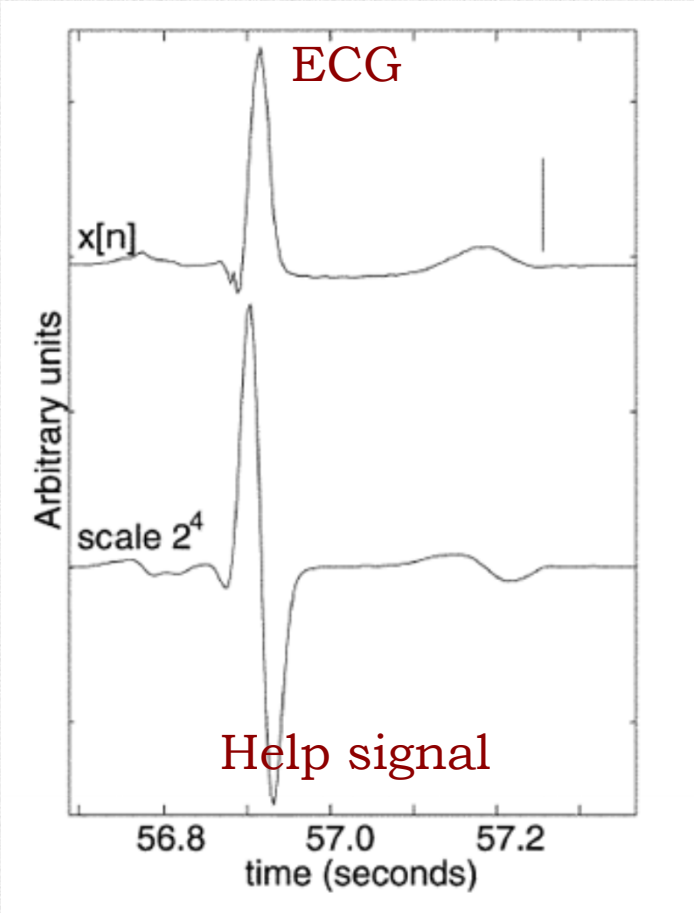
Waves of the ECG: P-QRS-T



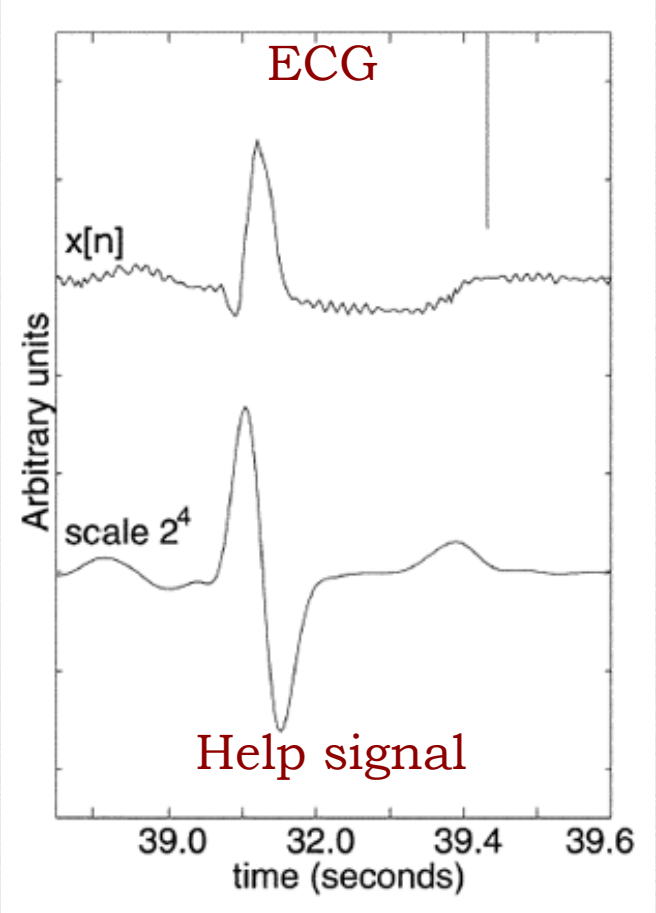
Large differences, even, between manual marks form different cardiologist...

Waves delineation

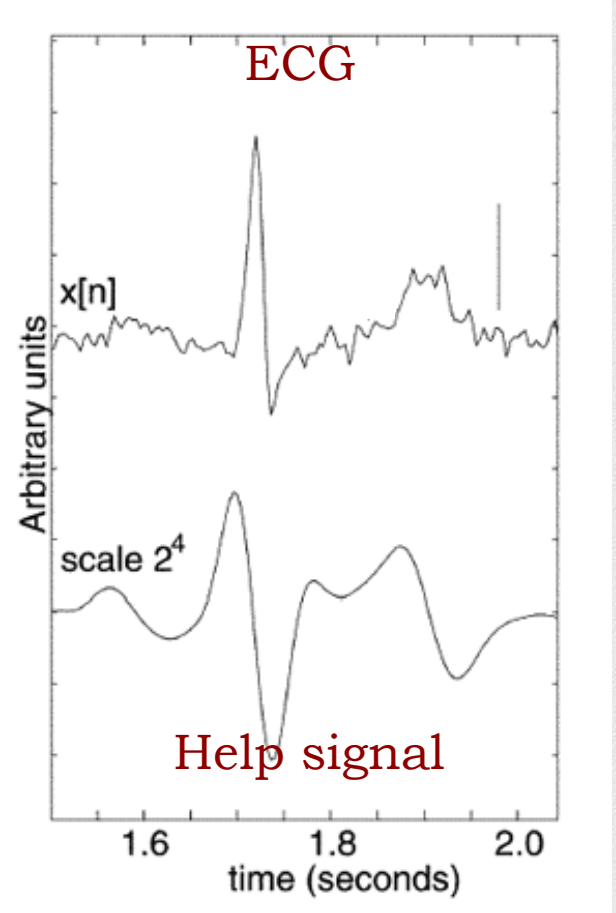
Easy



Medium

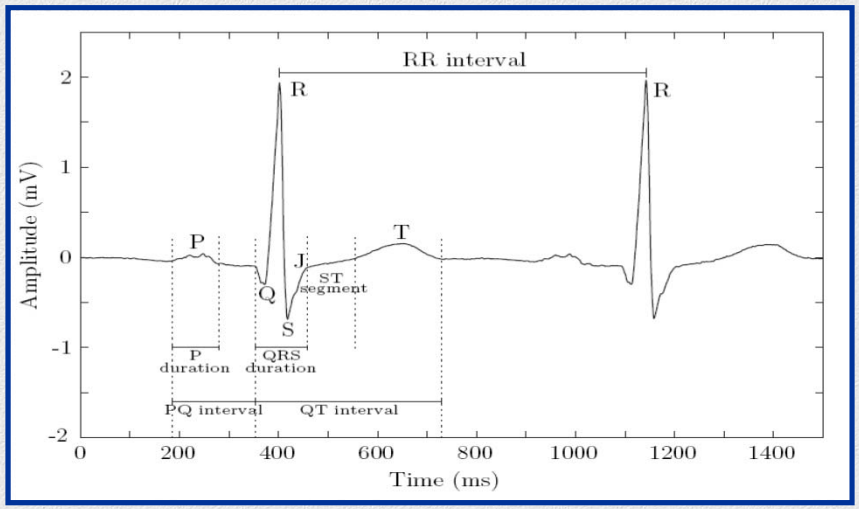


Difficult

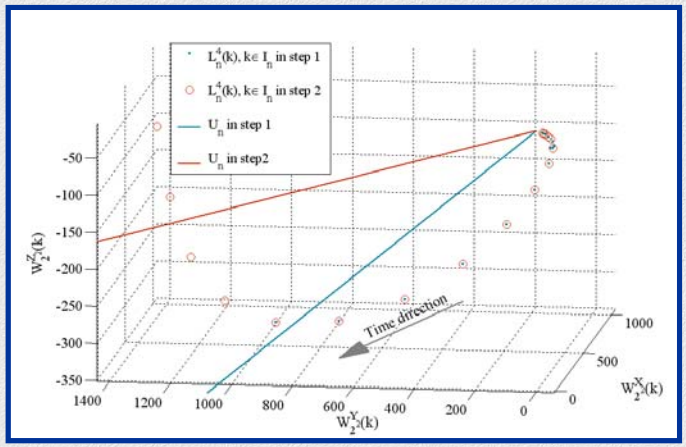


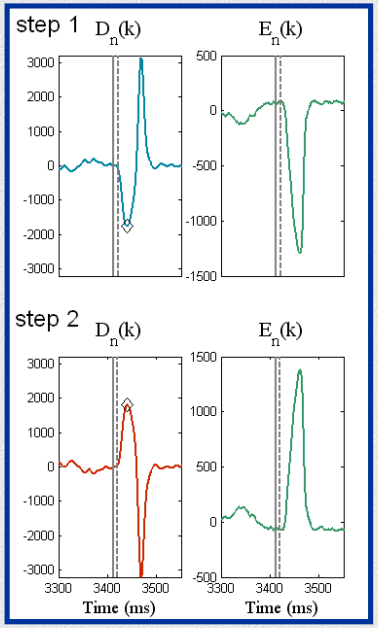
Where is the real onset and end of waves? Multilead ECG delineation

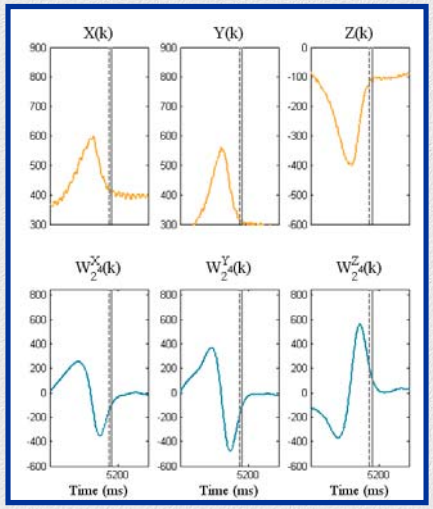
Single lead

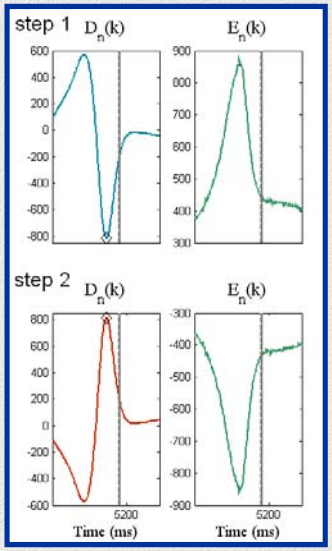


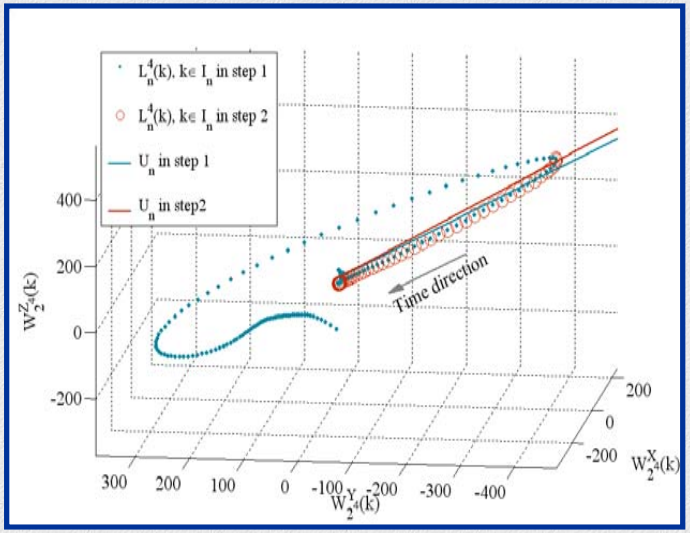
Multi-lead

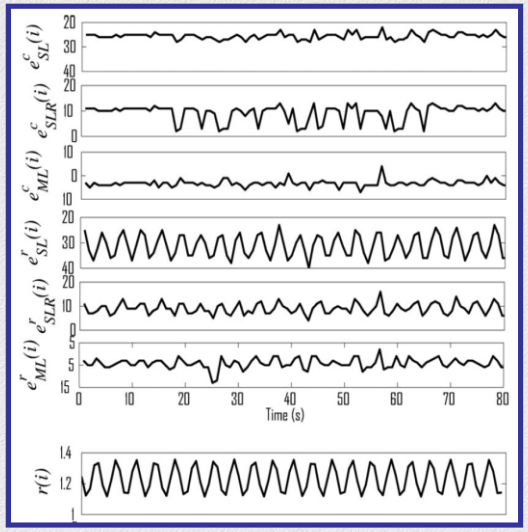










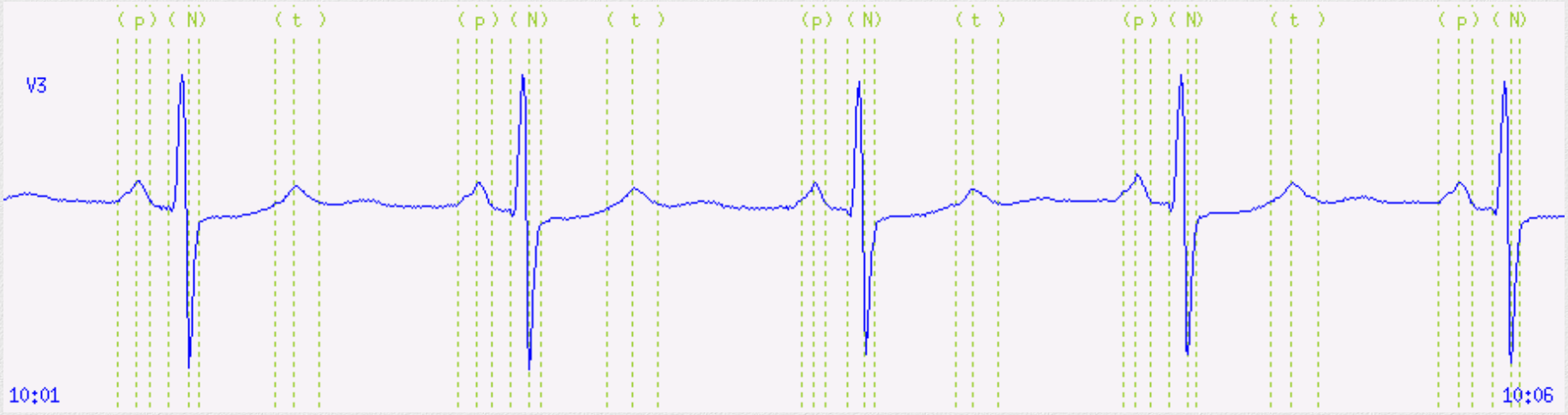


Group 1 :

Well detected
end of T- wave

me < 40 ms
SD < 50 ms

Automatic annotations:



Manual annotations:

Delineación de ECG: Validación

Bias (in ms) between automatic and manual anotations								
Detector	***Pon***	***P***	***Poff***	***QRSon***	***QRSoff***	***Ton***	***T***	***Toff***
WT	1.3	-7.8	0.3	-6.6	-0.4	2.3	-6.1	0.7
LPD	-9.4	-0.1	5.4	3.5	1.3	-3.3	-24.0	-19.7

Mean Standard Deviation (in *ms*)								
Detector	***Pon***	***P***	***Poff***	***QRSon***	***QRSoff***	***Ton***	***T***	***Toff***
WT	10.7	8.2	9.9	8.9	9.5	26.6	20.3	22.9
LPD	11.2	9.3	12.7	9.5	9.3	24.7	25.6	26.9
Tolerance	10.2	-	12.7	6.5	11.6	-	-	30.6

Noise reduction

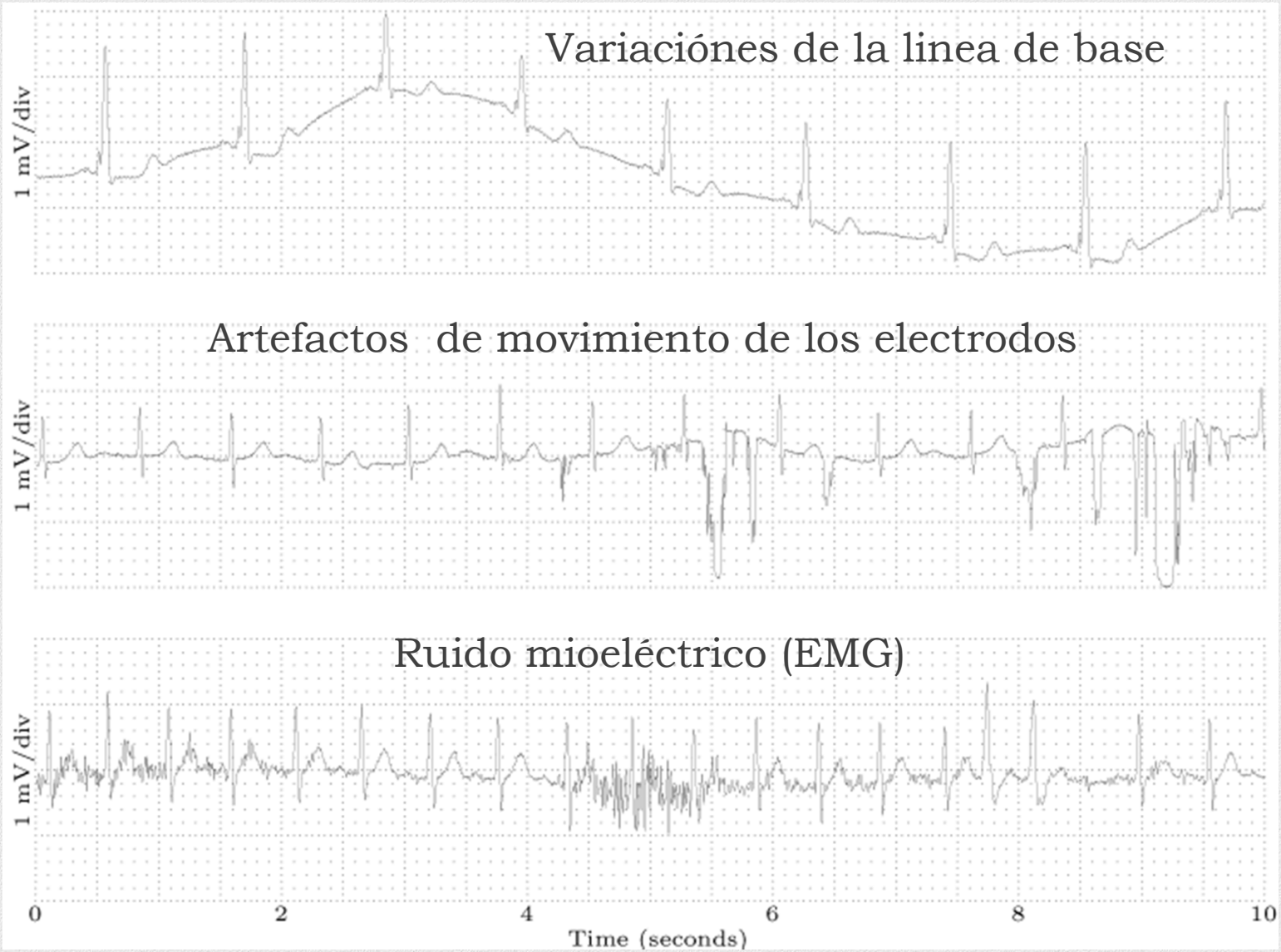
Noise

- External origin, as 50/60 Hz, other equipment, etc.
- Physiological origin, as EMG in ECG analysis.

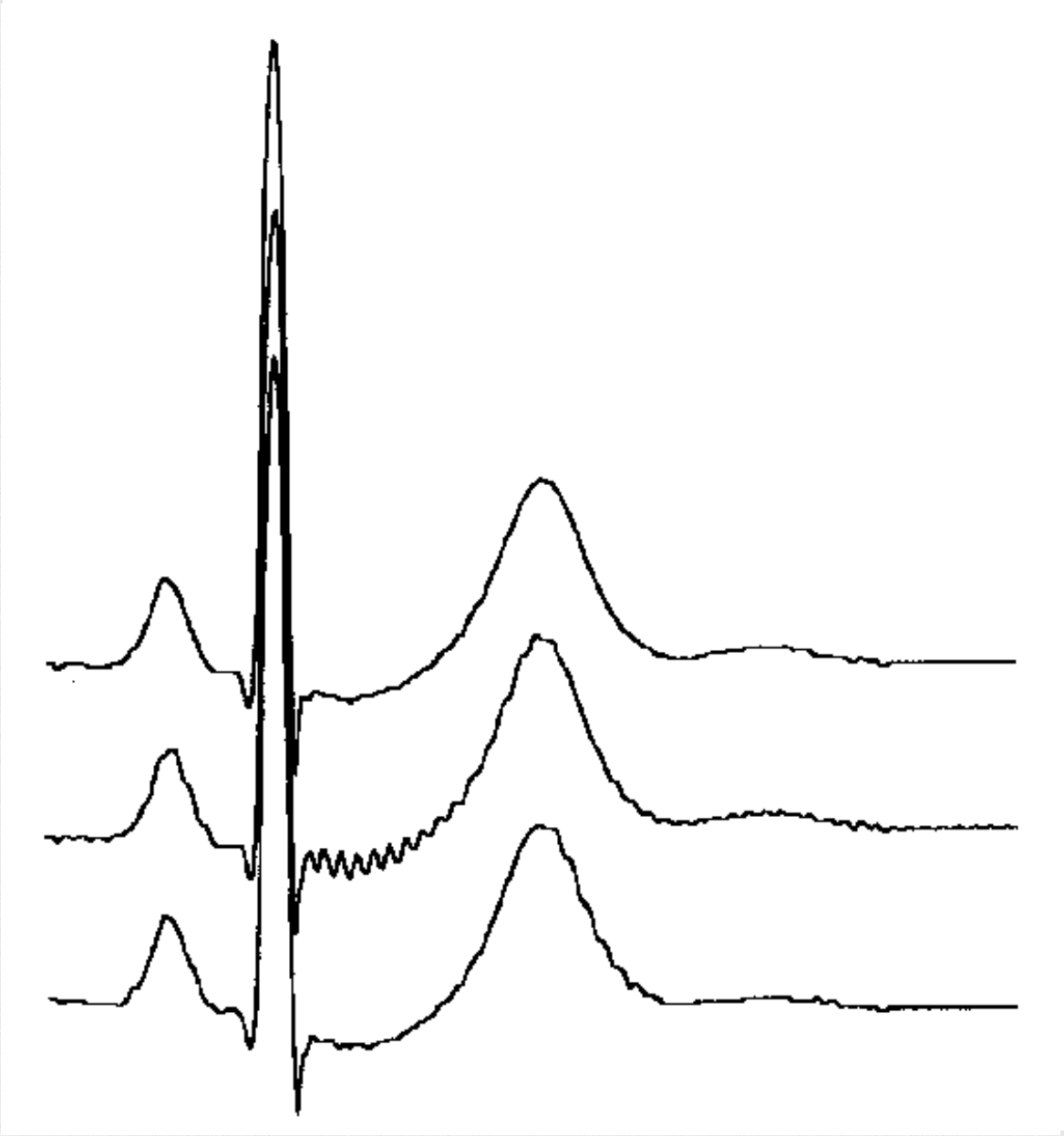
Basics with noise

- Every noise context should be address with a specific strategy, no generalization
  - Rarely one algorithm can be extrapolated without mayor considerations.
  - Their adaptation is very important NOT to destroy signal characteristics.

Ruido electrocardiográfico



Filtering 50/60 Hz

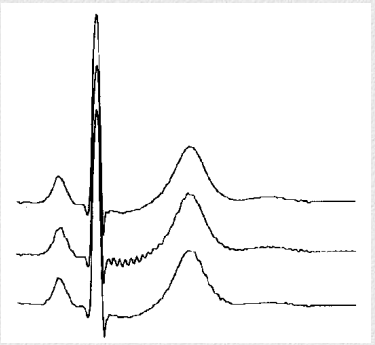


Original signal

Notch Filter (stándar)

Nonlineal Filter

Filtering 50/60 Hz



Solution: **non-lineal filter**

- Substract a sinusoid

$$v(n) = w_0 \sin(\omega_0 n)$$

$$H(z) = \frac{V(z)}{U(z)} = \frac{1}{1 - 2\cos\omega_0 z^{-1} + z^{-2}}$$

- Error function

$$e(n) = x(n) - v(n)$$

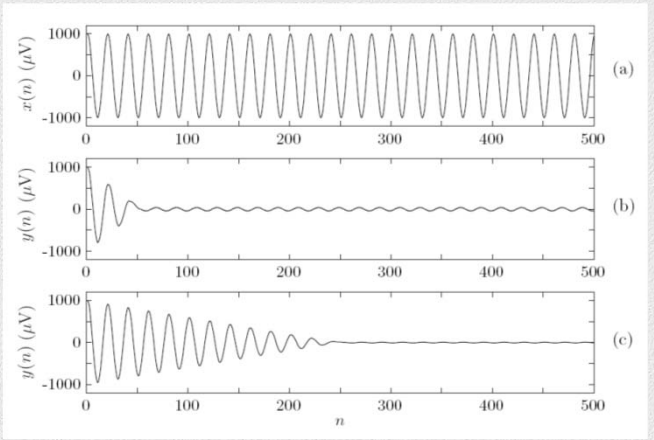
$$\begin{aligned} e'(n) &= e(n) - e(n-1) \\ &= x(n) - x(n-1) - (v(n) - v(n-1)) \end{aligned}$$

- Non-linear sinusoid update

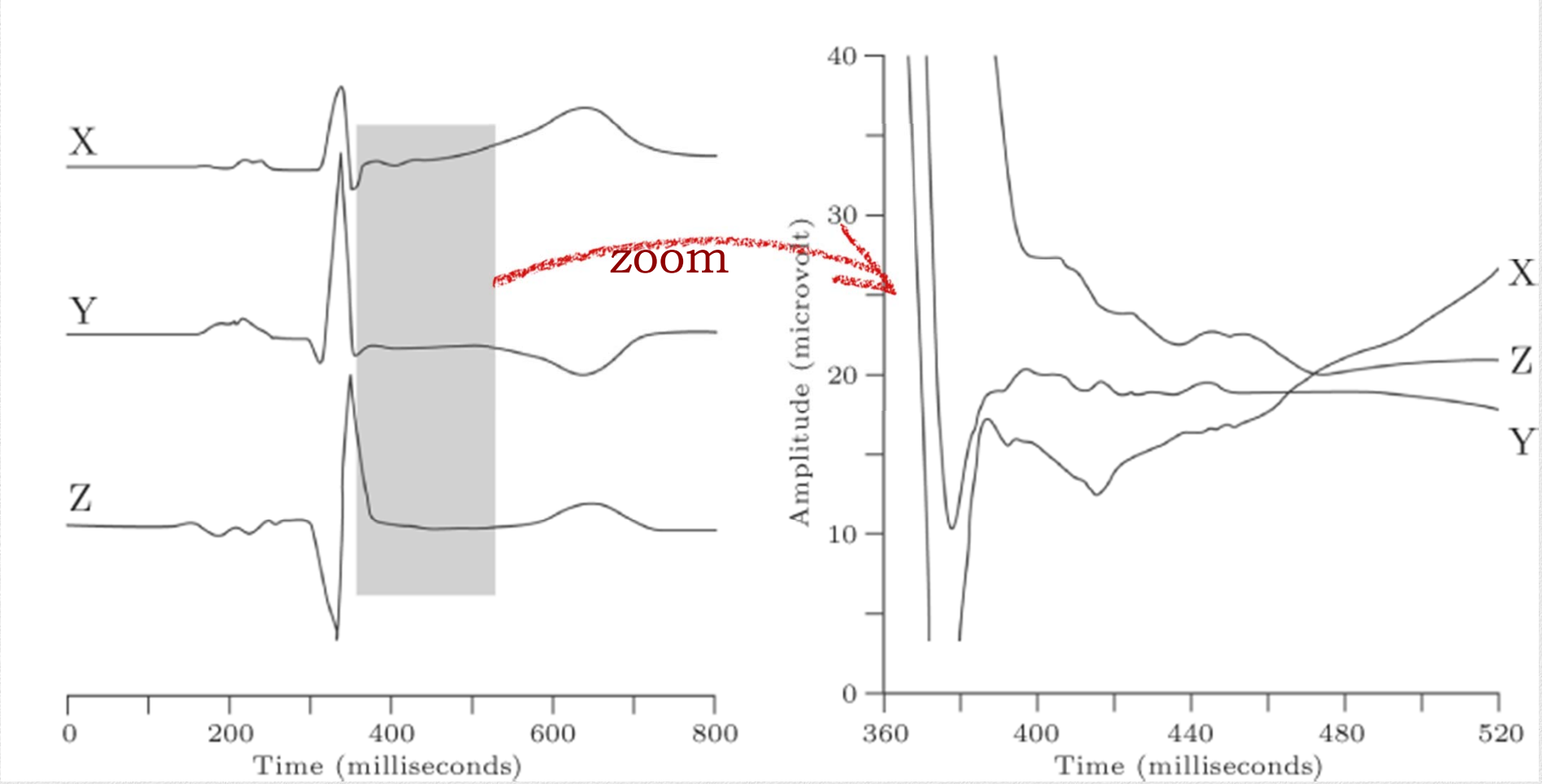
$$\hat{v}(n) = v(n) + \alpha\ \mathrm{sgn}(e'(n))$$

- Noise subtraction

$$y(n) = x(n) - \hat{v}(n)$$

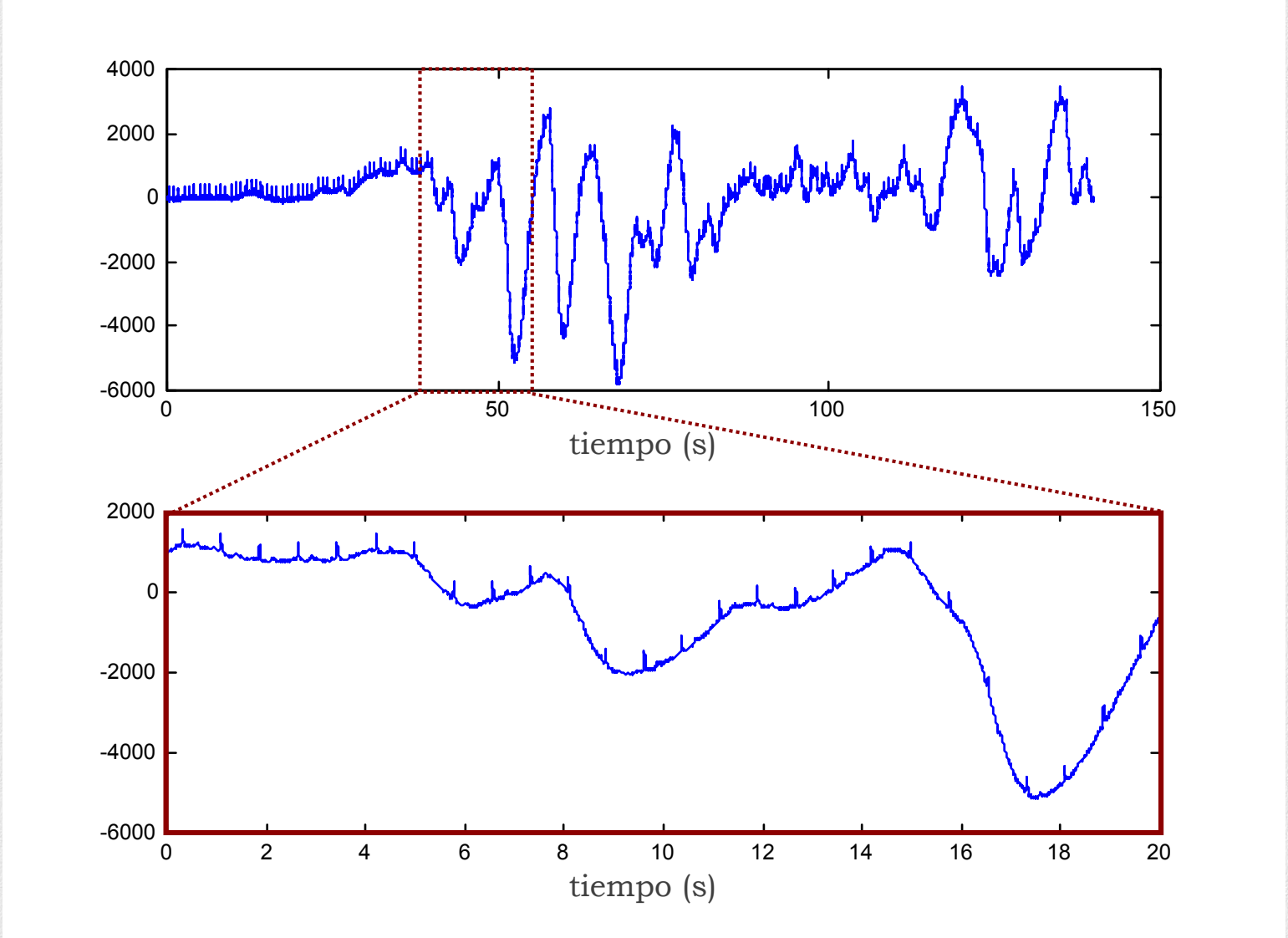


Warning: artifacts interpreted as late potentials.



Late potentials as arrhythmia risk markers in post MI patients

Baseline variations at the ECG



Baseline filtering

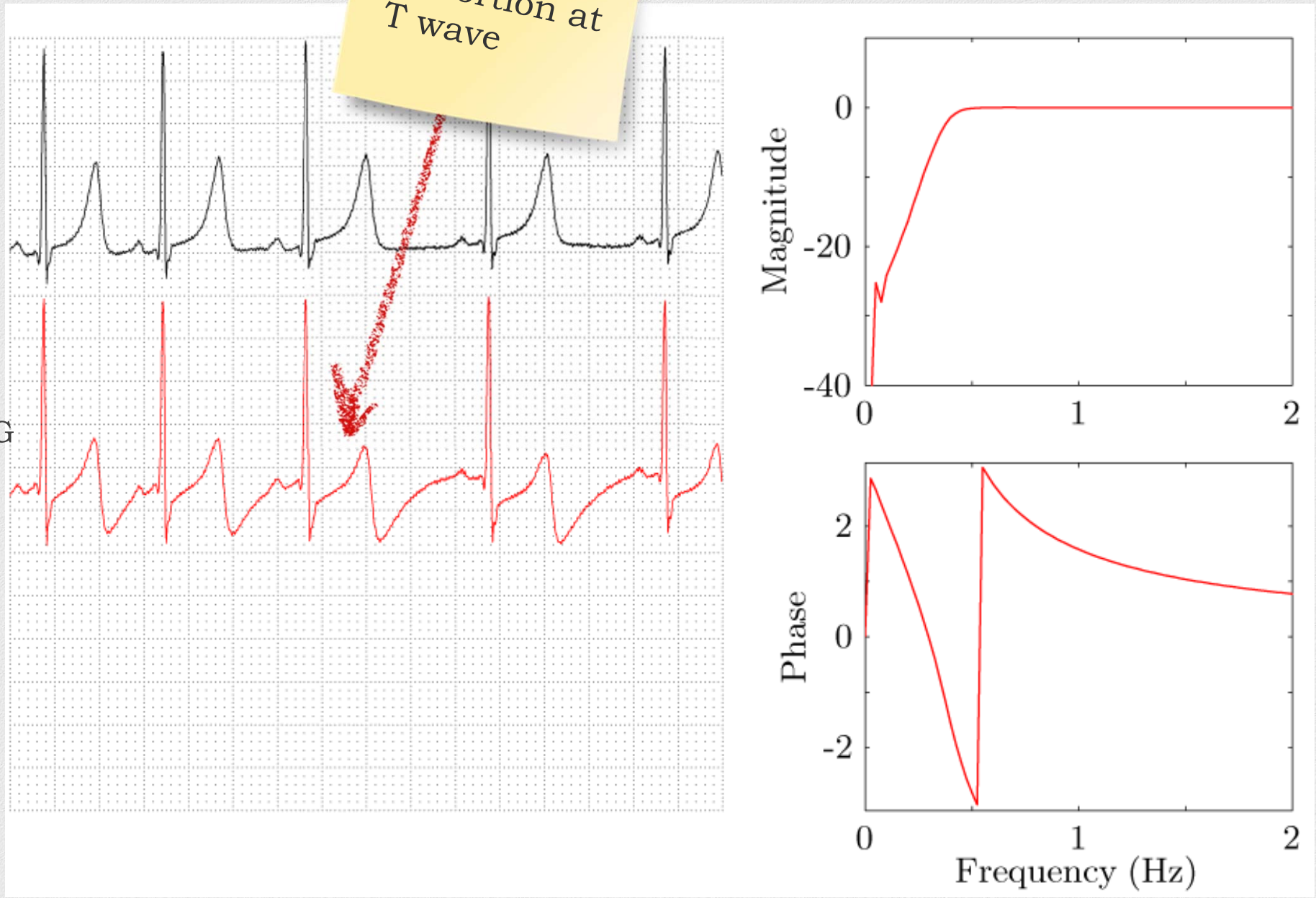
Original ECG

Baseline filtering

Note Large distortion at T wave

Original ECG

Filtered ECG (Nonlinear phase)

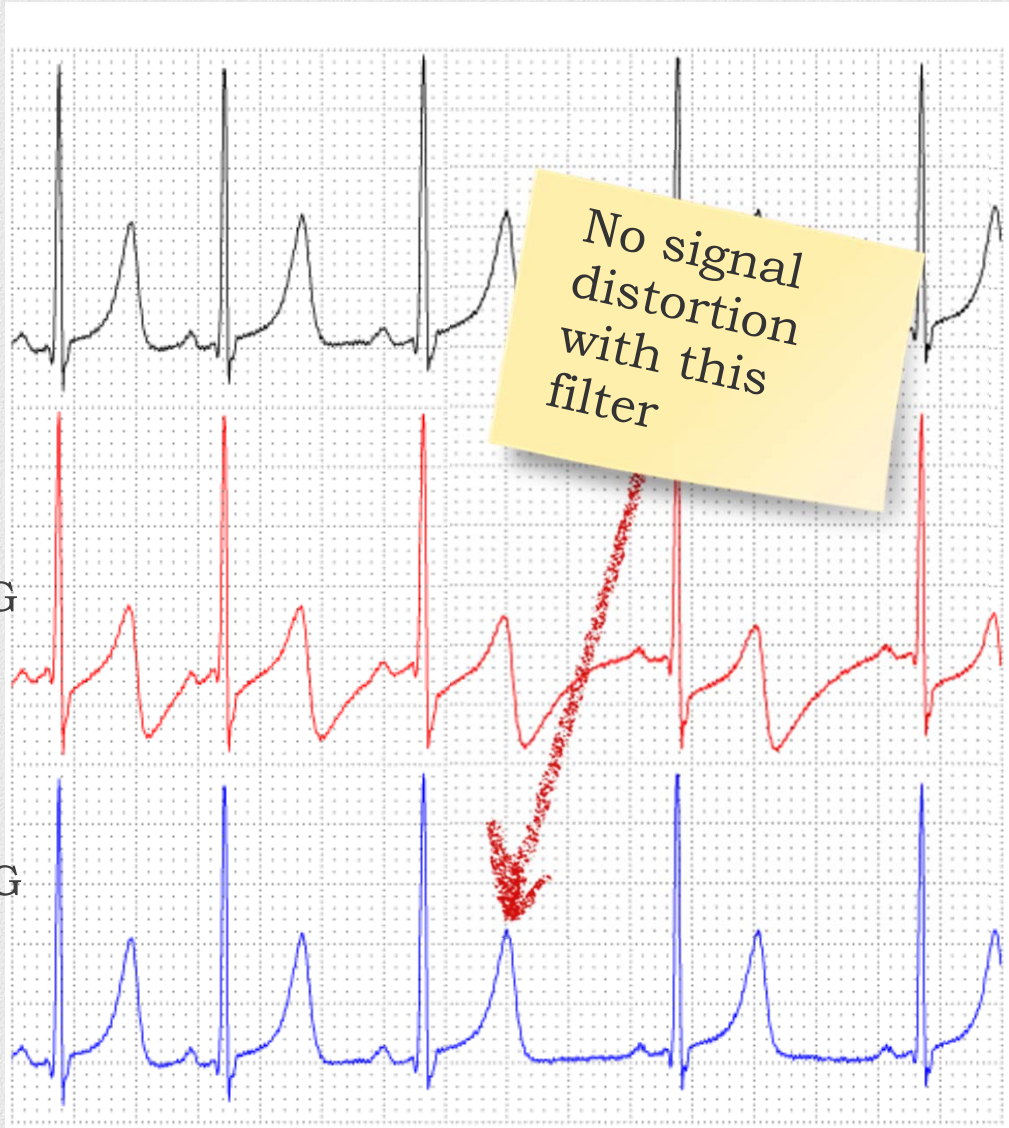


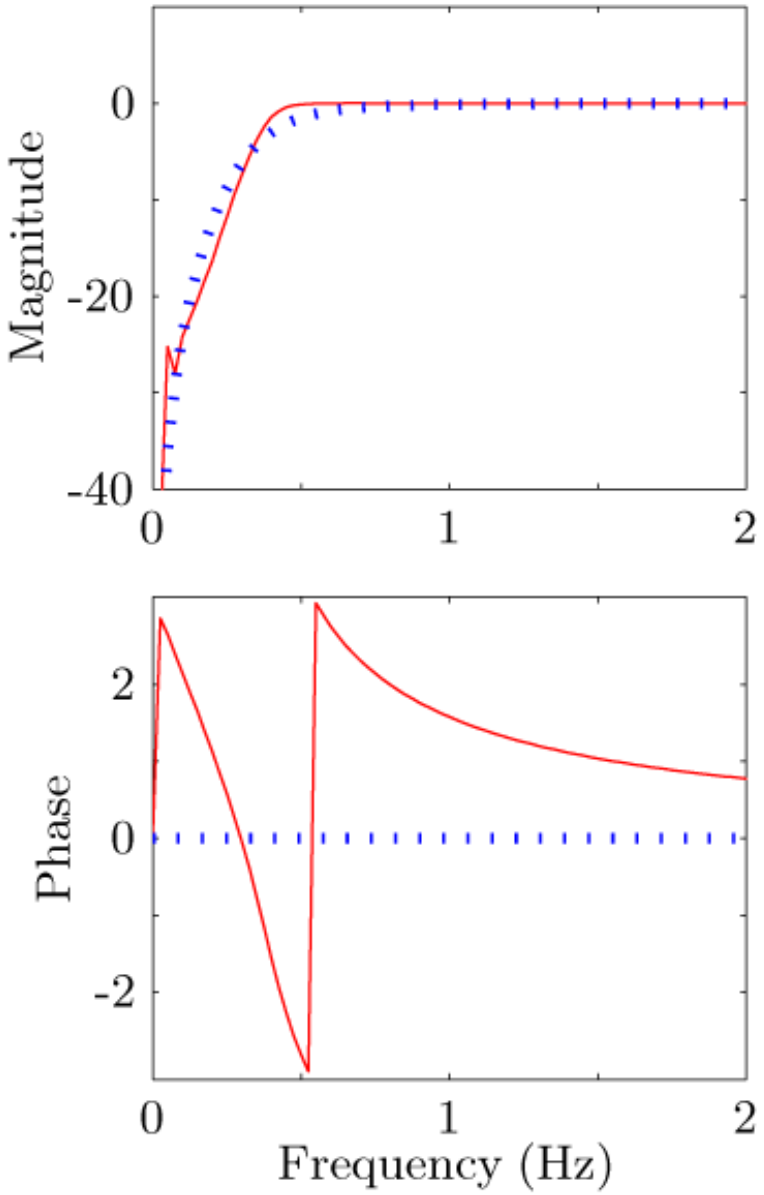
Baseline filtering

Original ECG

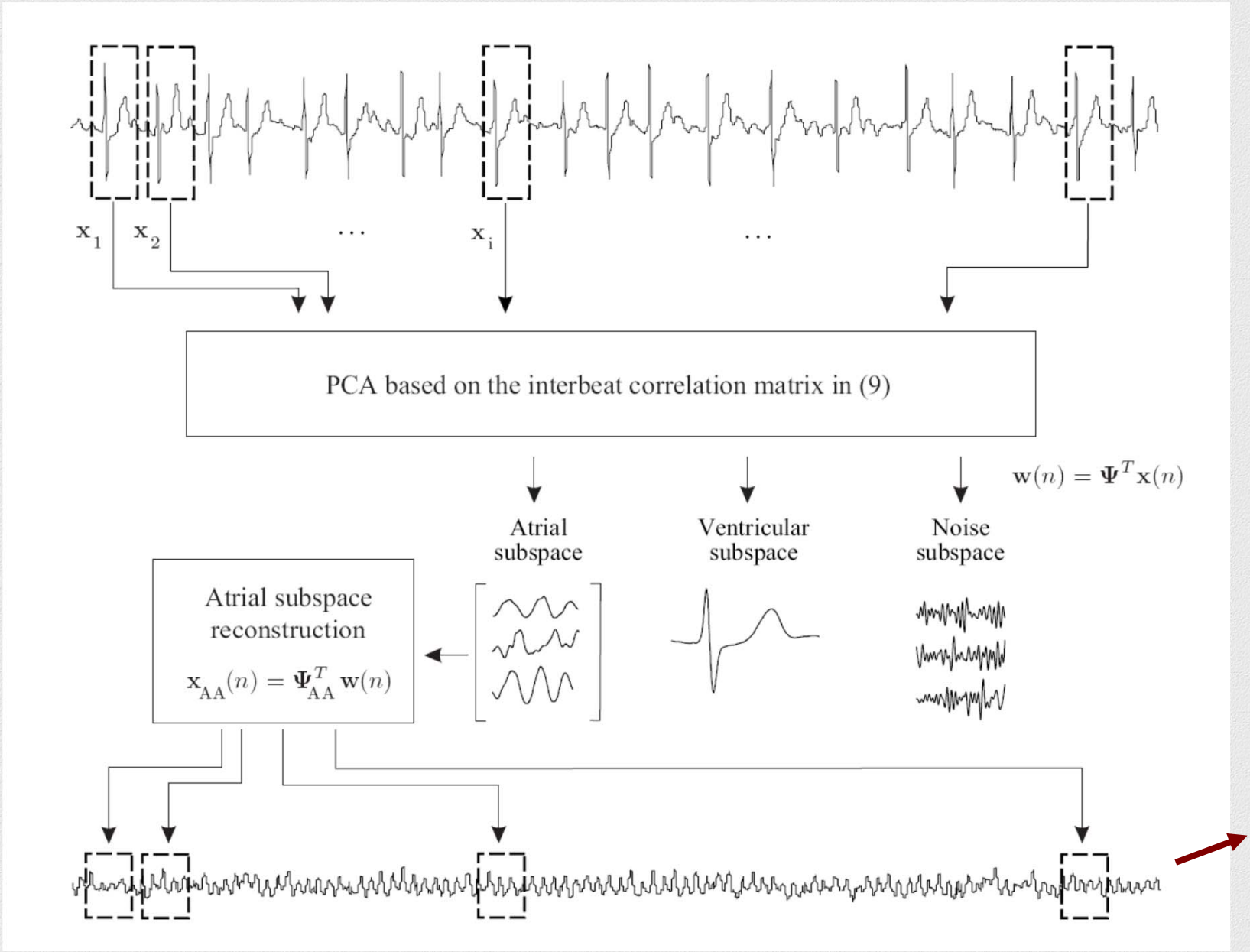
Filtered ECG (Nonlinear phase)

Filtered ECG (linear phase)



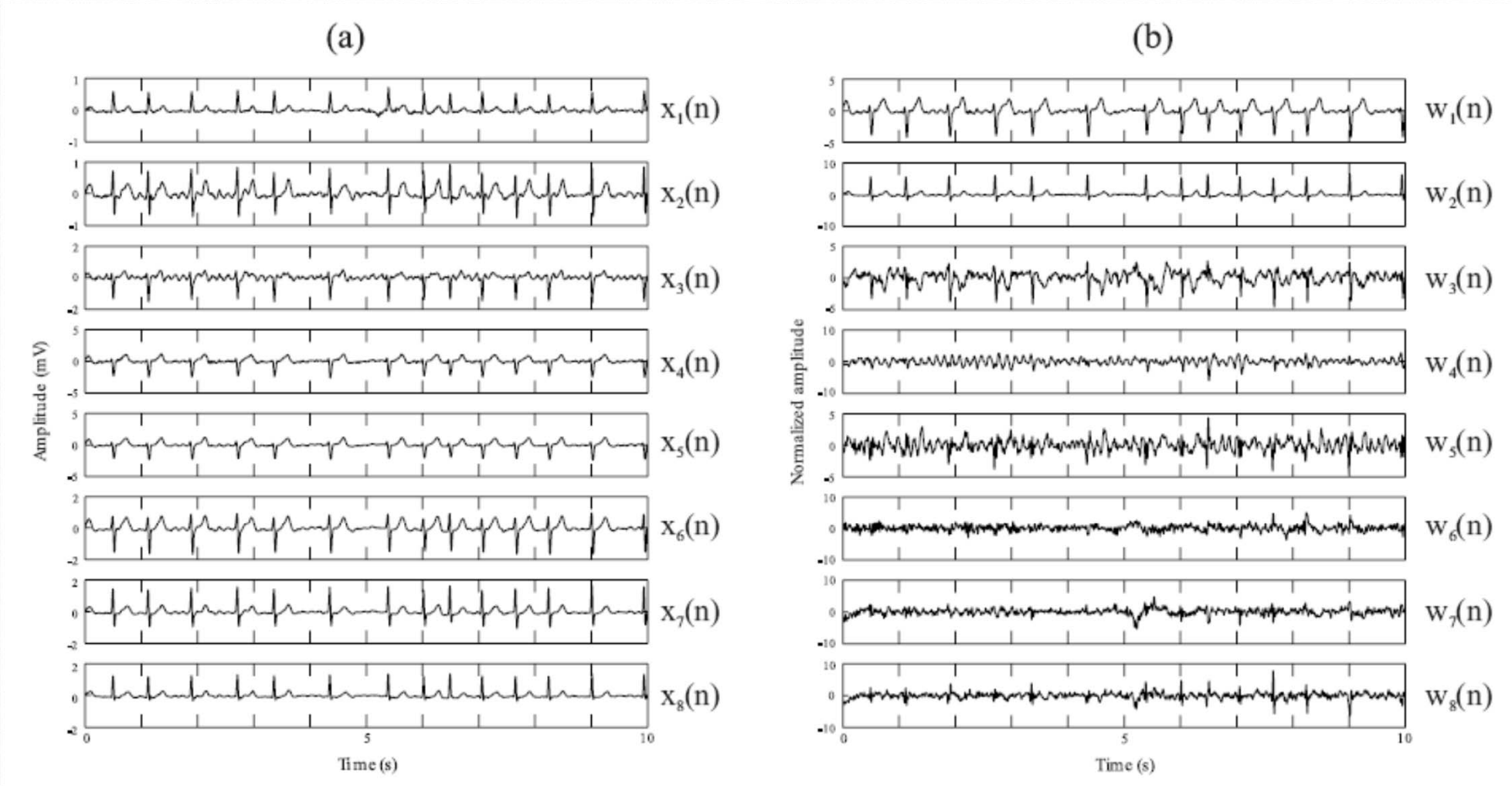


Atrial fibrillation



Spectral Estimation of the AA

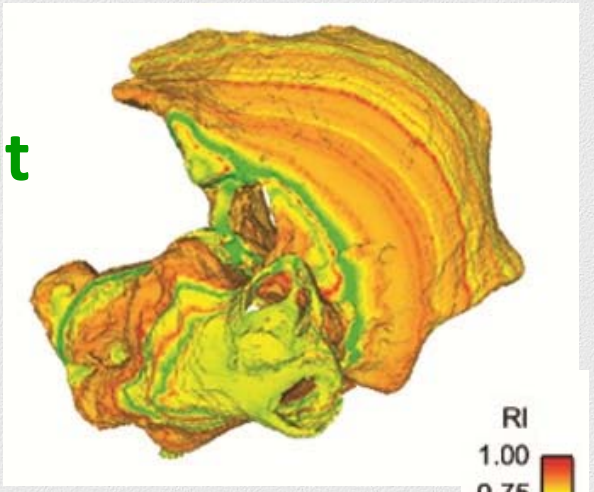
Atrial fibrillation: Multi-lead



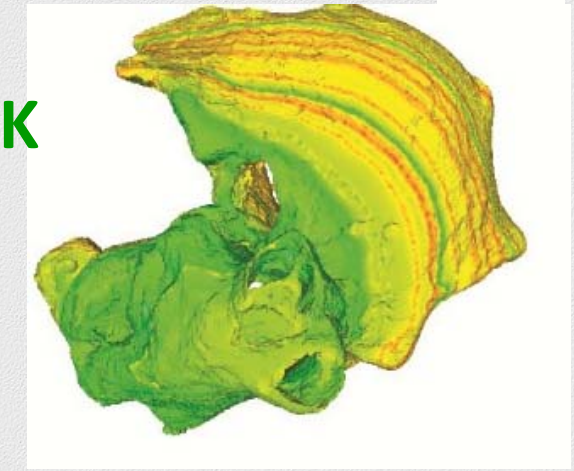
Ionic modulation of Atrial Fibrillation dynamics

Regularity

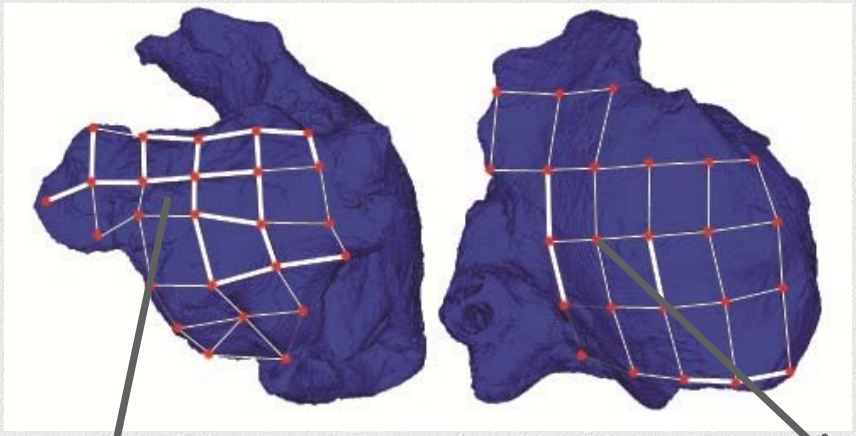
Default

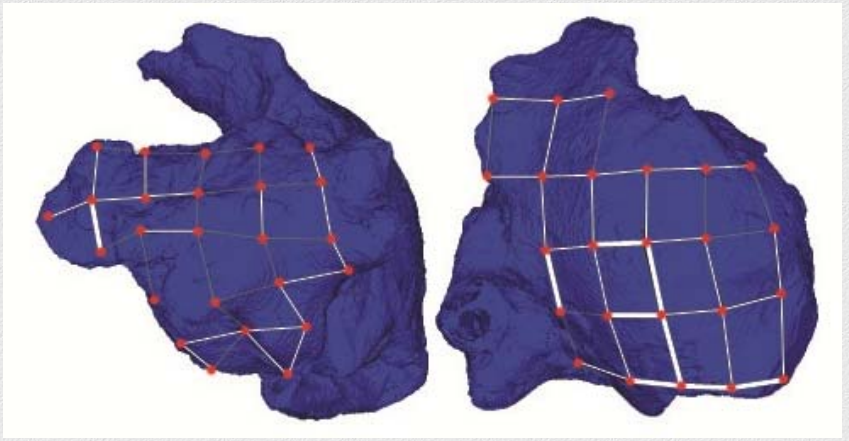


30% INaK block

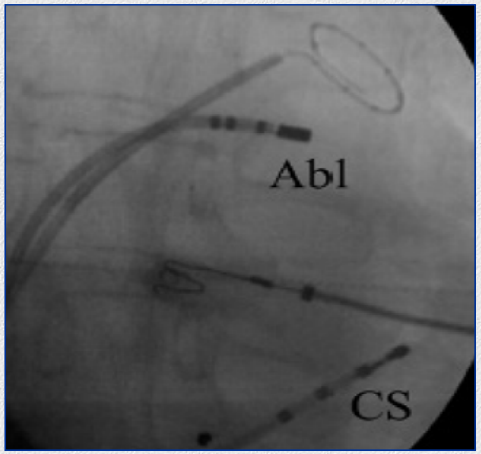


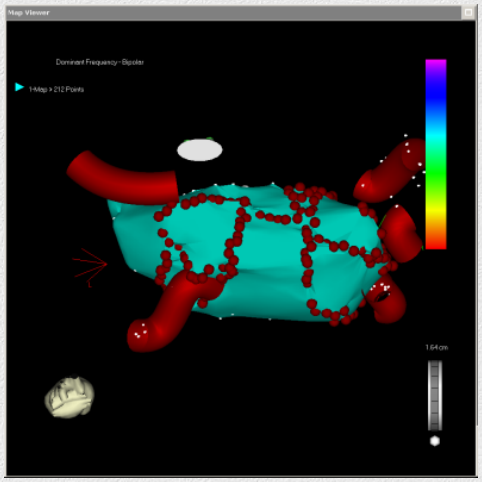
Coupling

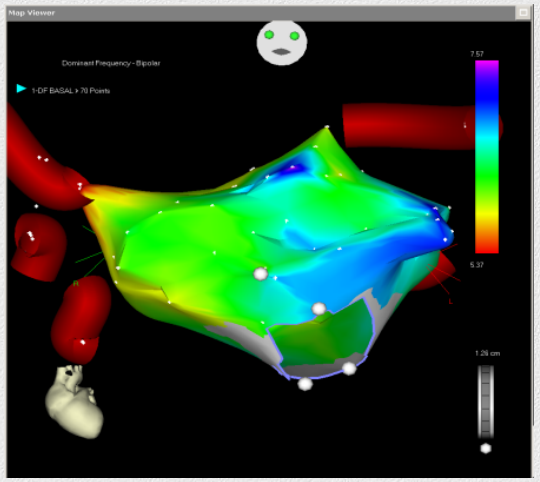




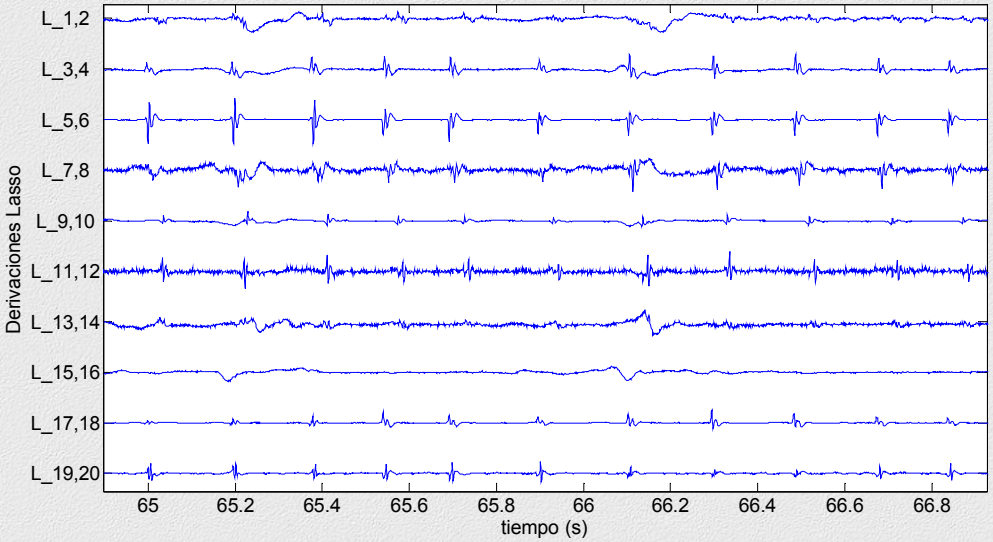
Atrial fibrillation: Where to Ablate? Guiding

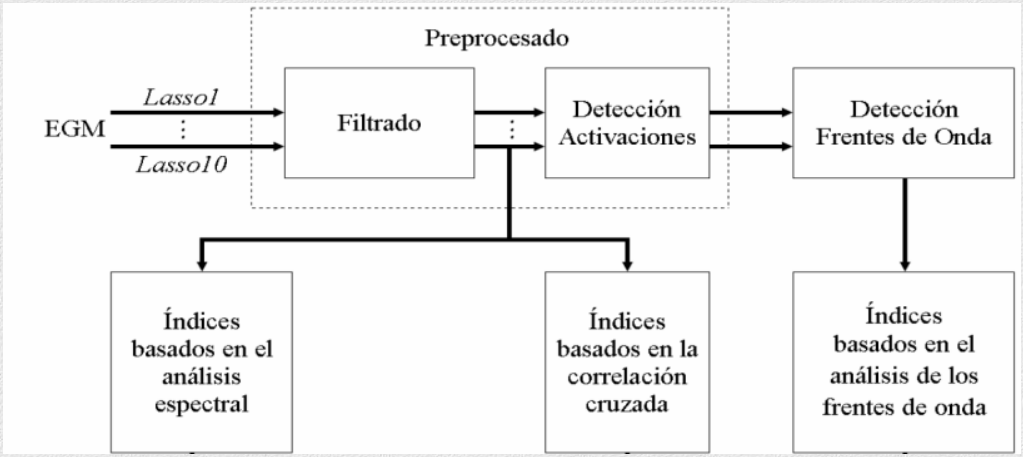




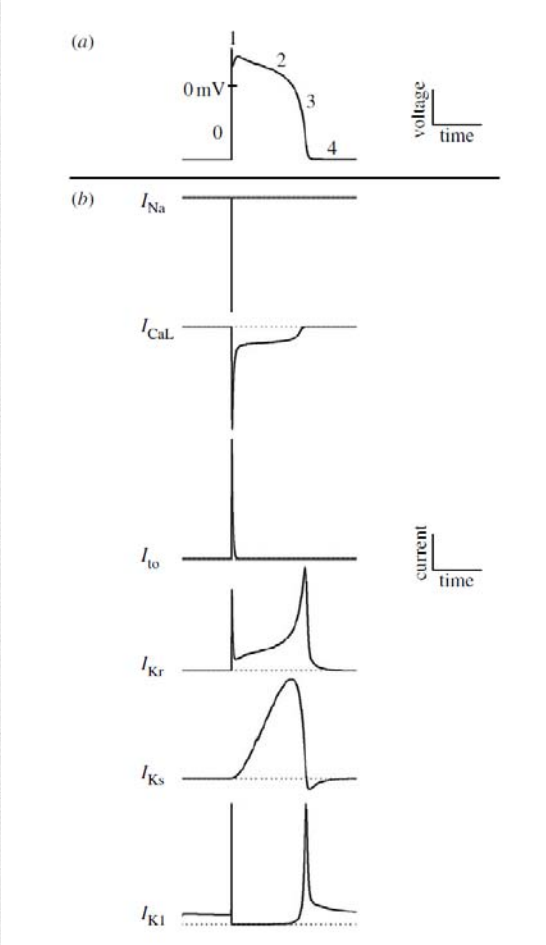


Organization, synchronization and Coherence in EGM





Ventricular arrhythmic risk indexes



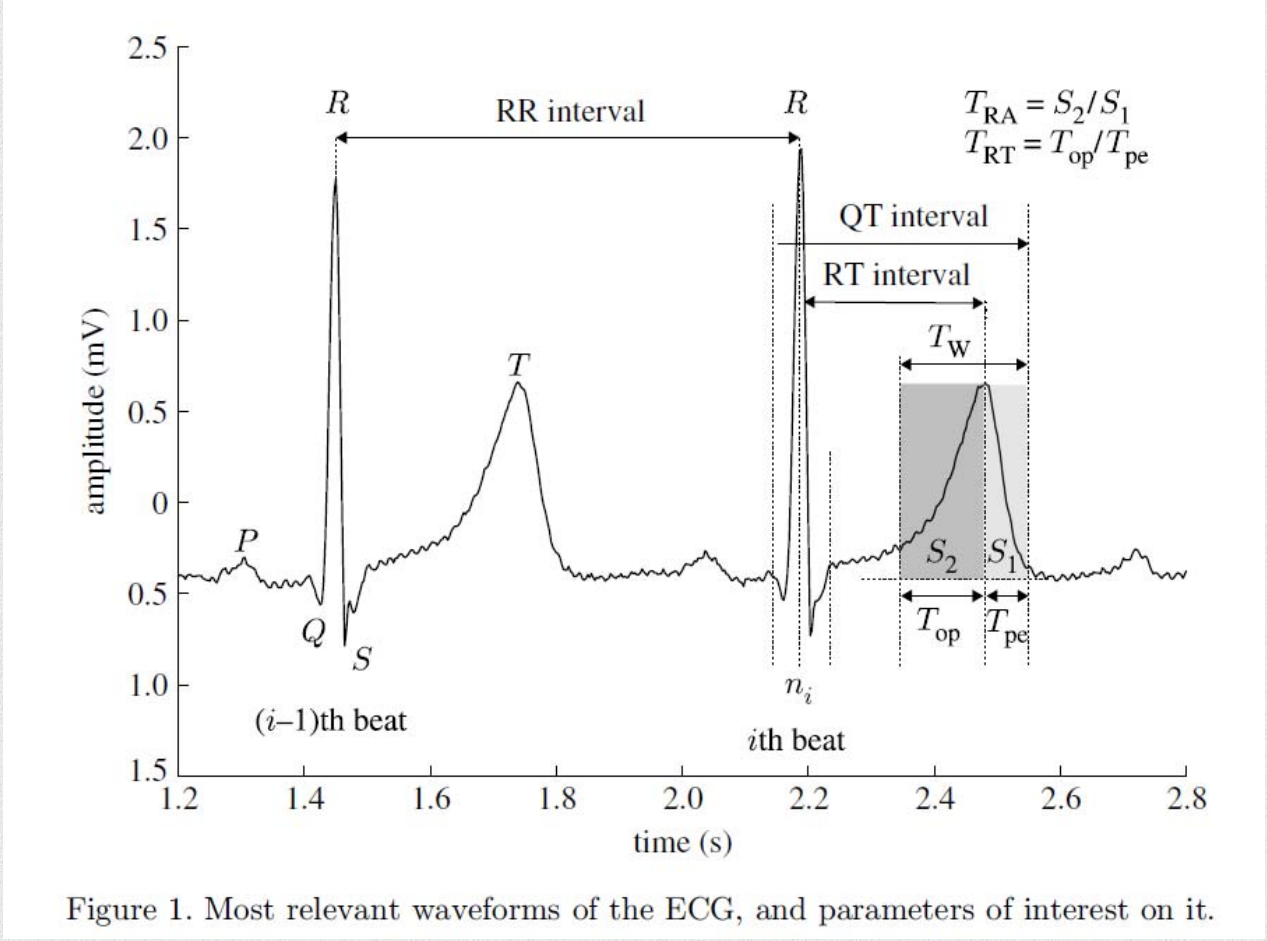
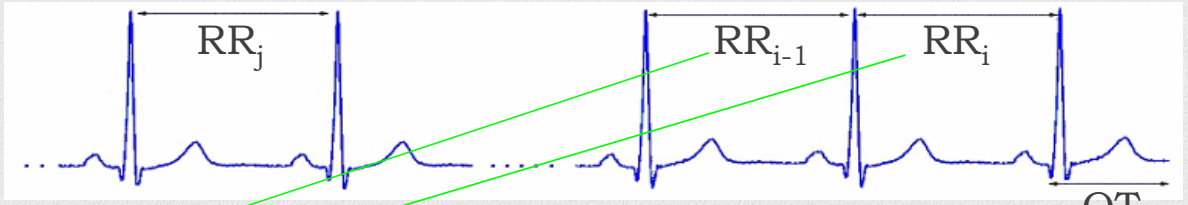
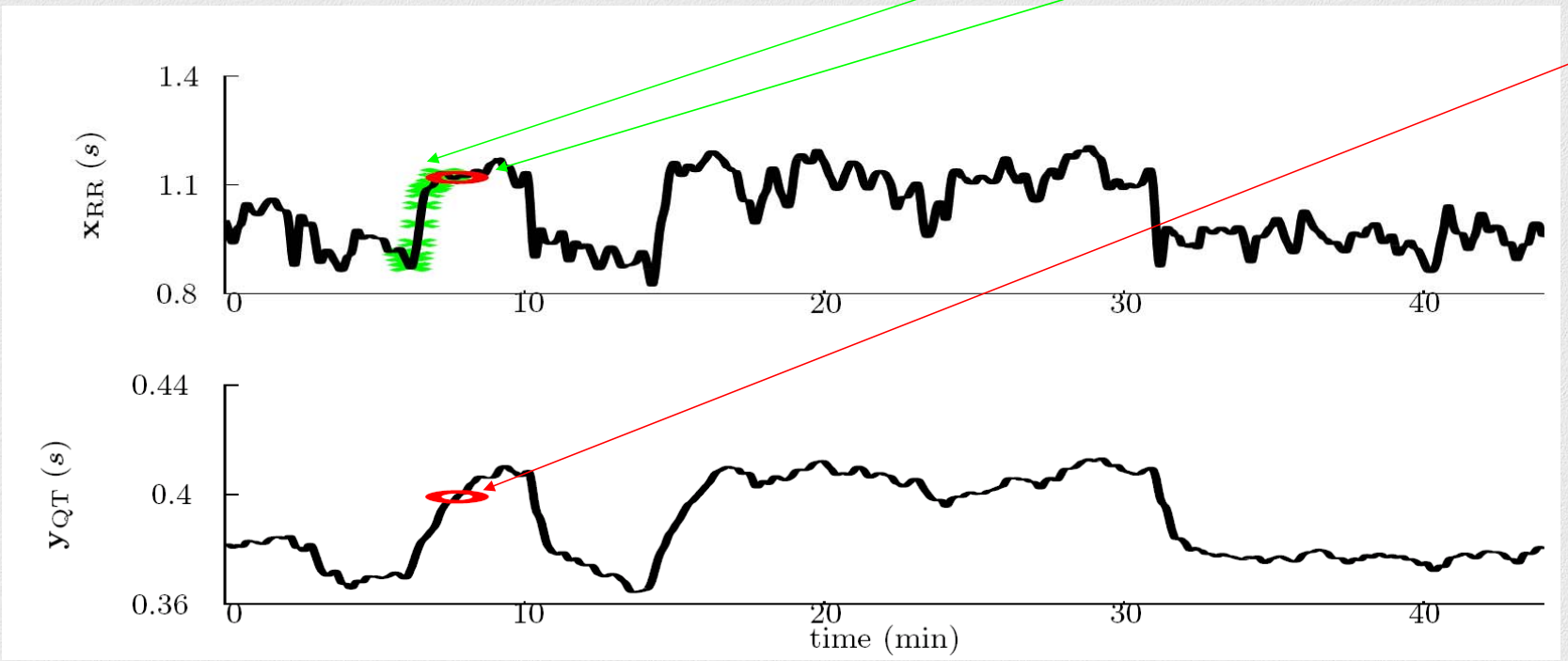


Figure 1. Most relevant waveforms of the ECG, and parameters of interest on it.

Time-invariant analysis of the QT / RR relationship

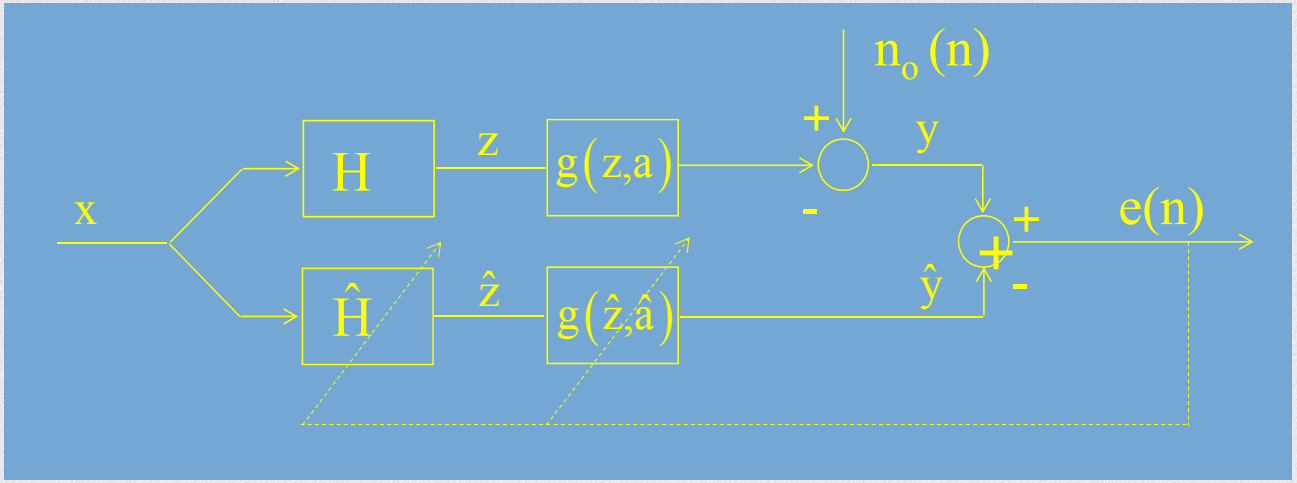
- QT lags behind RR changes:



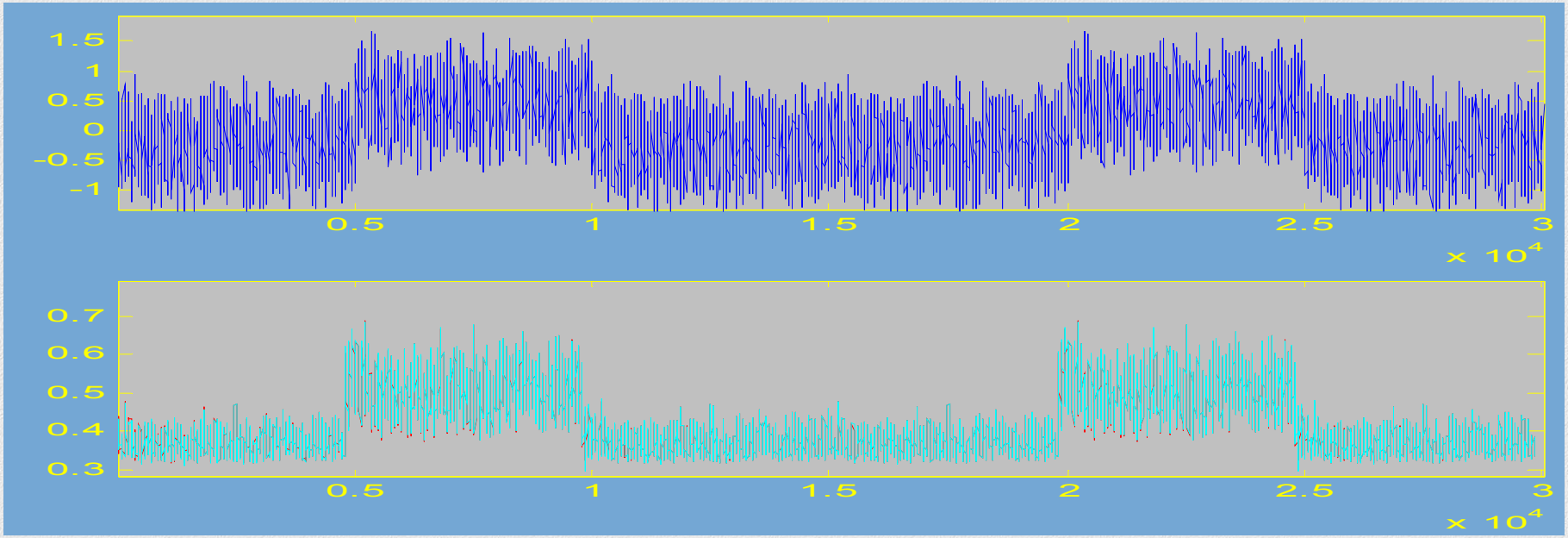


Hypothesis: QT is affected by a history of RR intervals that can be expressed as an RR weighted average ($\overline{RR}$)

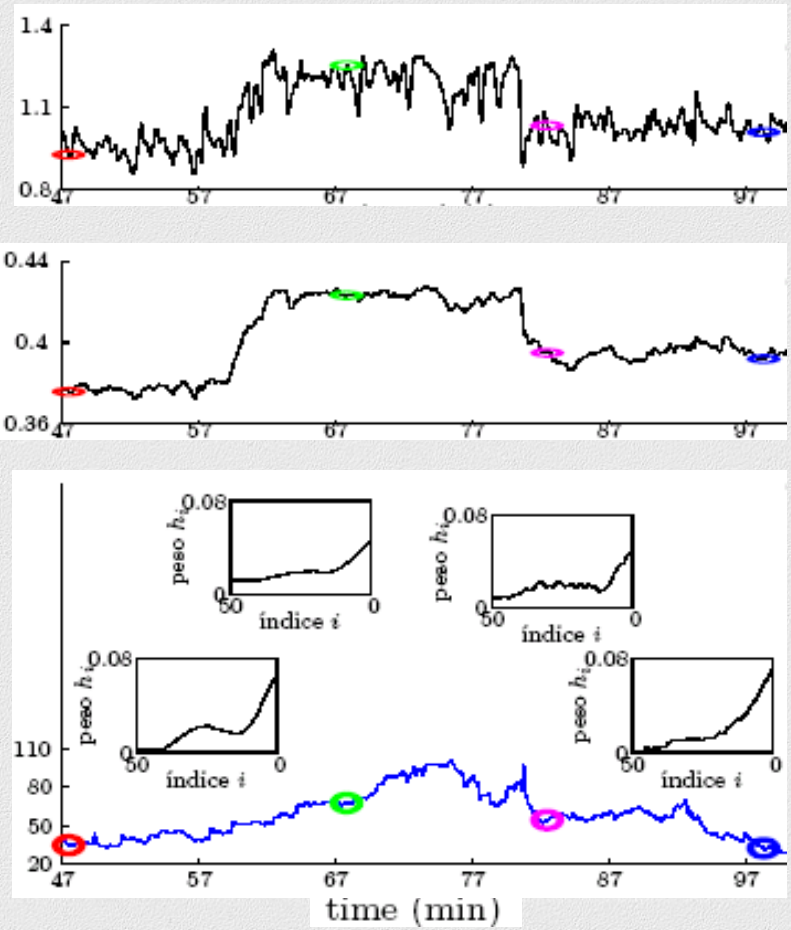
Time-invariant analysis of the QT / RR relationship

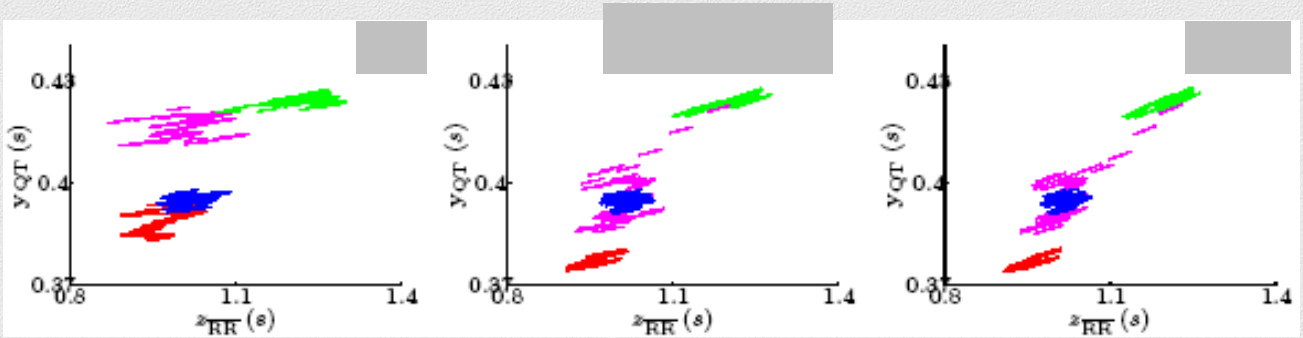


Repolarization Analysis and modelling



Beat-to-beat response of QT to abrupt changes

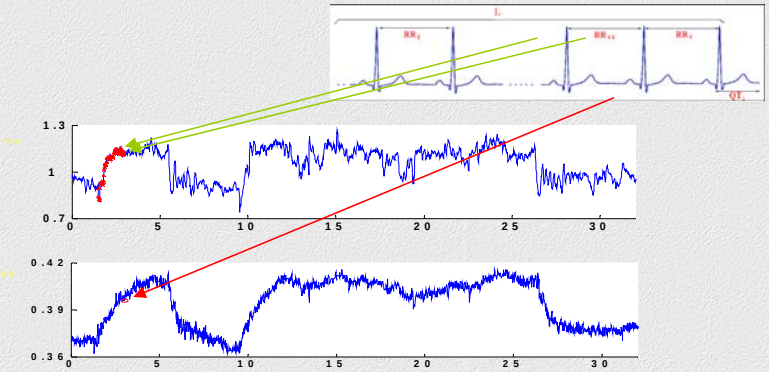




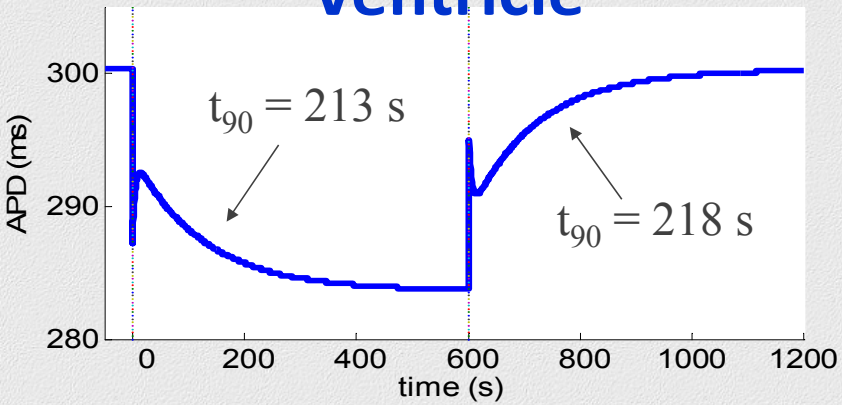
N = 1 N = 30 N = 50

Rate Adaptation of Repolarization

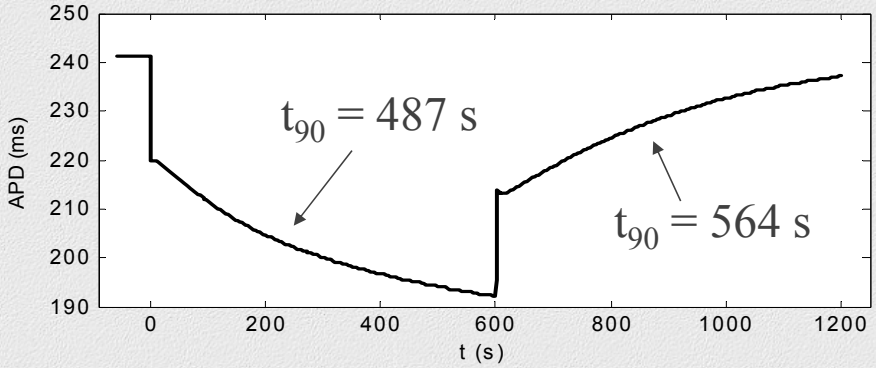
Repolarization response to heart rate changes



Ventricle



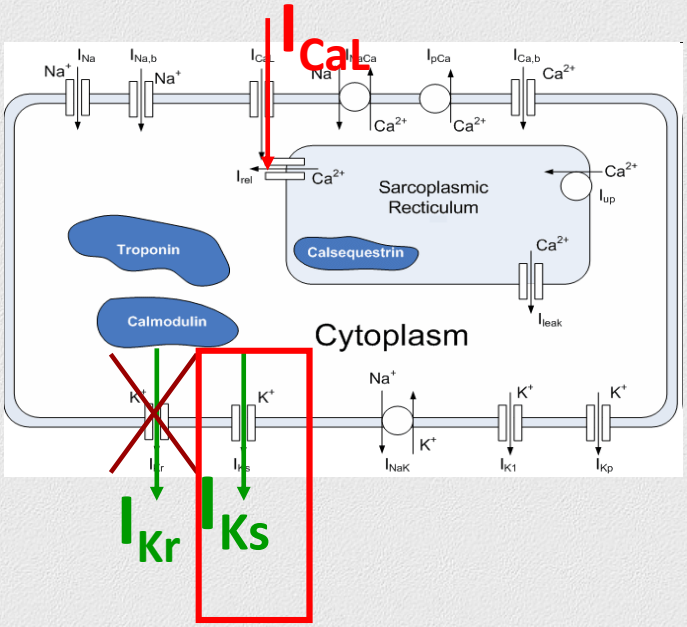
Atria



1. **Ionic mechanisms of APD rate adaptation:**
   - Fast phase: I_{CaL} and I_{Ks} dynamics in ventricle and maximal conductances of I_{CaL} and I_{NaCa} in atria
   - Slow phase: intracellular Na^+ dynamics in both cavities
2. **Abnormally slow APD rate adaptation → higher arrhythmic risk**

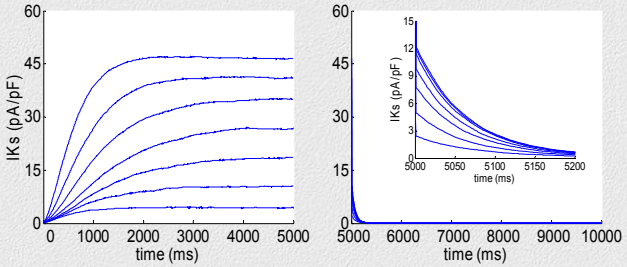
Repolarization variability and arrhythmic risk

Human ventricular model

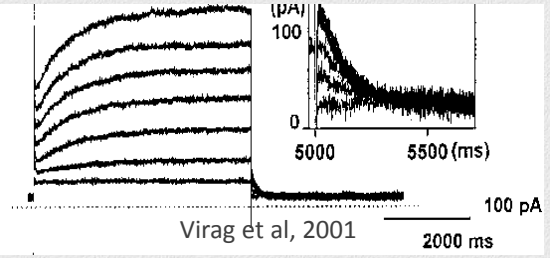


Stochastic IKs current

Simulation

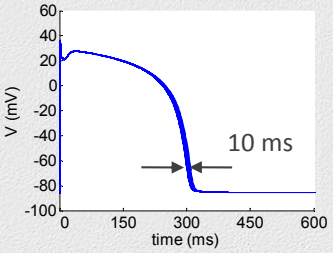


Experiment

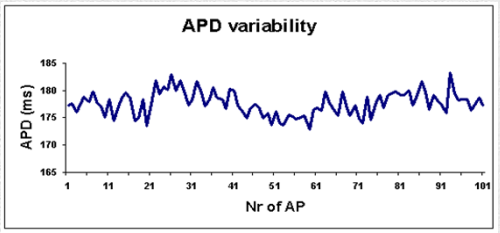


APD variability

Simulation



Experiment



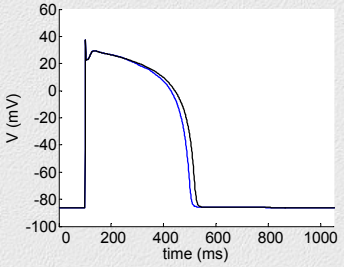
Stochastic differential equation

$$dx_s = \frac{x_{s,\infty} - x_s}{\tau_{xs}} dt + \sqrt{\gamma}\, dW_t$$

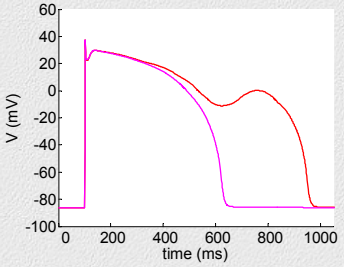
$$\gamma \prec \frac{1}{N_{Ks}}$$

Arrhythmic risk

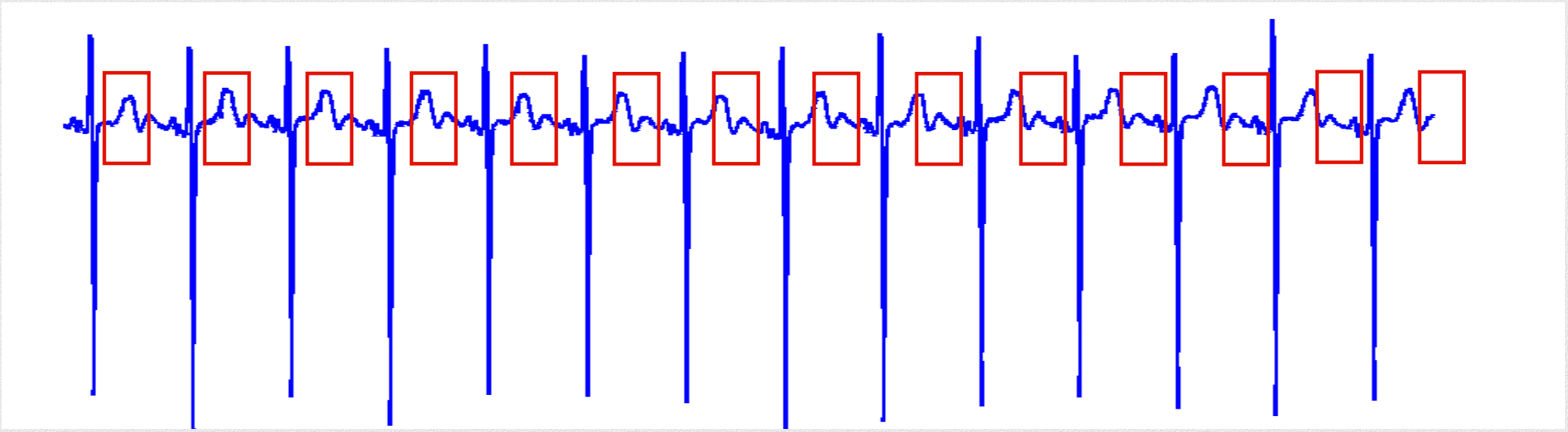
Control



LQT2

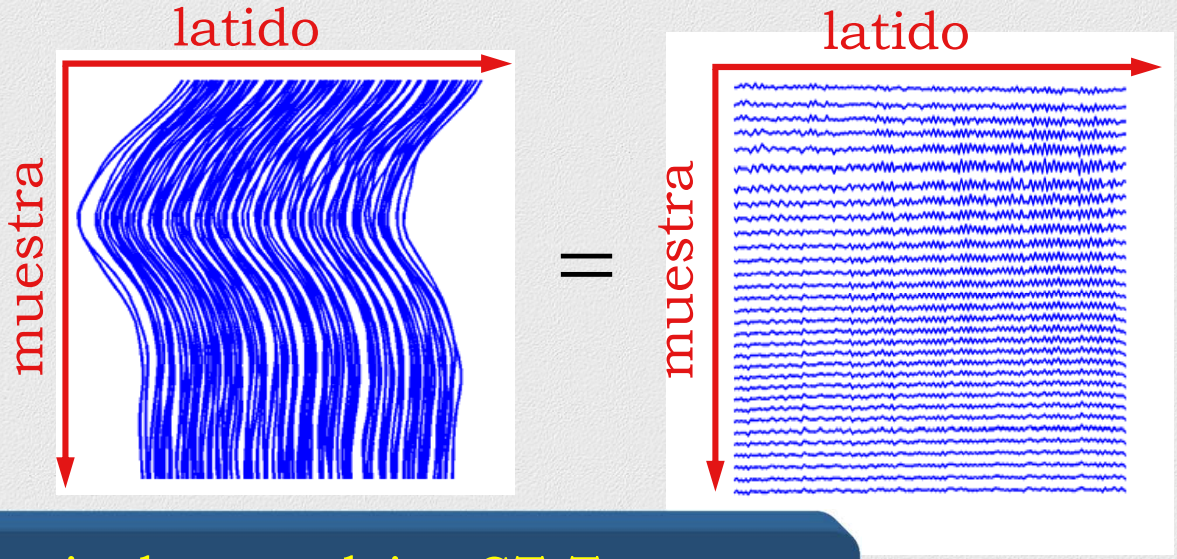


Repolarization alternans



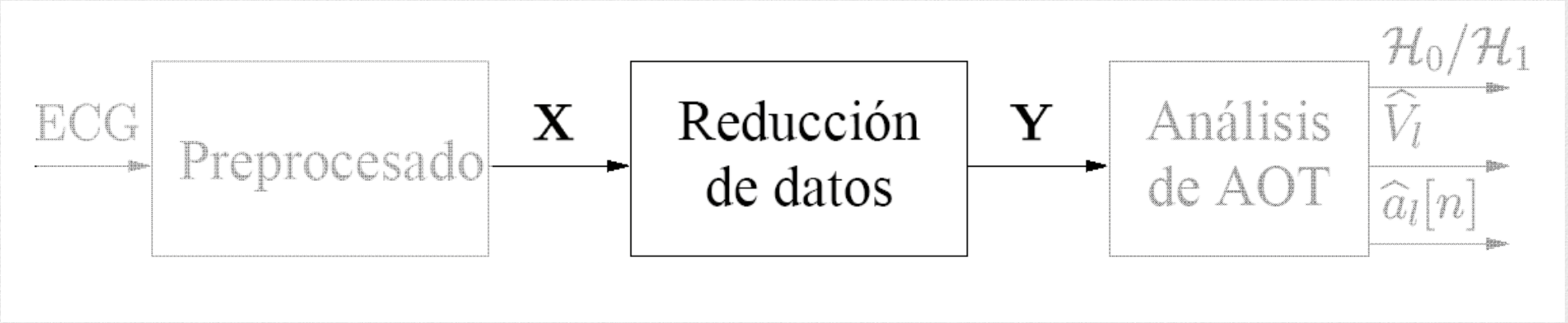
Detección de Alternancias

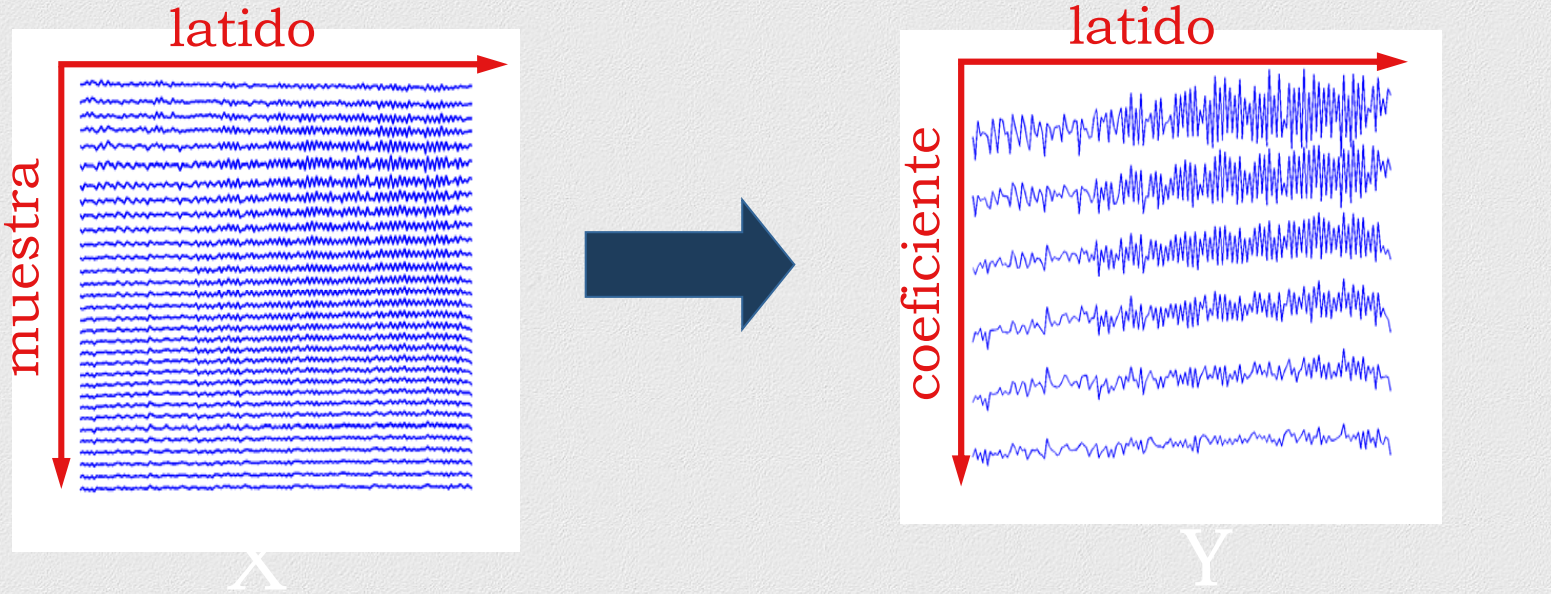
$$\mathbf{X} = [\mathbf{x}_0 \ldots \mathbf{x}_{M-1}] =$$



Matriz de complejos ST-T:
M latidos, con N muestras por complejo

Deteccion de alternancias

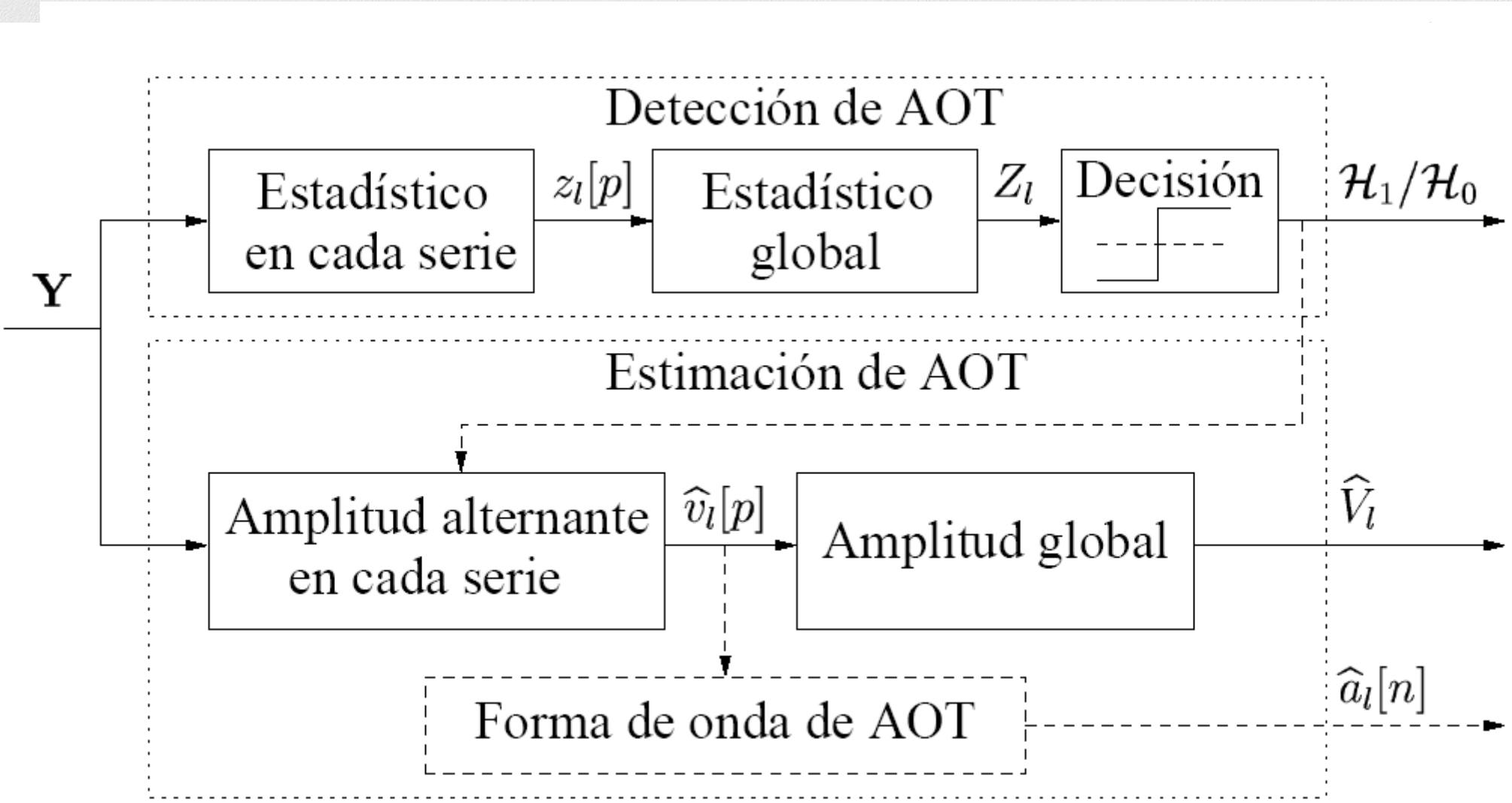




N series de muestras

P series de coeficientes

Detección de alternnacias



Detección de alternnacias

$$x(i) = A + a(-1)^i + v(i), \quad i = 1, \ldots, M$$

Repo a una muestra dada para latido i

$$y(i) = x(i) - \bar{x}$$

Detector Gausiano

$$T_G = \left(\sum_{i=1}^{M} y(i)(-1)^i \right)^2$$

Detector Laplaciano

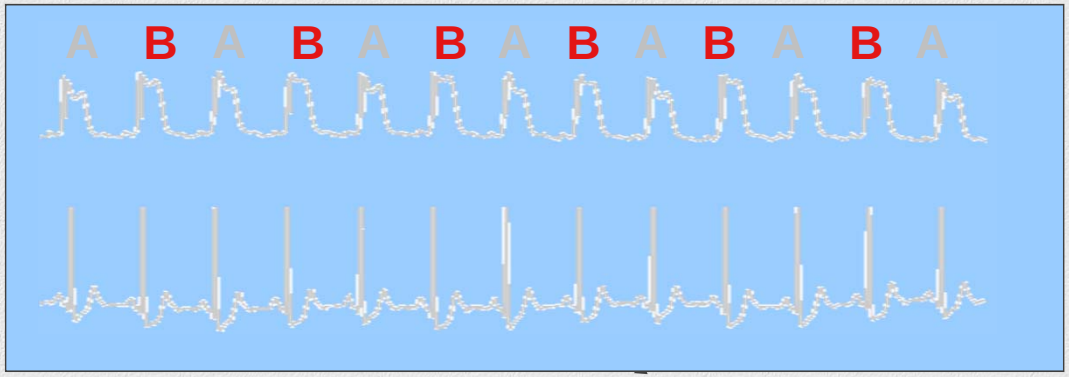
$$T_L = \sum_{i=1}^{M} (|y(i)(-1)^i| - |y(i)(-1)^i - \hat{a}|)$$

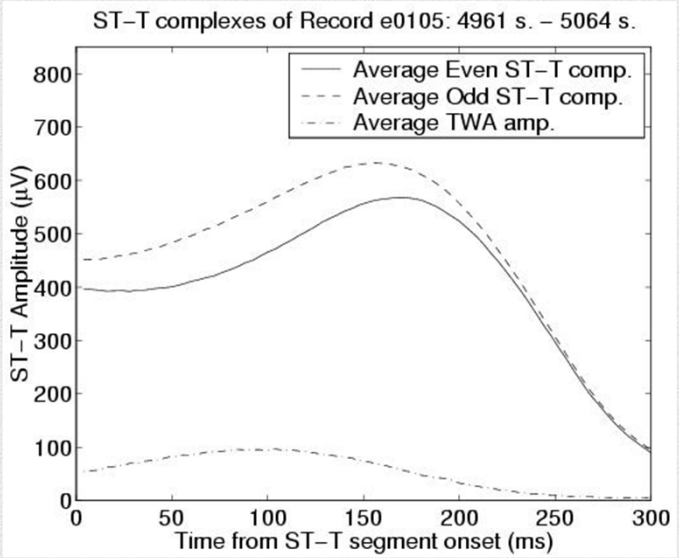
Estimación de la alternancia

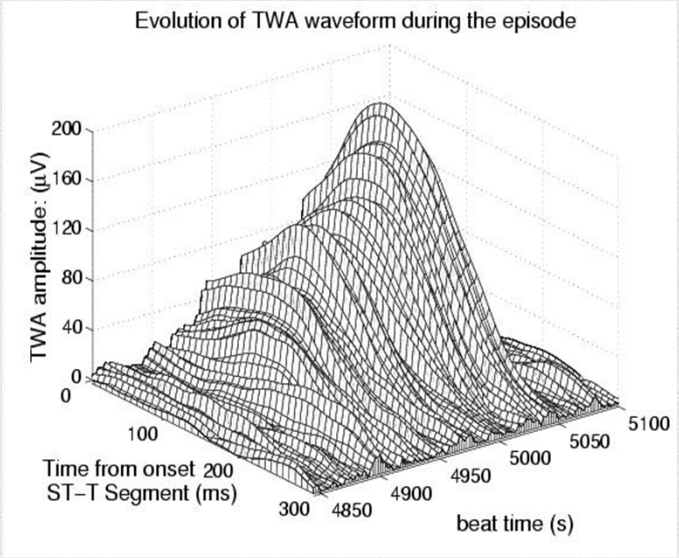
$$\hat{a} = \text{median}(y(1) \cdot (-1), y(2) \cdot 1, \ldots, y(M) \cdot (-1)^M)$$

Tratamiento de señales biomédicas

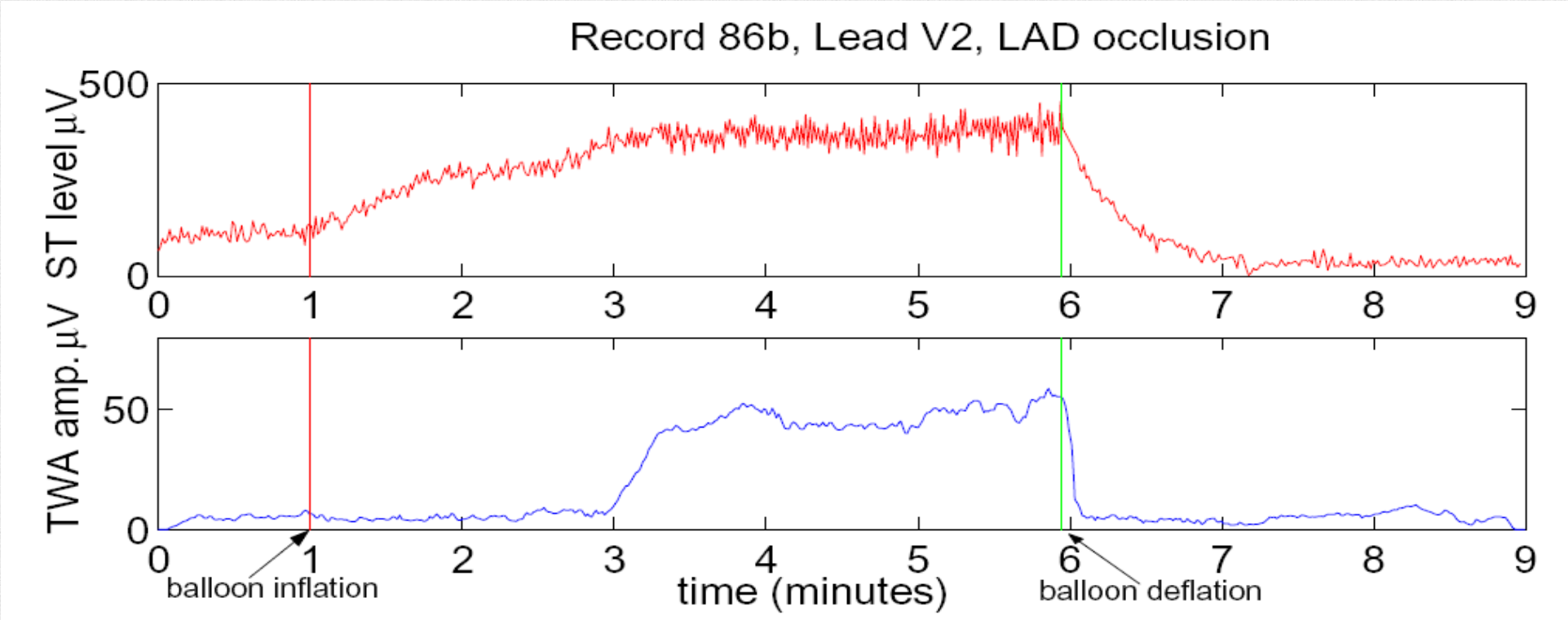
Indices de riesgo cardiaco: Alternancias







Alternancias de onda T en isquemia



Does a multilead approach improve the clinical utility of TWA?

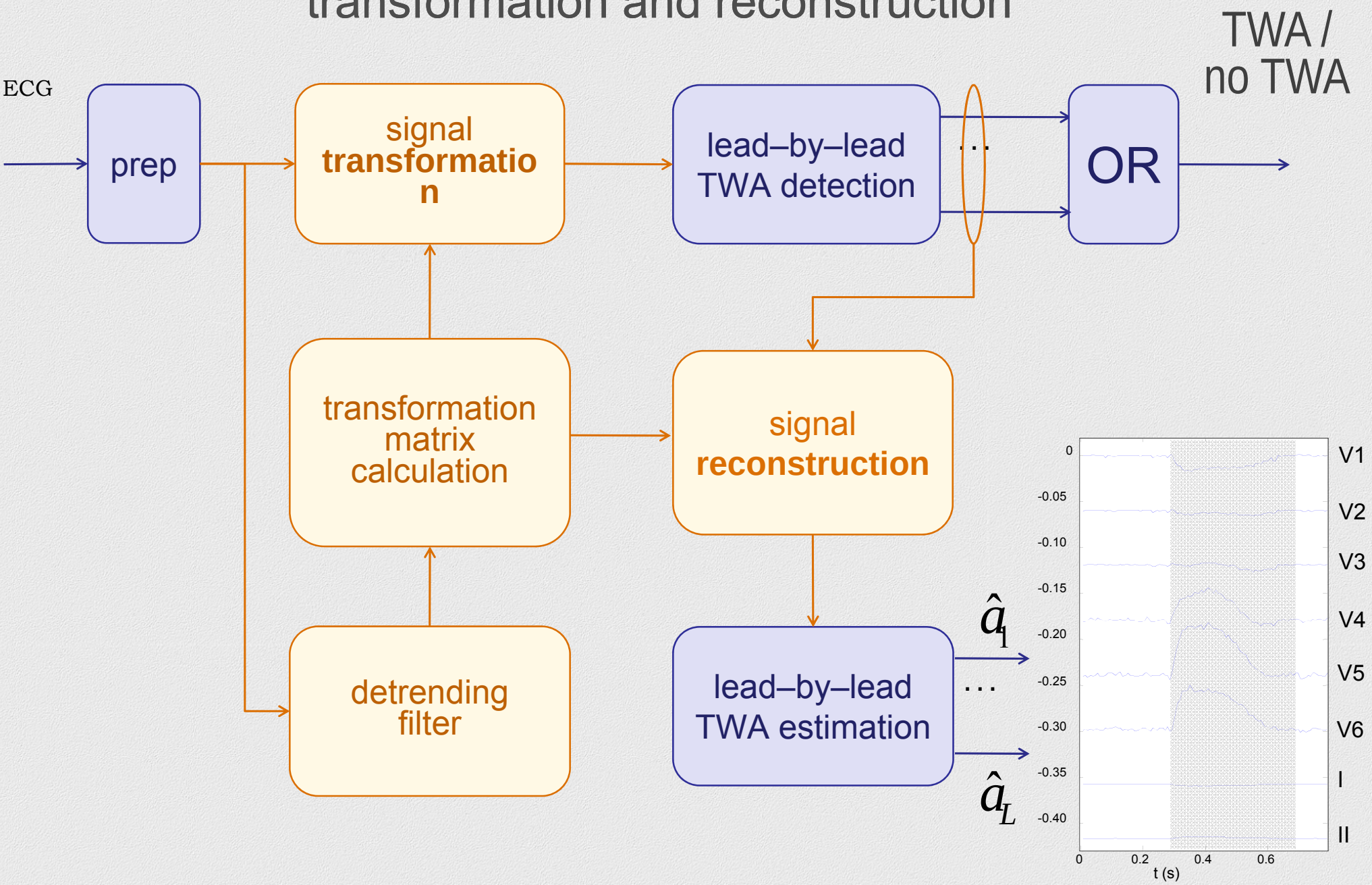
presence / absence of TWA

TWA amplitude at each instant

distribution of TWA among leads

. . .

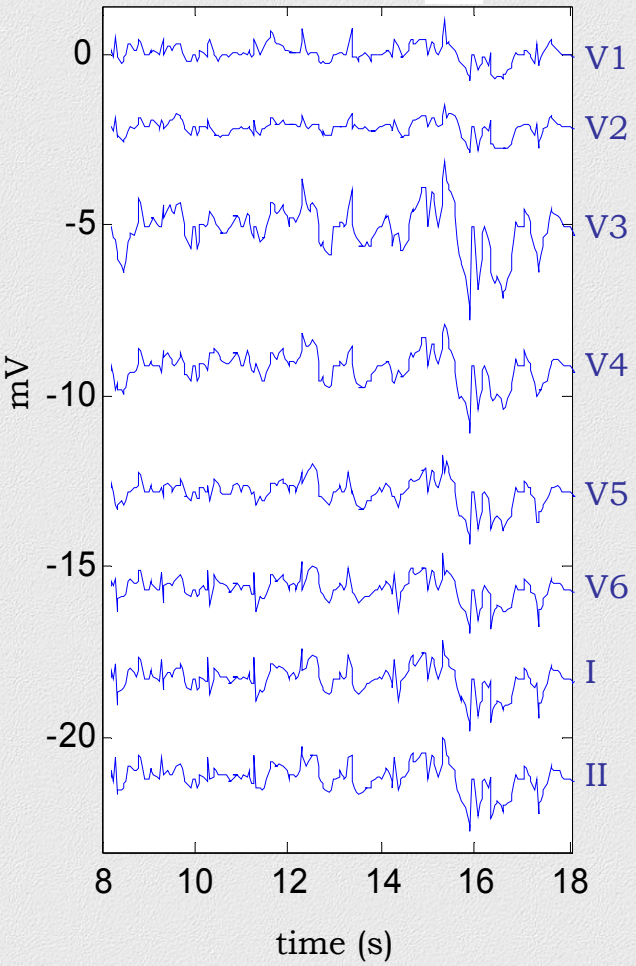
The multilead scheme includes additional stages: transformation and reconstruction



Evaluation of the PCA-based scheme

PCA converts the input signal into a set of uncorrelated components sorted in descending order of variance

Input signal $\mathbf{X}$



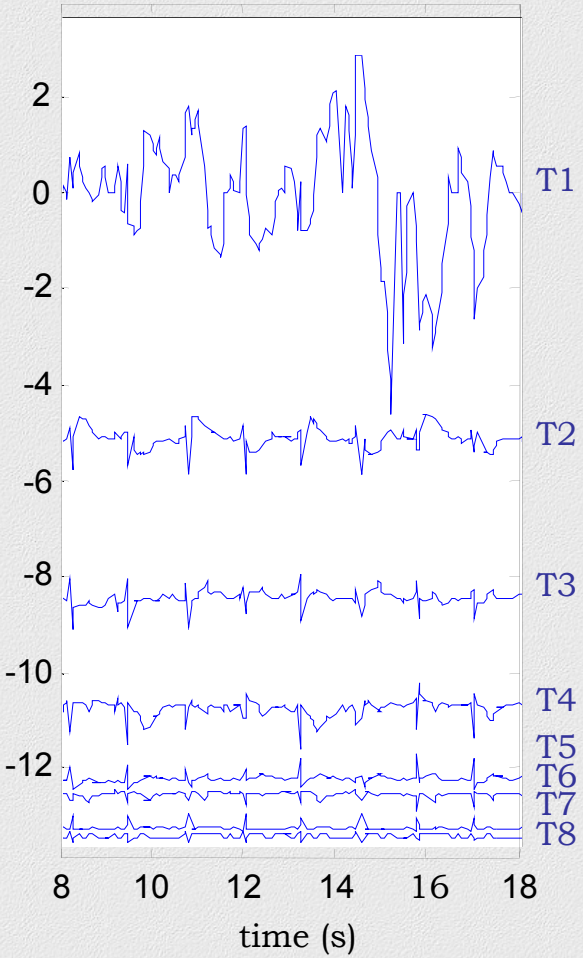
1 - detrending filter $\mathbf{X}'$

2 - $\hat{\mathbf{R}}_{X'} = \frac{1}{(K-1)N}\mathbf{X}'\mathbf{X}'^{T}$

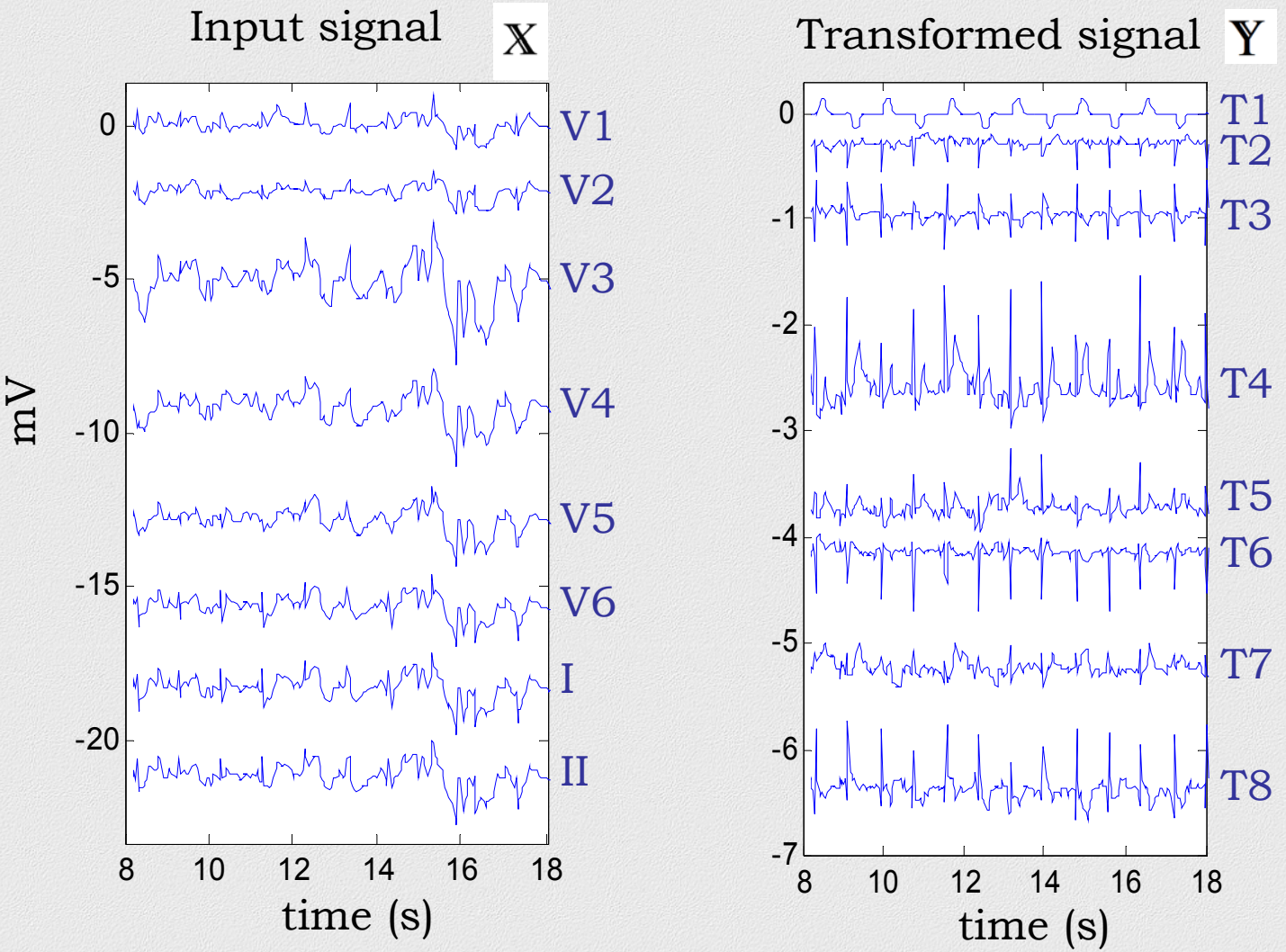
3 - $\hat{\mathbf{R}}_{X'}\boldsymbol{\Psi} = \boldsymbol{\Psi}\boldsymbol{\Lambda}$

4 - $\mathbf{Y} = \boldsymbol{\Psi}^{T}\mathbf{X}$

Transformed signal $\mathbf{Y}$

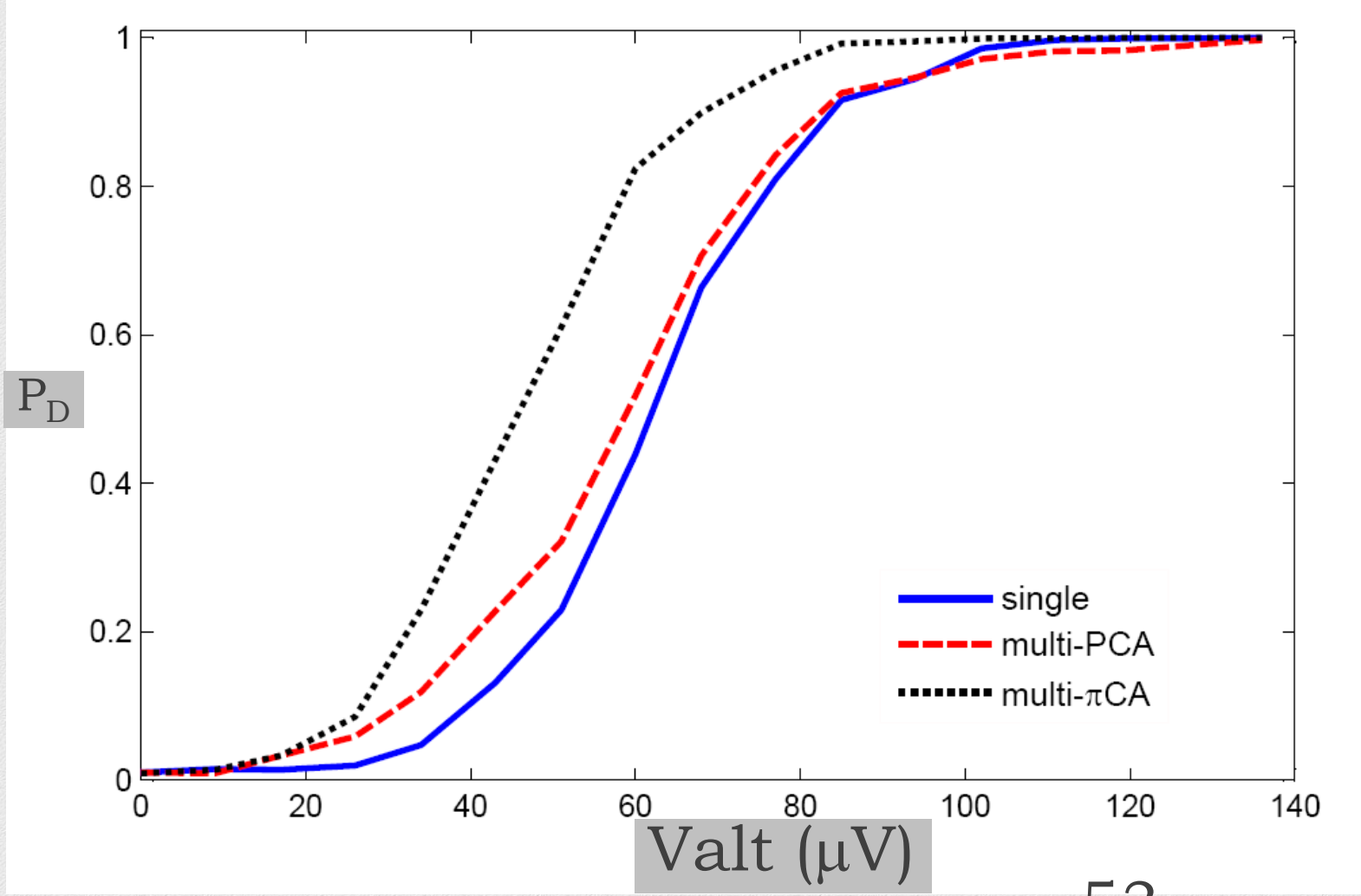


The component with 2-beat period is projected onto the first transformed lead



3.2. Results: detection performance

In synthetic signals, the multi-πCA scheme presents the best P_D for V_{alt} between 20 and 105 dB

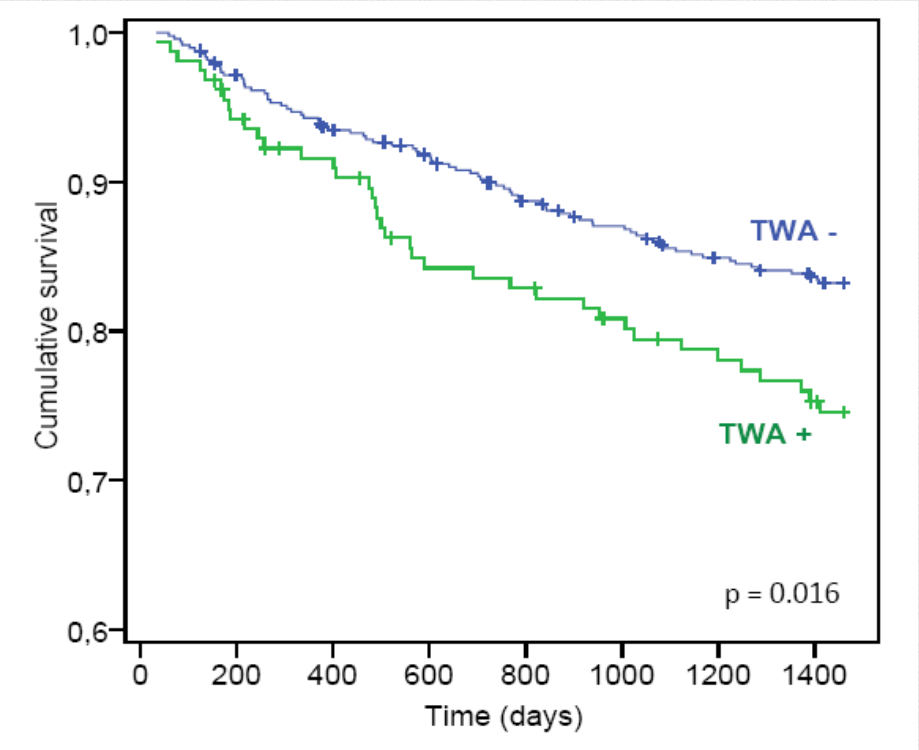


Results: association of TWA indices and mortality risk

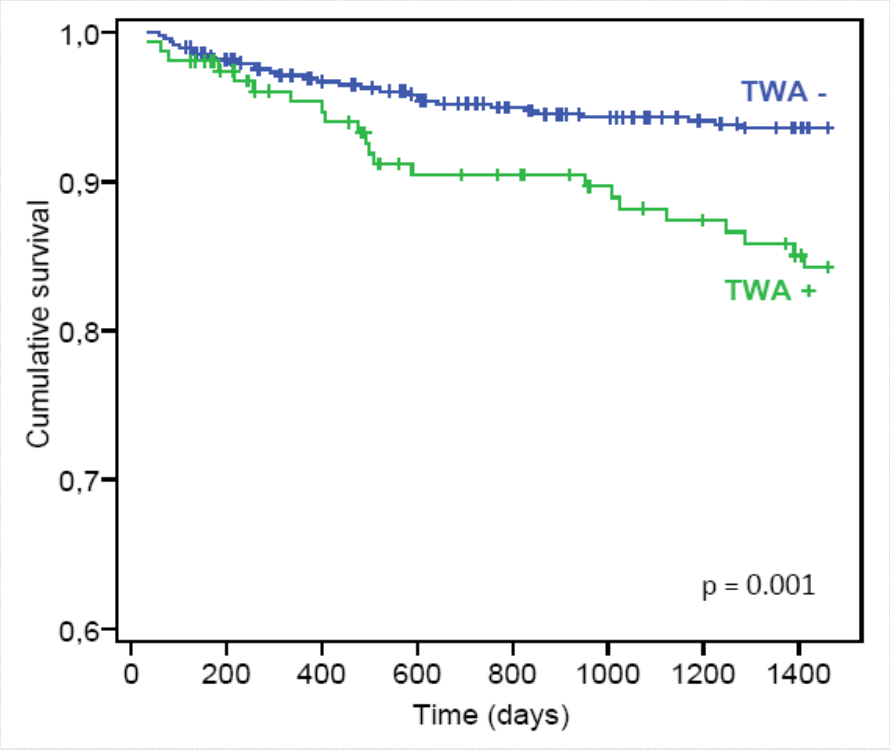
The rate of deaths was significantly higher in TWA+ group for all end points

	Total Population (n = 650)	TWA− (n = 493)	TWA+ (n = 157)	p
Total mortality	146 (22.5%)	99 (20.1%)	47 (30.0%)	**0.012**
CD	119 (18.3%)	81 (16.4%)	38 (24.2%)	**0.033**
SCD	52 (8.0%)	30 (6.1%)	22 (14.0%)	**0.003**

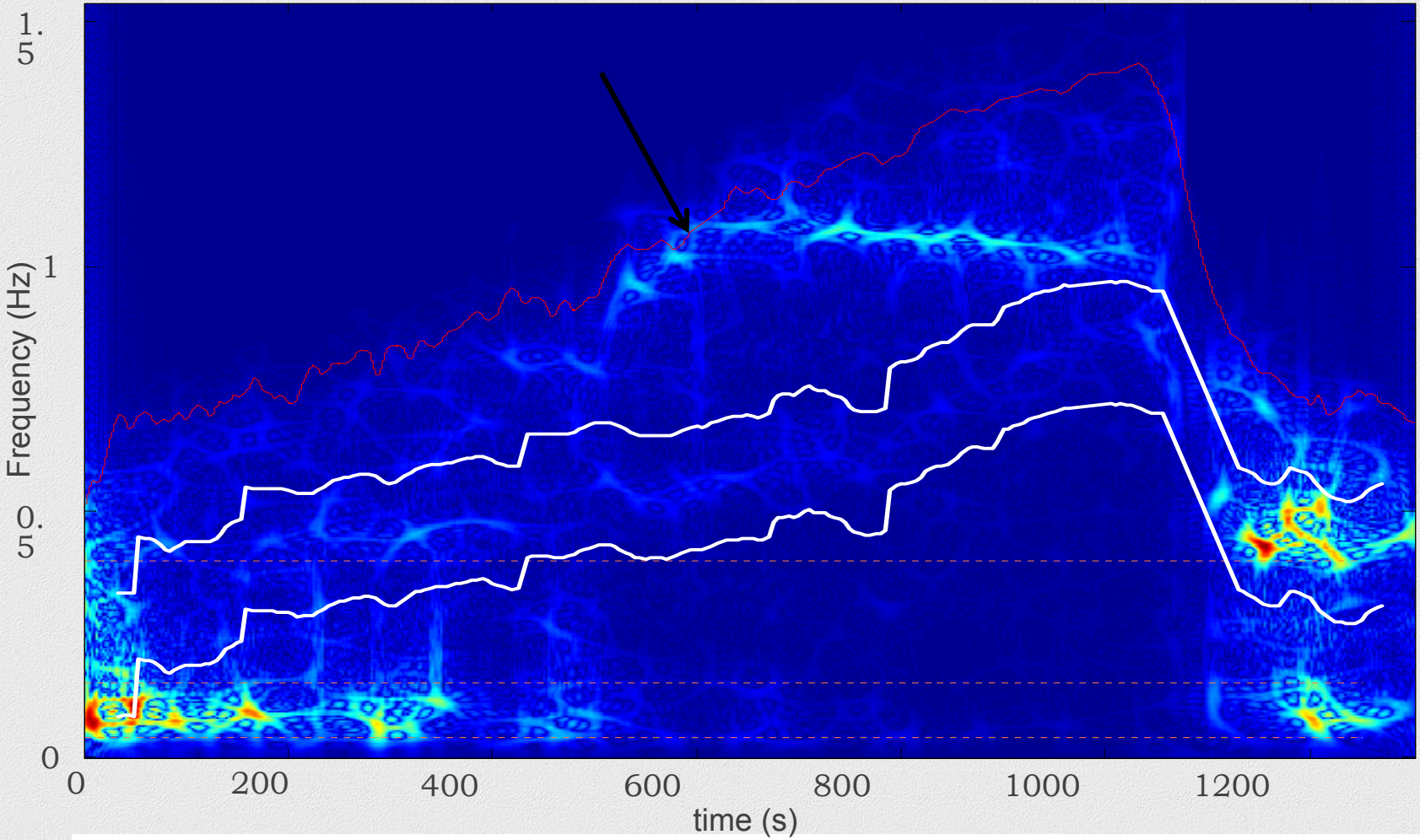
CD

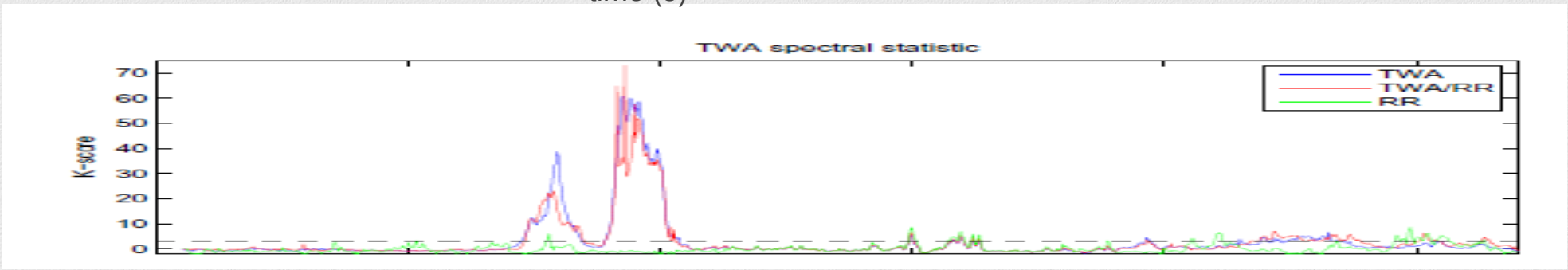


SCD



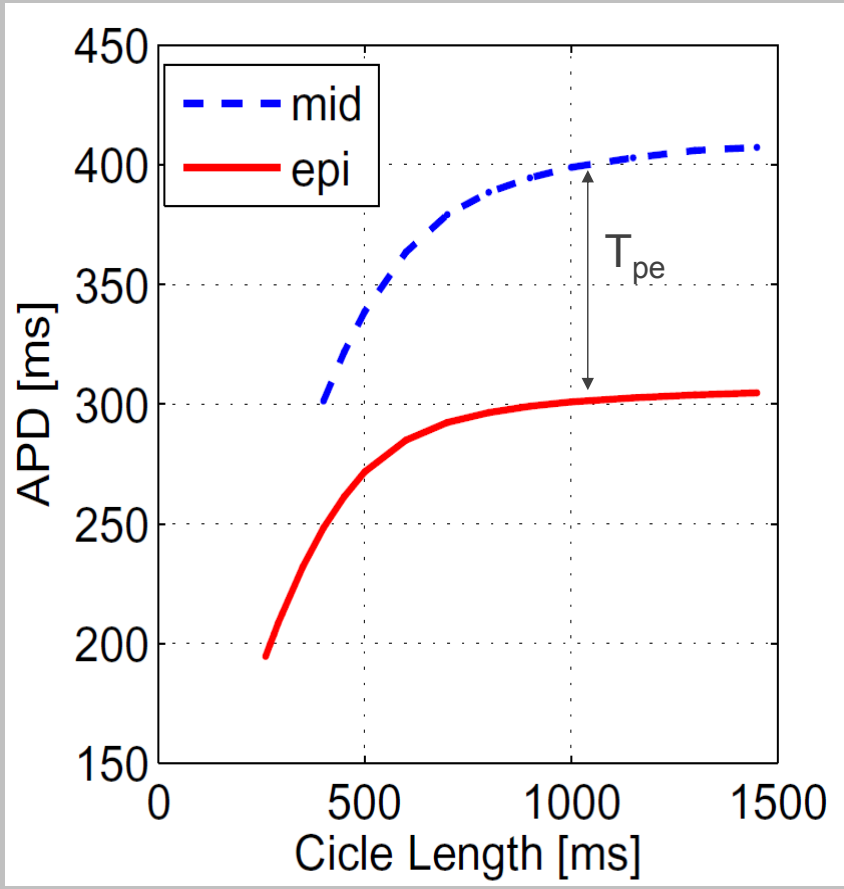
Artefacted alternans from pedaling or stride cadence

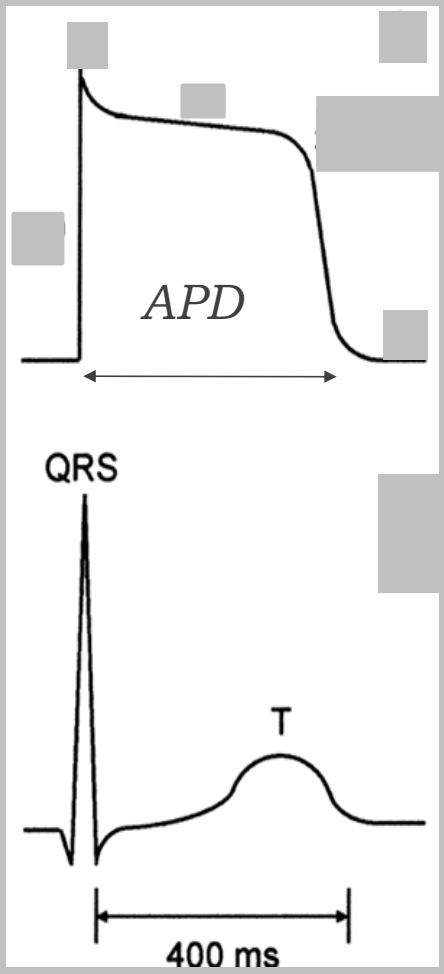




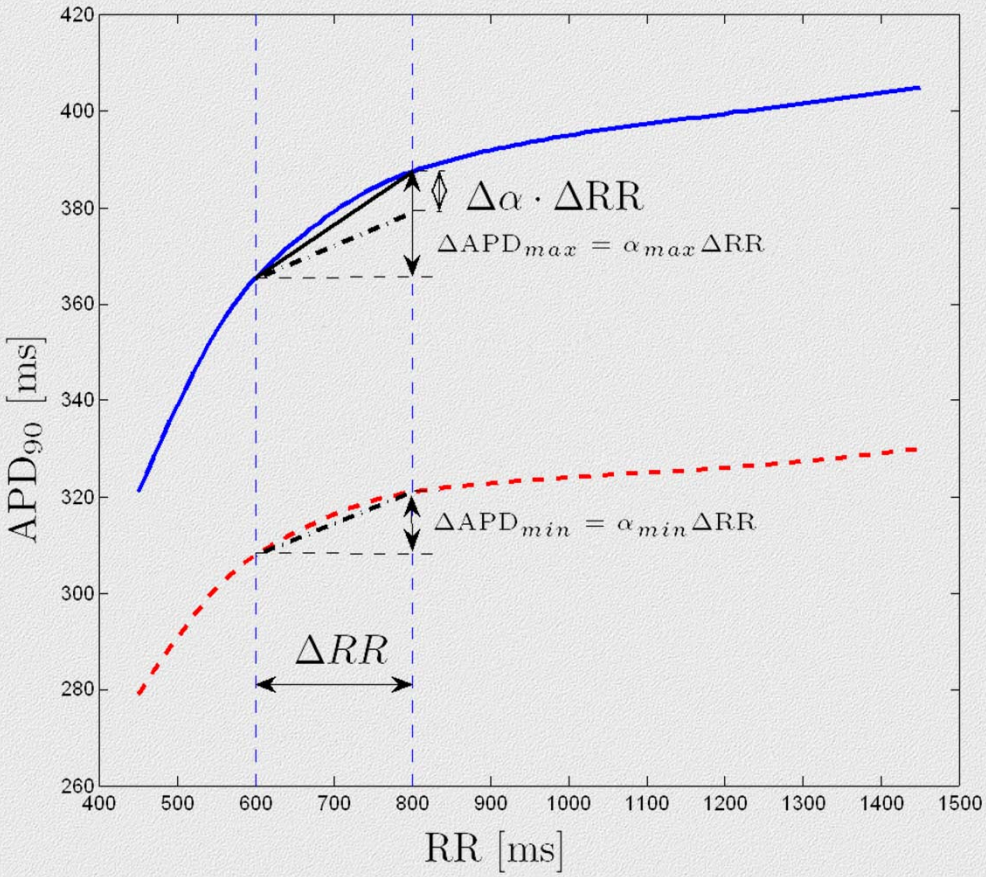
Dispersion of APD restitution from ECG

- **APD restitution curves→** *APD vs RR (steady-state conditions)*
- **APD restitution dispersion →** *Arrhythmogenic substrate*





Dispersion of APD restitution from ECG



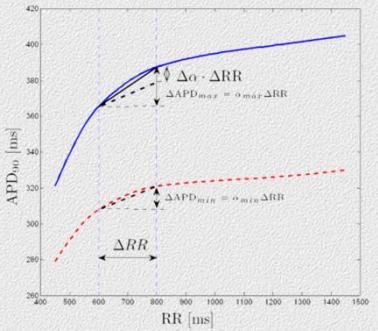
$\Delta\alpha = \alpha_{max} - \alpha_{min}$

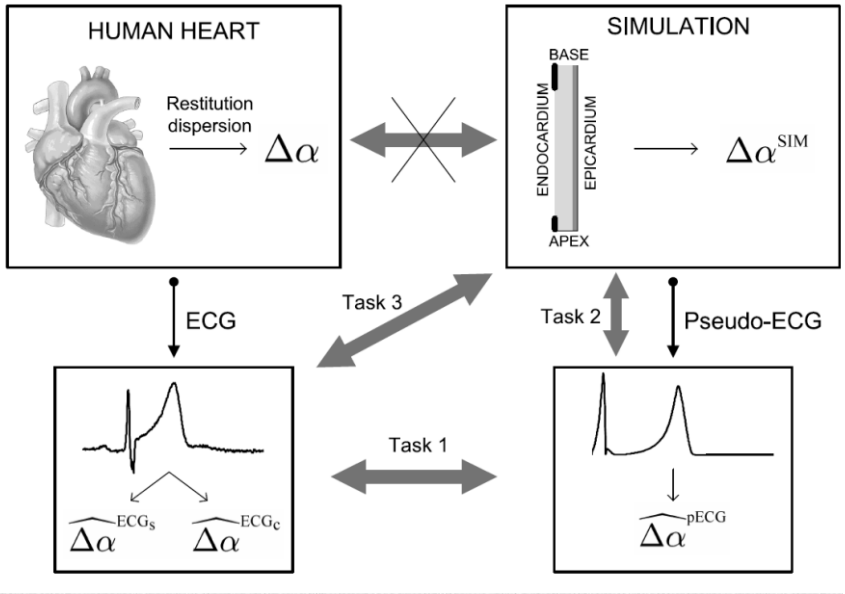
QUANTIFICATION FROM SURFACE ECG

$$\Delta\alpha = \frac{\partial T_{pe}^{dyn}}{\partial RR}$$

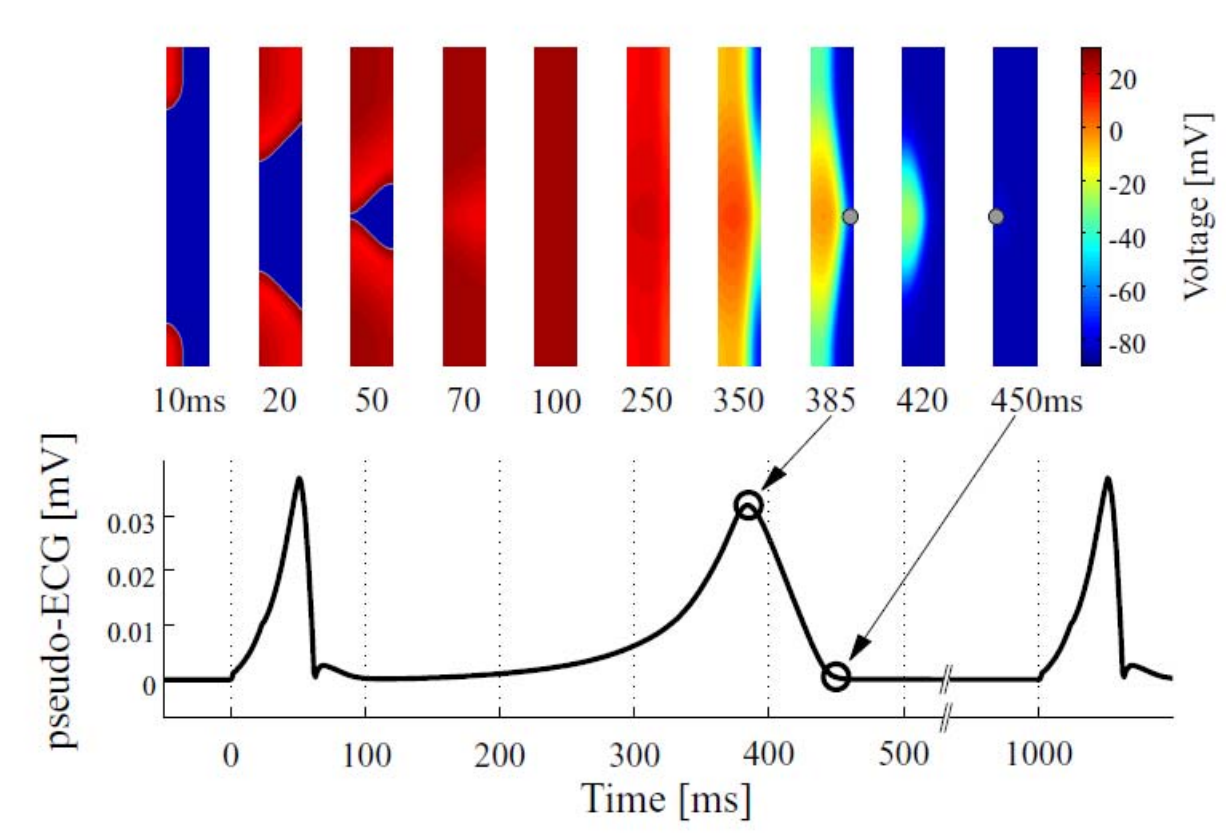
Increased restitution dispersion associated to ventricular tachyarrhythmia

Dispersion of APD restitution from ECG

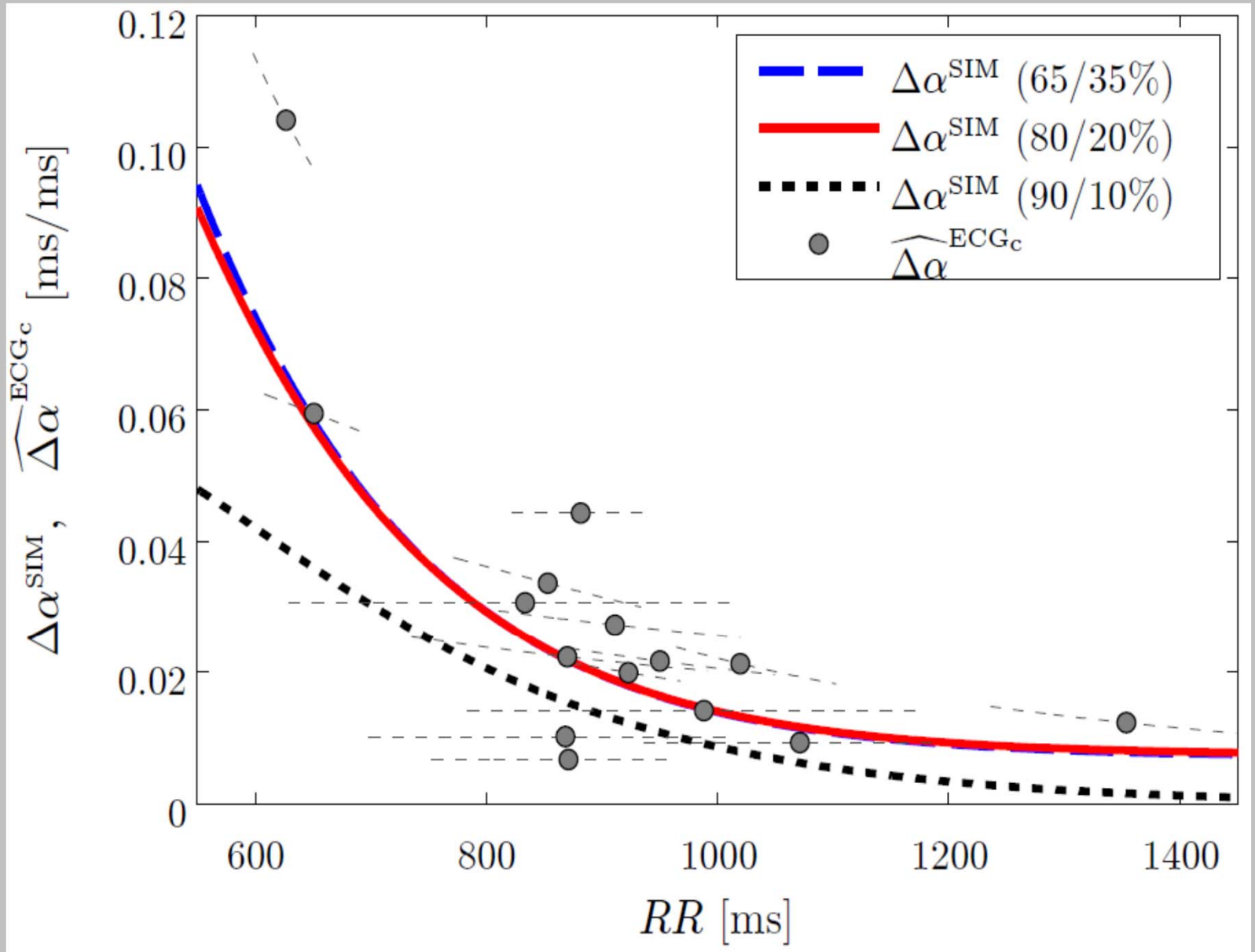




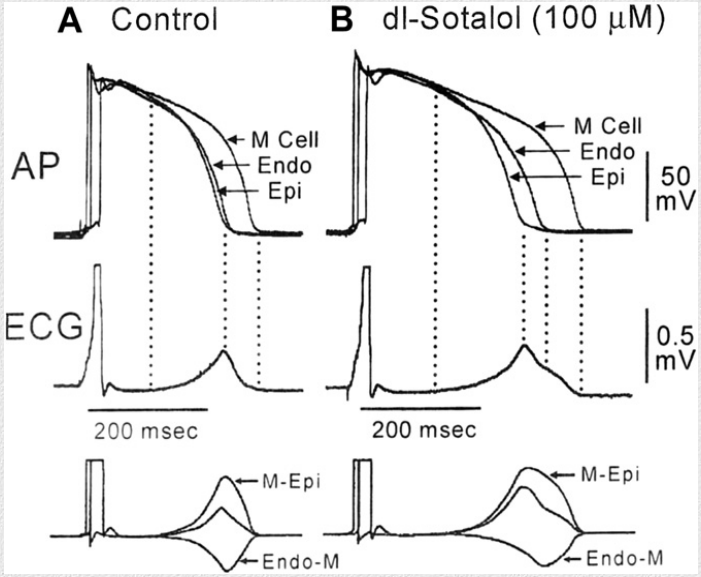
$$\widehat{\Delta\alpha} = \frac{\Delta T_{pe}}{\Delta RR}$$



Agreement between simulated APDR slope dispersion and estimates from clinical ECG data

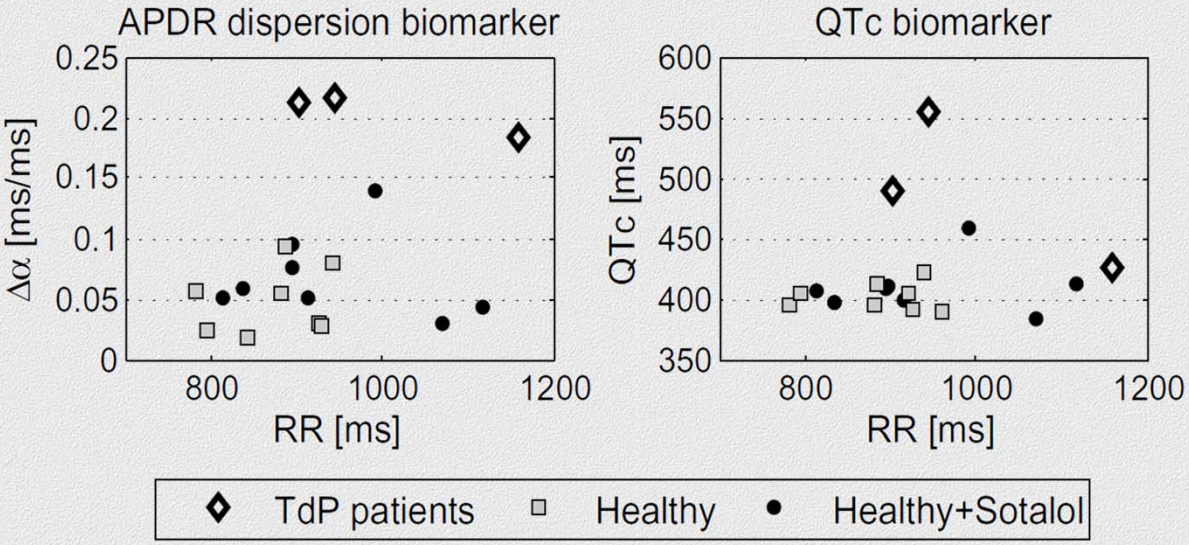


APPLICATION: Drug Cardiotoxicity



Database

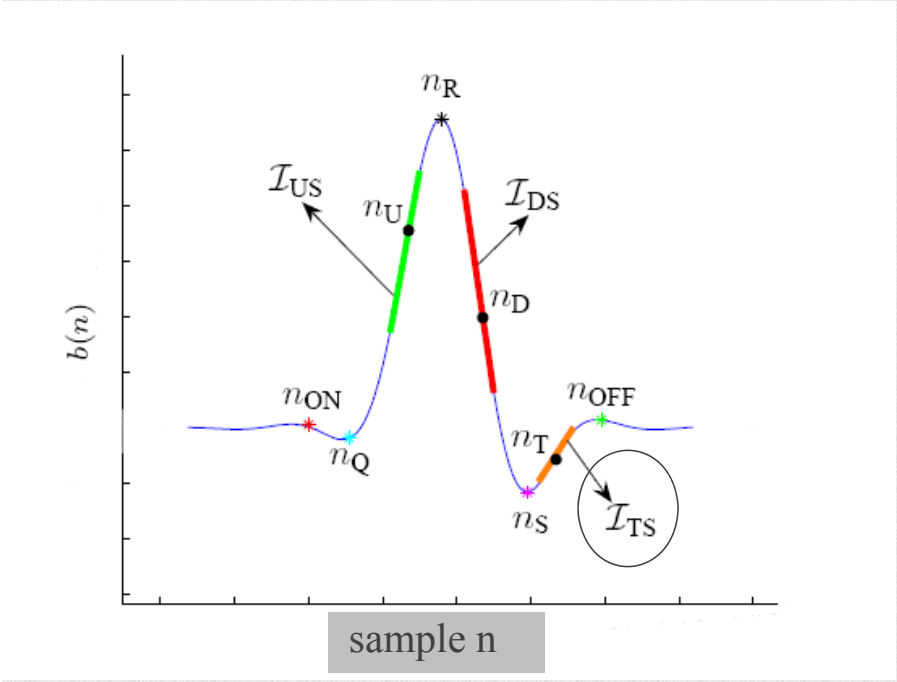
	Baseline	+ Sotalol
3 patients	X	**TdP**
8 volunteers	YES	no TdP



APDR dispersion (Δα) has been shown to provide better risk stratification after sotalol administration than standard ECG-biomarkers such as QTc.

Depolarization Analysis. Ischemia monitoring and quantification

QRS slopes



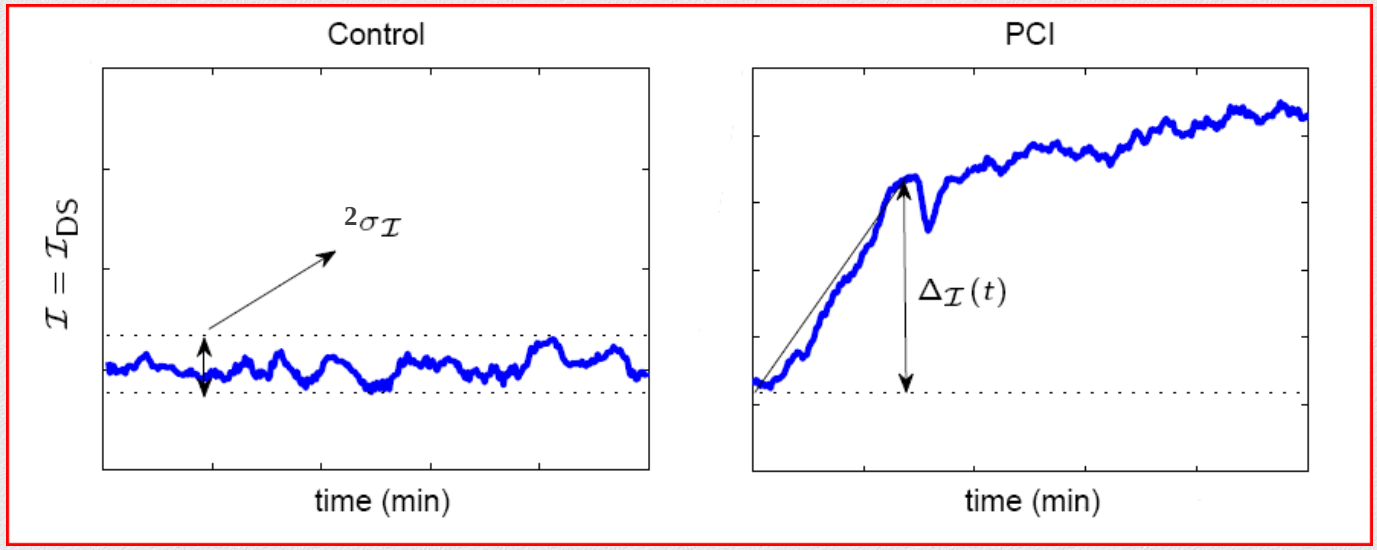
$\mathcal{I}_{US}$: up-slopes of the R wave

$\mathcal{I}_{DS}$: down-slope of the R wave

$\mathcal{I}_{TS}$: terminal slopes of the S wave

Methods PCI

Quantification of the dynamic changes during ischemia



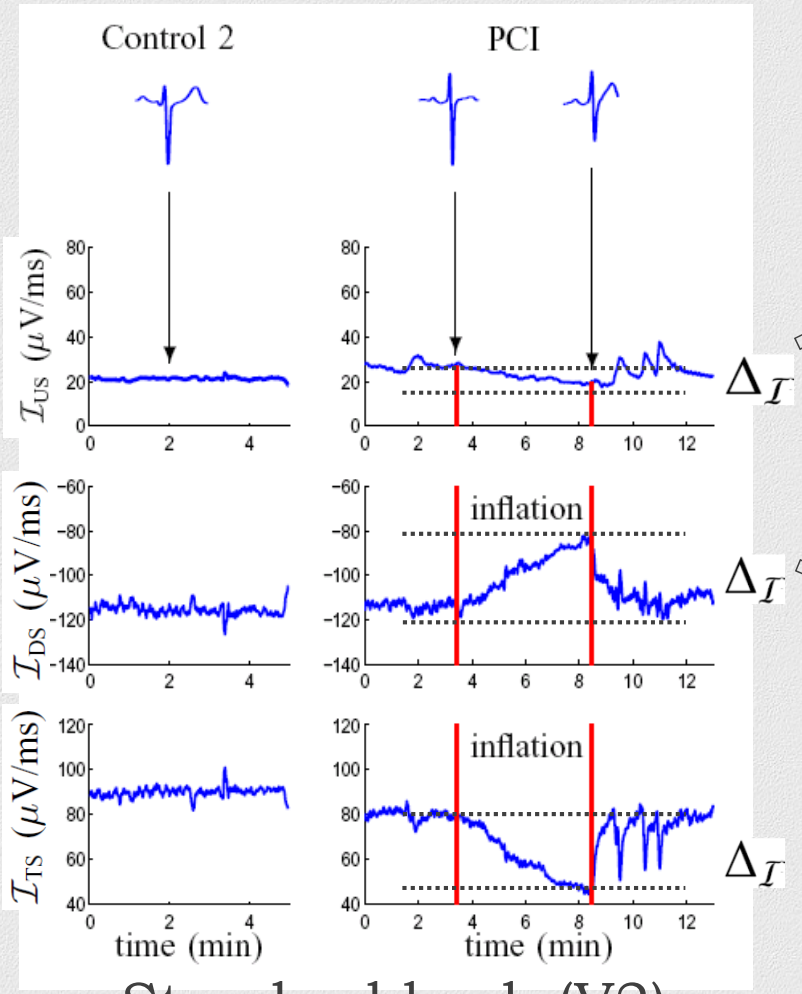
$$\mathcal{R}_{\mathcal{I}}(t_j) = \frac{\Delta_{\mathcal{I}}(t_j)}{\sigma^{\mathcal{I}}}$$

: absolute change during PCI

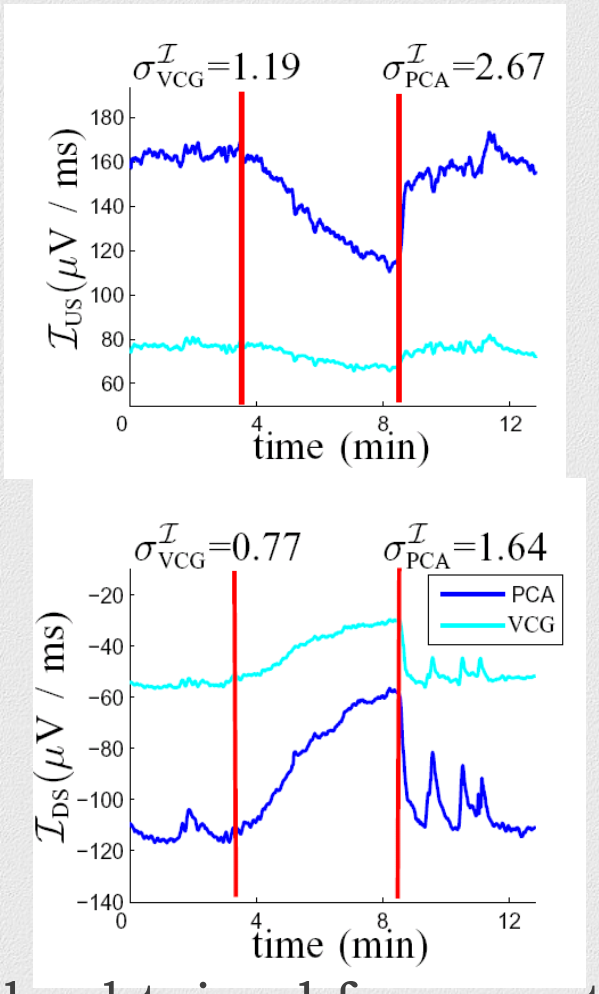
: standard deviation (SD) of $\mathcal{I}$ at control

Results in PCI

QRS slopes measured in a control and PCI recording for a particular patient



Standard lead (V2)

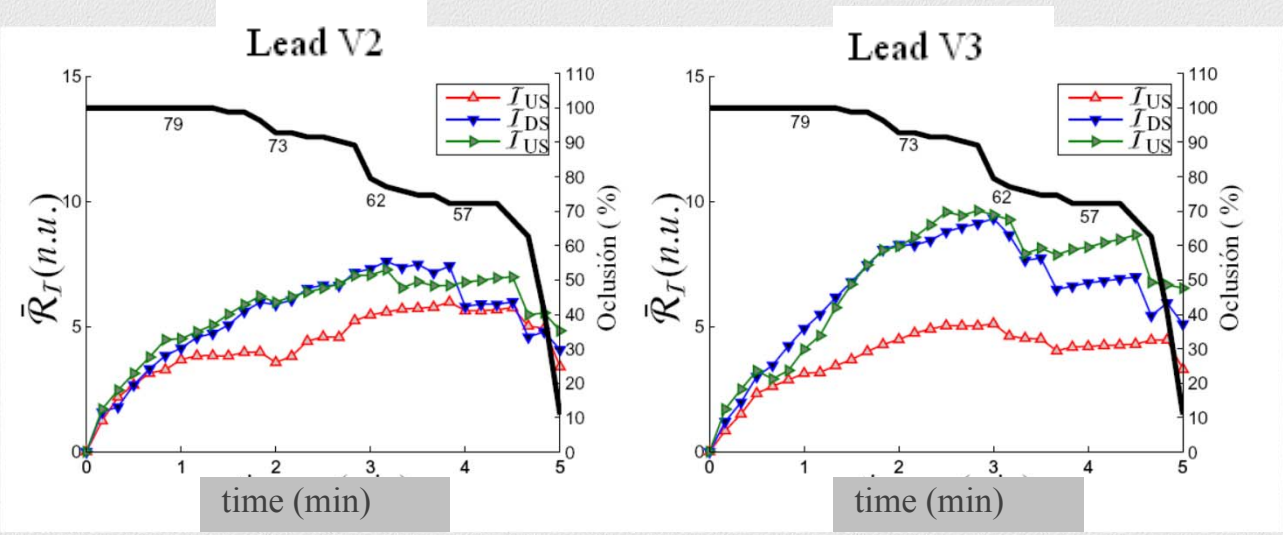


Leads obtained from spatial QRS loops.

Results PCI

Temporal analysis

Averaged relative factor of change for the QRS slopes in leads V2 and V3 during the occlusion.



Leads that presented the greatest changes.

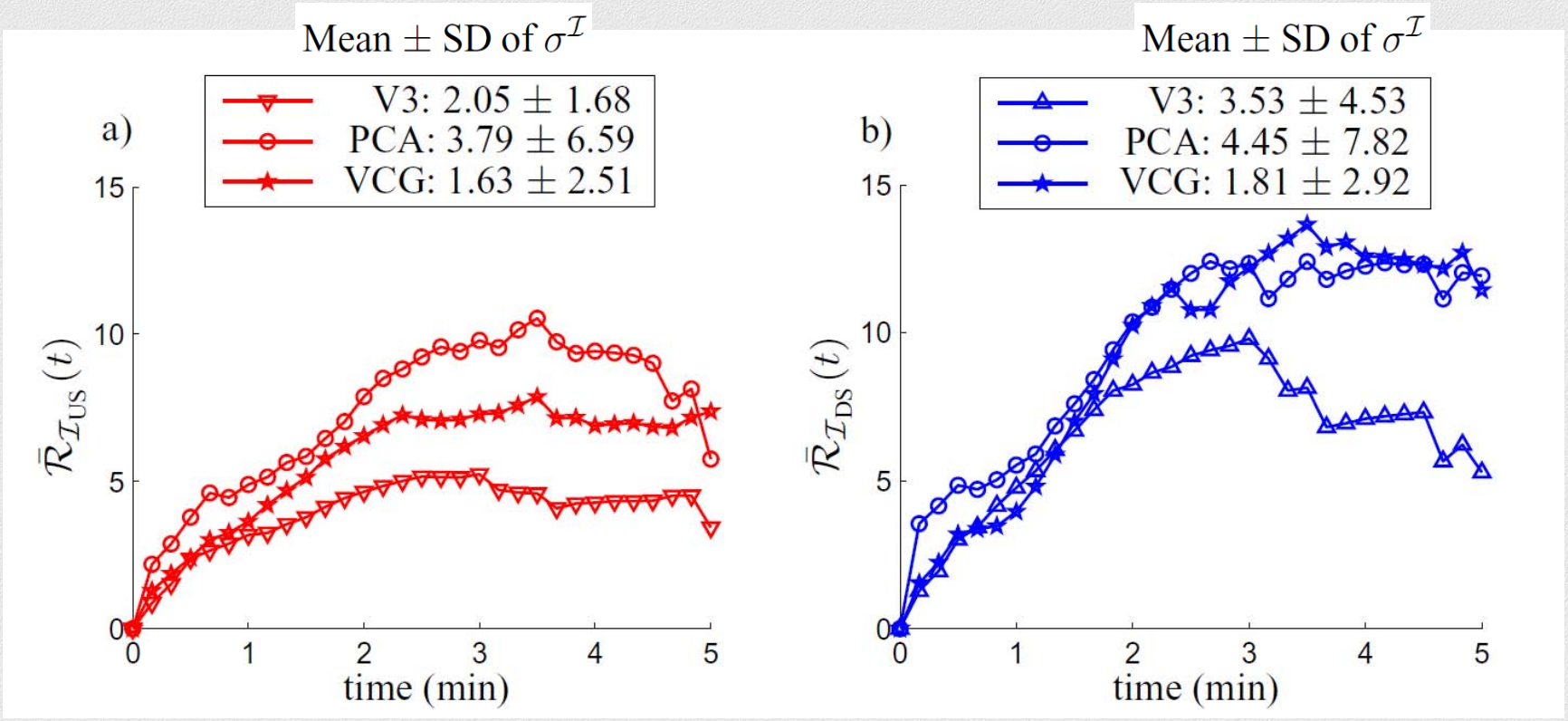
$\mathcal{R}_{\mathcal{I}}$

Index	V3	V5
$\mathcal{I}_{US}$	5.11	9.31
$\mathcal{I}_{DS}$	6.01	8.06

Results PCI

Comparison between standard and derived leads

Averaged relative factor of change for the lead V3 and those leads obtained from the spatial QRS loops.

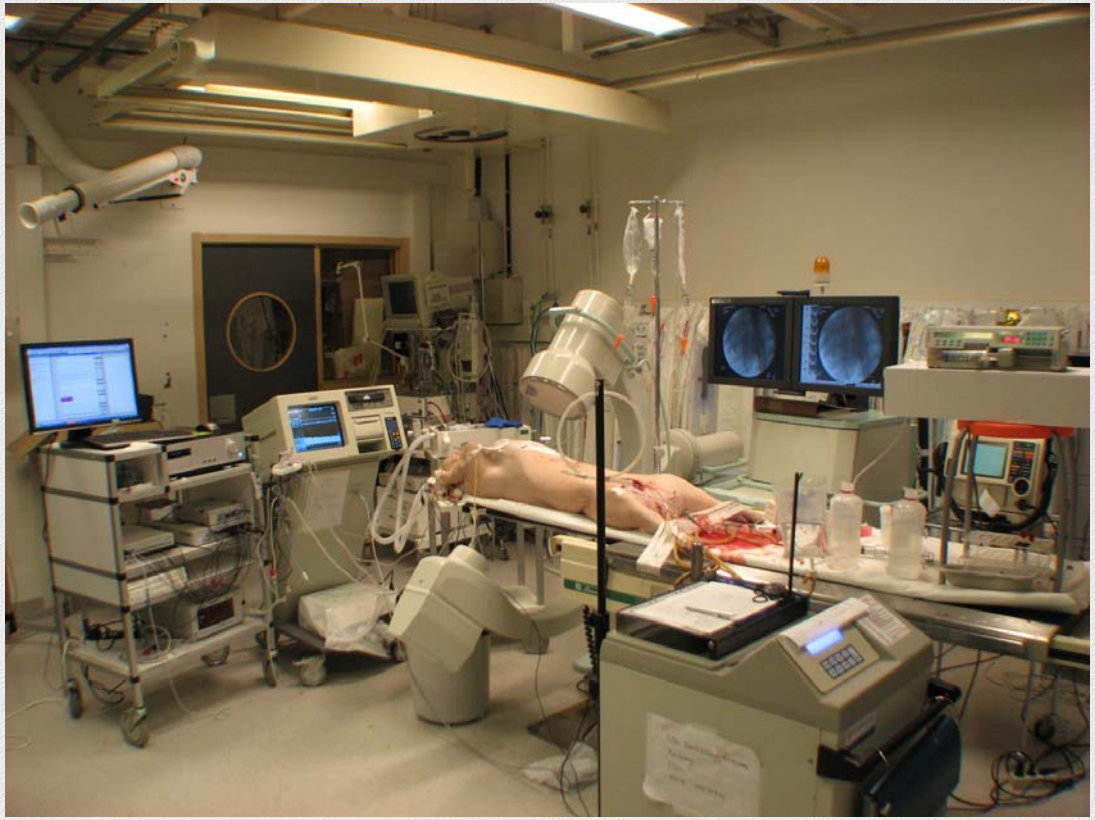


Results PCI

Multiple linear regression (also including R wave changes)

Predictor variables	Dependent variable Extent (% of LV), R^2 (p)	Dependent variable Severity (% of LV), R^2 (p)
ST	0.593 (<.0001)	0.665 (<.0001)
ST, US	0.722 (<.0001), ↑12.9%	0.705 (<.0001), ↑4.0%
ST, DS	0.715 (<.0001), ↑12.2%	0.736 (<.0001), ↑7.1%
ST, DS, US	0.738 (<.0001), ↑14.5%	0.736 (<.0001), ↑7.1%
ST, Ra sum neg	0.688 (<.0001), ↑9.5%	0.693 (<.0001), ↑2.8%
ST, Ra sum pos	0.593 (<.0001), ↑0.0%	0.669 (<.0001), ↑0.4%
ST, Ra sum tot	0.644 (<.0001), ↑5.1%	0.673 (<.0001), ↑0.8%

Animal Models



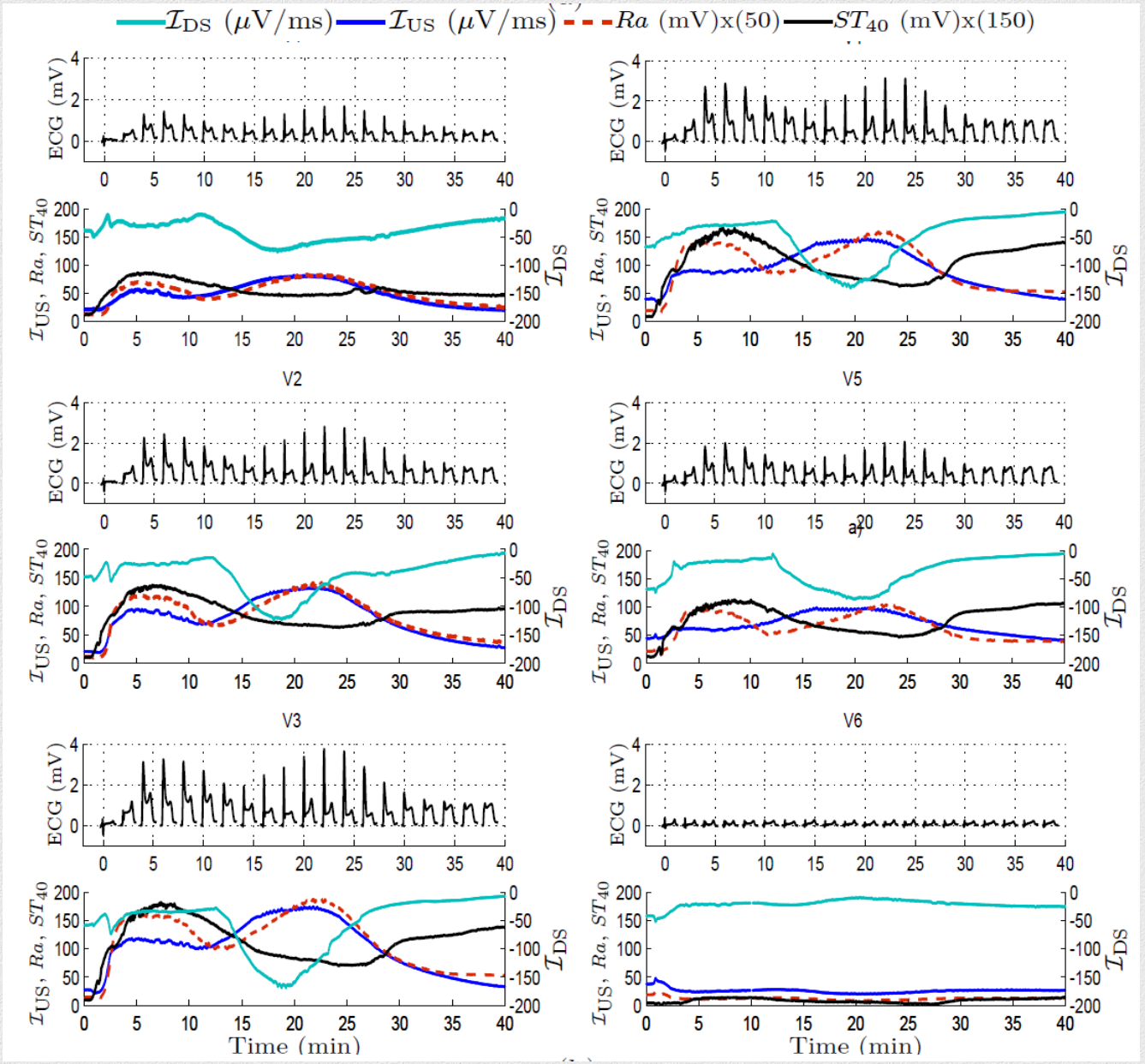
13 Healthy pigs weighing 40-50 kg

Balloon Angioplasty in the mid LAD

12 lead ECG monitoring:

- control
- occlusion (40 min)
- reperfusion (4 hours)

Time course evolution during occlusion (for one pig)

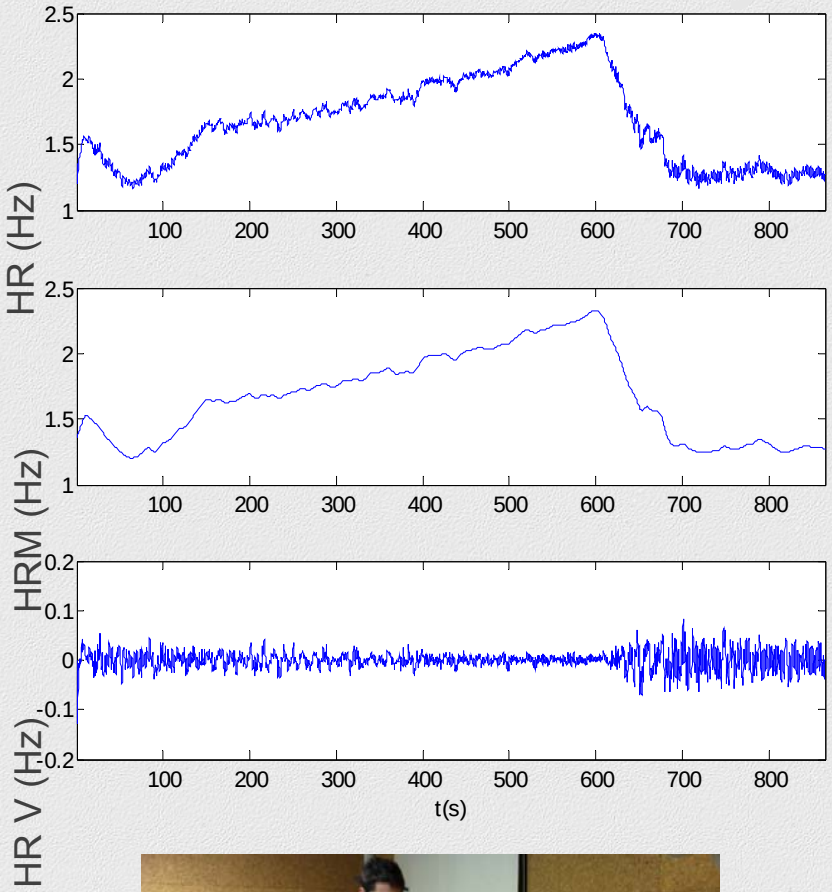


Correlation analysis between Mar/IS and the quantified ECG changes

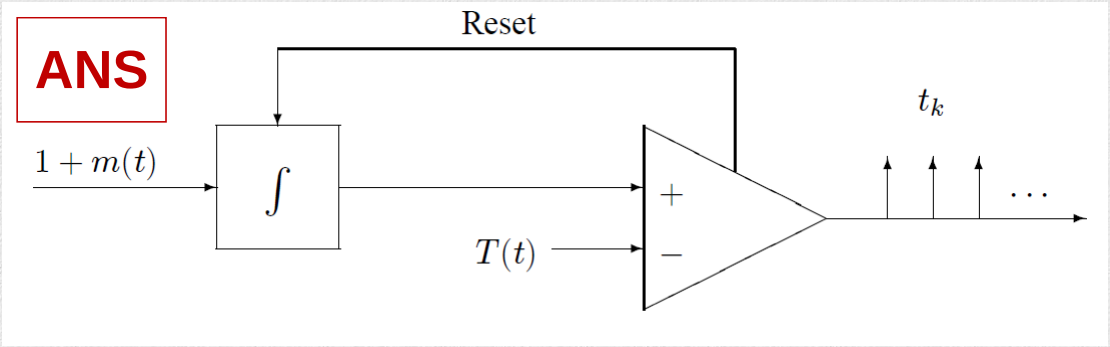
MaR vs $\Delta\mathcal{Y}$	$\Delta\mathcal{Y}_{max}$ $r(p)$	$\Delta\mathcal{Y}_{pos}$ $r(p)$	$\Delta\mathcal{Y}_{abs}$ $r(p)$	$\Delta\mathcal{Y}_{real}$ $r(p)$
$\mathcal{I}_{\mathrm{US}}$ 1^{st} peak	0.54 (0.0850)	0.52 (0.0971)	0.69 (0.0167)*	0.26 (0.4312)
$\mathcal{I}_{\mathrm{US}}$ 2^{nd} peak	0.42 (0.1929)	0.44 (0.1774)	0.41 (0.2092)	0.36 (0.2692)
R_a 1^{st} peak	0.21 (0.5353)	0.43 (0.1825)	0.51 (0.1115)	0.44 (0.1724)
R_a 2^{nd} peak	0.28 (0.4230)	0.34 (0.3025)	0.32 (0.3307)	0.20 (0.5628)
$\mathcal{I}_{\mathrm{DS}}$ 1^{st} peak	-0.75 (0.0045)*	-0.65 (0.0220)*	-0.63 (0.0265)*	-0.66 (0.0184)*
$\mathcal{I}_{\mathrm{DS}}$ 2^{nd} peak	-0.67 (0.0237)*	-0.71 (0.0345)*	-0.08 (0.8101)	-0.77 (0.0054)*
ST_{40} peak	-0.25 (0.4351)	-0.34 (0.2814)	-0.34 (0.2805)	-0.34 (0.2828)

IS vs $\Delta\mathcal{Y}$	$\Delta\mathcal{Y}_{max}$ $r(p)$	$\Delta\mathcal{Y}_{pos/neg}$ $r(p)$	$\Delta\mathcal{Y}_{abs}$ $r(p)$	$\Delta\mathcal{Y}_{real}$ $r(p)$
$\mathcal{I}_{\mathrm{US}}$ 1^{st} peak	0.51 (0.1099)	0.46 (0.1543)	0.61 (0.1518)	0.25 (0.4512)
$\mathcal{I}_{\mathrm{US}}$ 2^{nd} peak	0.20 (0.5573)	0.18 (0.5952)	0.24 (0.4854)	0.07 (0.8388)
R_a 1^{st} peak	0.30 (0.3710)	0.17 (0.6144)	0.25 (0.4512)	0.18 (0.5952)
R_a 2^{nd} peak	0.26 (0.4345)	0.26 (0.4345)	0.20 (0.5575)	0.12 (0.7342)
$\mathcal{I}_{\mathrm{DS}}$ 1^{st} peak	-0.65 (0.0217)*	-0.51 (0.0923)	-0.49 (0.1085)	-0.53 (0.0265)*
$\mathcal{I}_{\mathrm{DS}}$ 2^{nd} peak	-0.42 (0.2695)	-0.13 (0.7435)	-0.13 (0.7435)	-0.13 (0.7435)
ST_{40} peak	-0.59 (0.0431)*	-0.67 (0.0162)*	-0.68 (0.0157)*	-0.67 (0.0168)*

ANS evaluation by HRV analysis in non stationary conditions



TVIPFM model



$$d_{\mathrm{HR}}(t) \approx \frac{1 + m(t)}{T(t)}$$

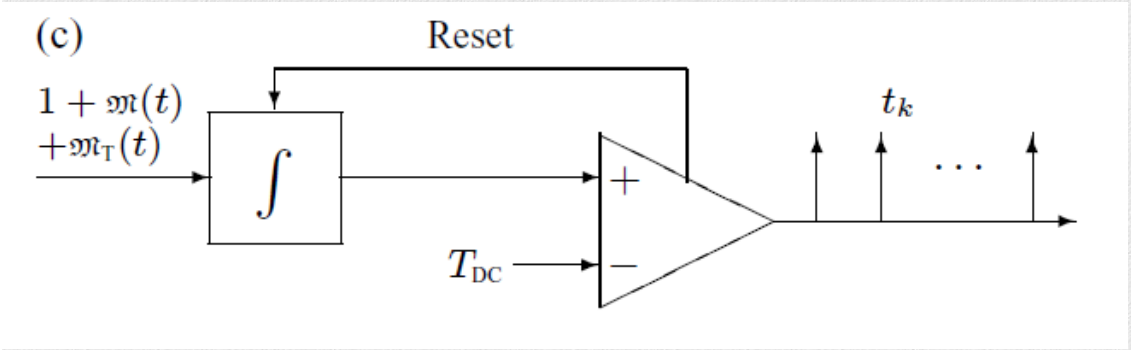
$$d_{\mathrm{HRM}}(t) \approx \frac{1}{T(t)}$$

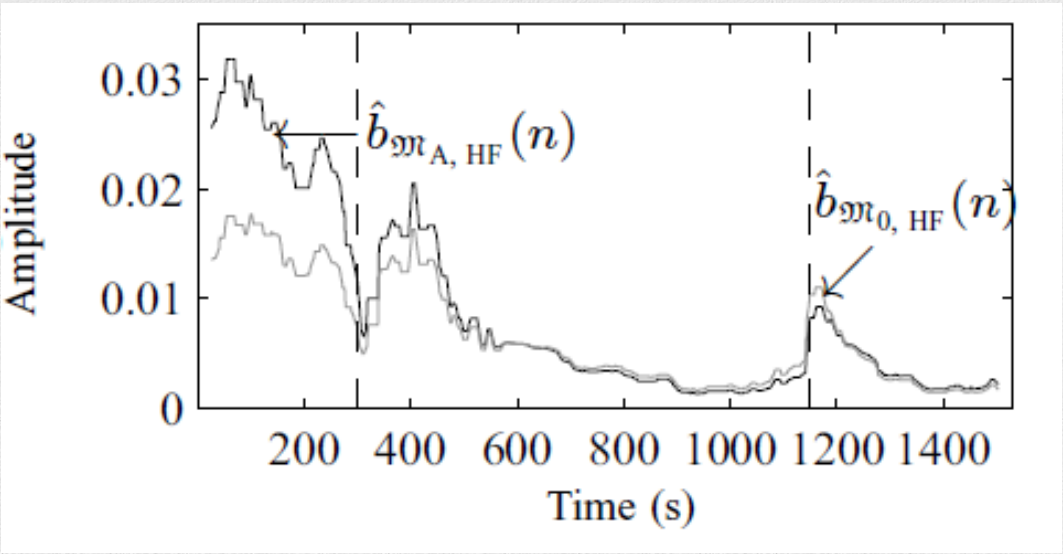
$$d_{\mathrm{HRV}}(t) = d_{\mathrm{HR}}(t) - d_{\mathrm{HRM}}(t) \approx \frac{m(t)}{T(t)}$$

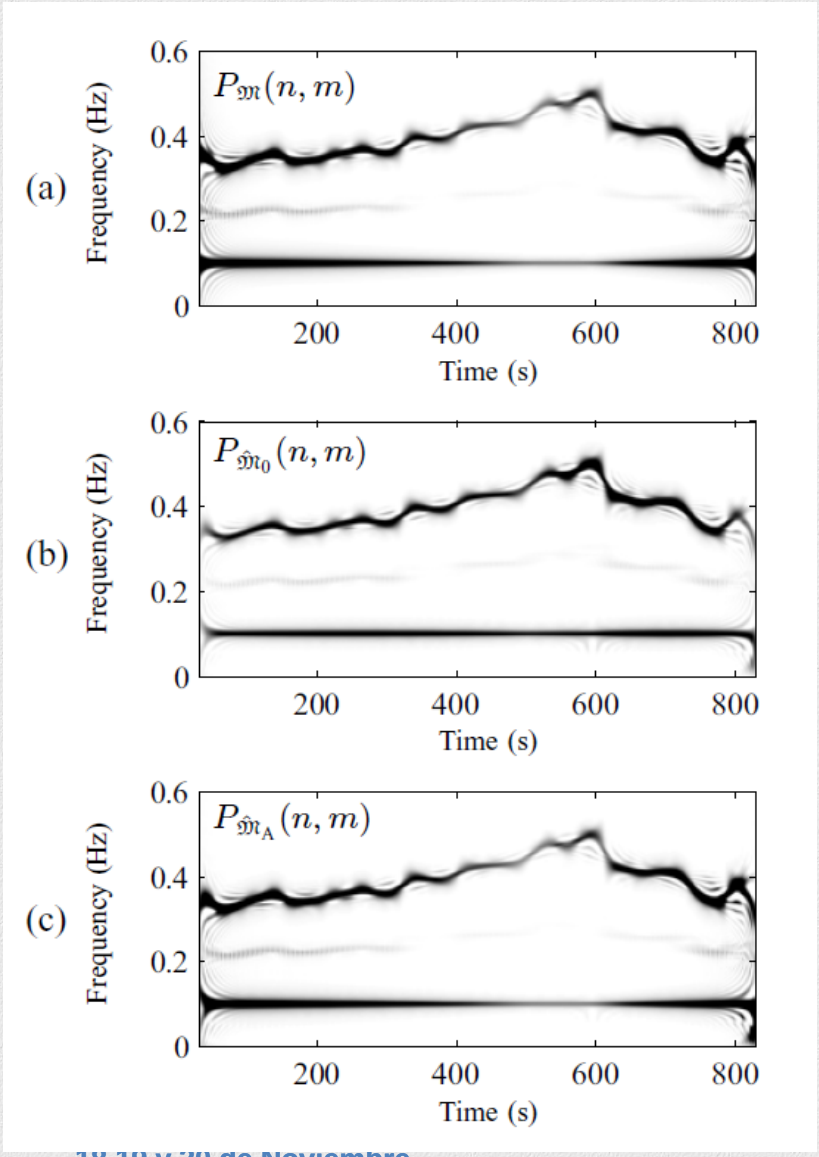
$$m(t) \approx d_{\mathrm{HRV}}(t)T(t) \approx \frac{d_{\mathrm{HRV}}(t)}{d_{\mathrm{HRM}}(t)}$$

ANS evaluation by HRV analysis at non stationary conditions

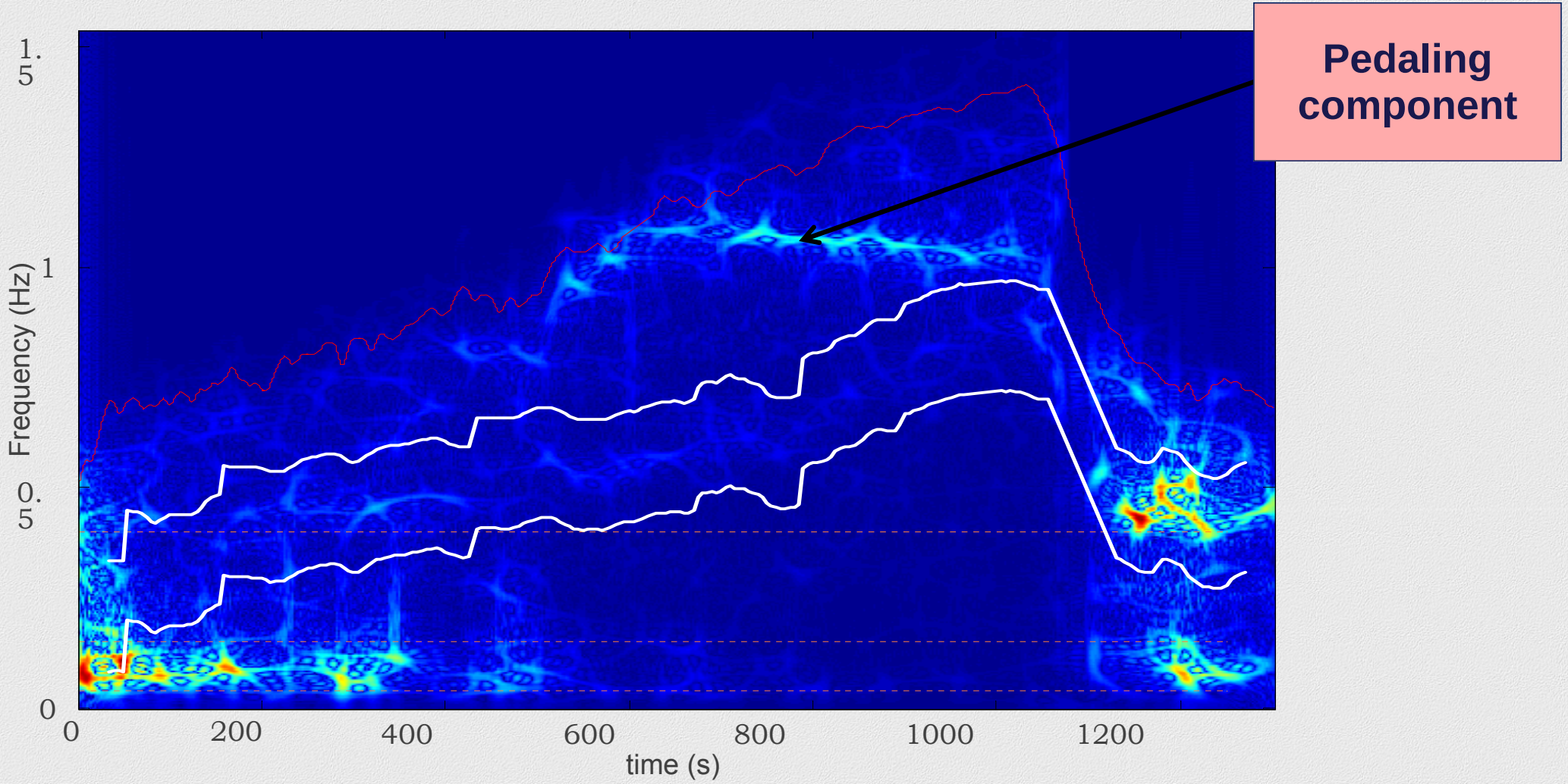
Stress test



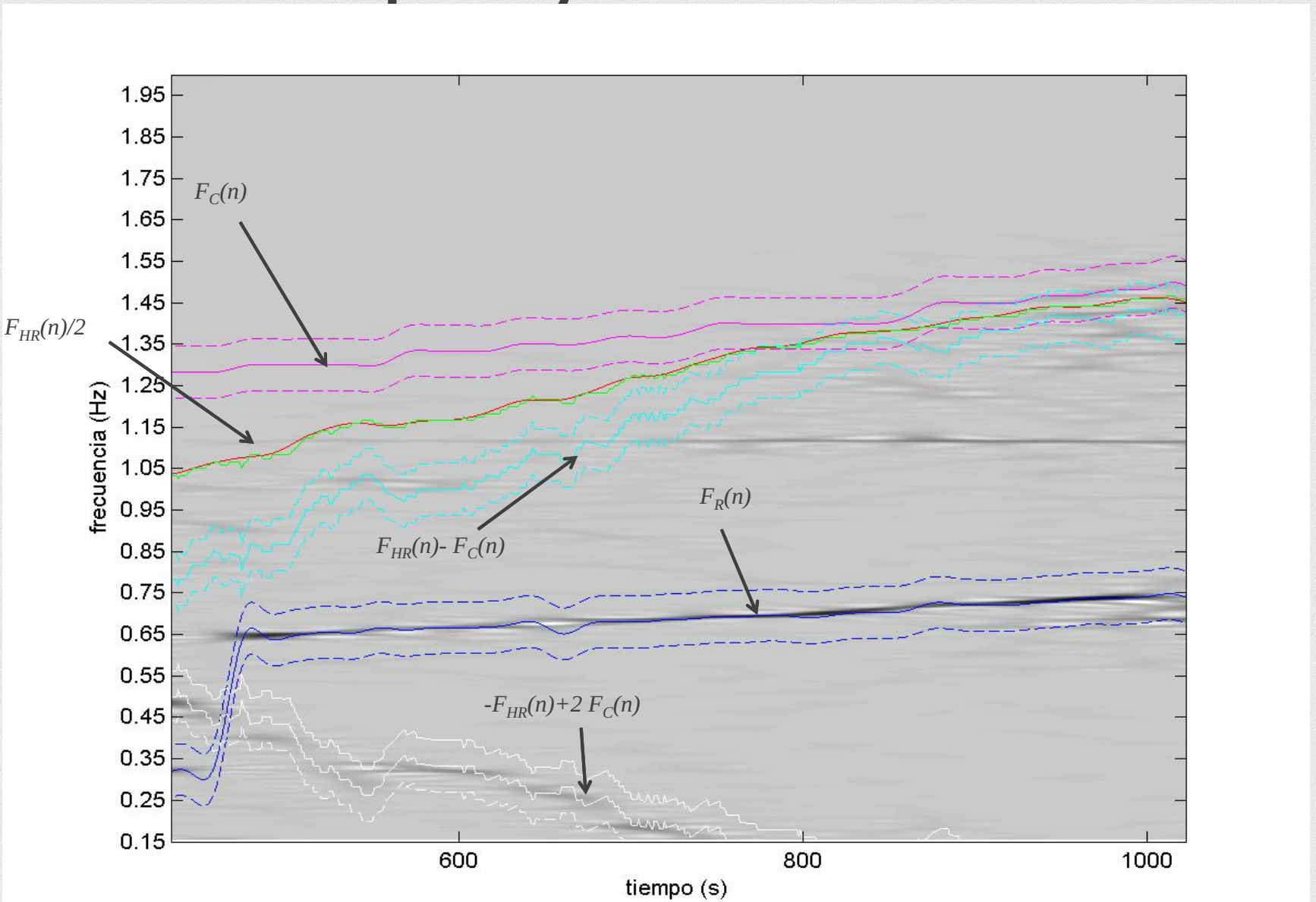


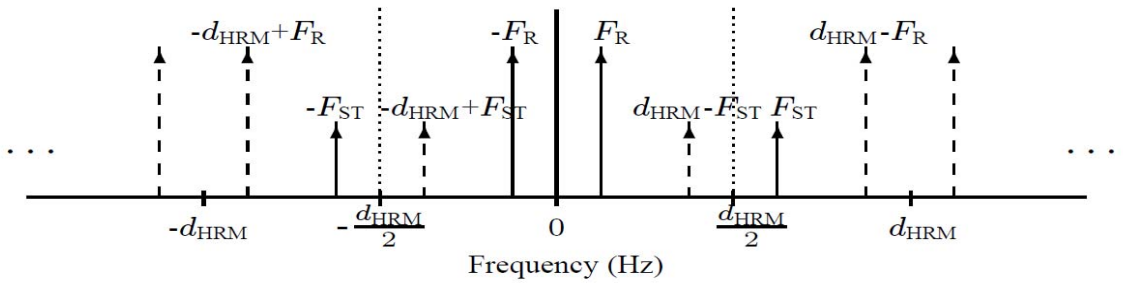


Cardiolocomotor coupling and Band re-definition

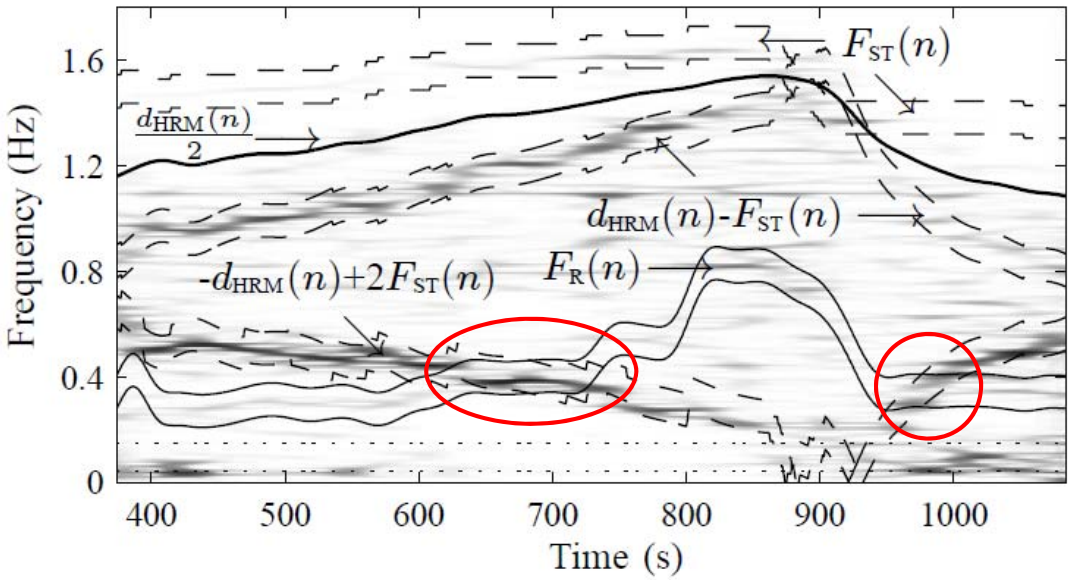


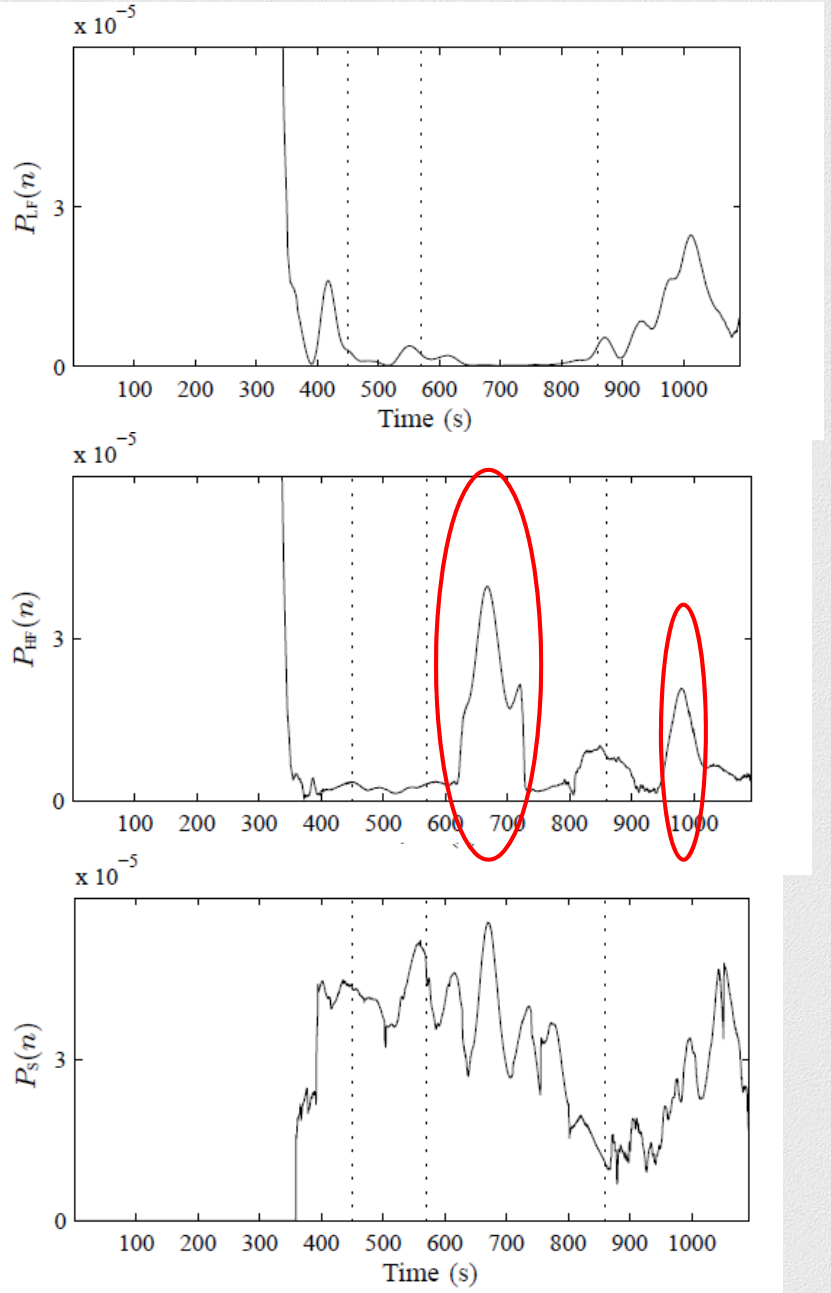
Frequency bands of interest





Results



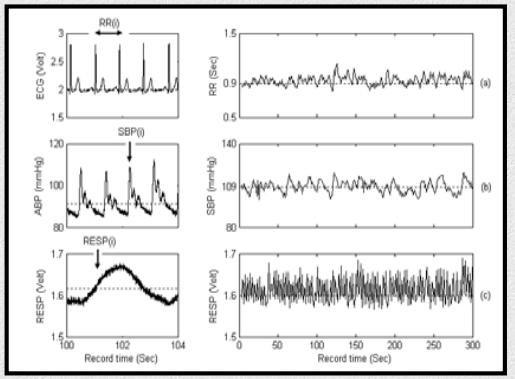


Overlapping!!!

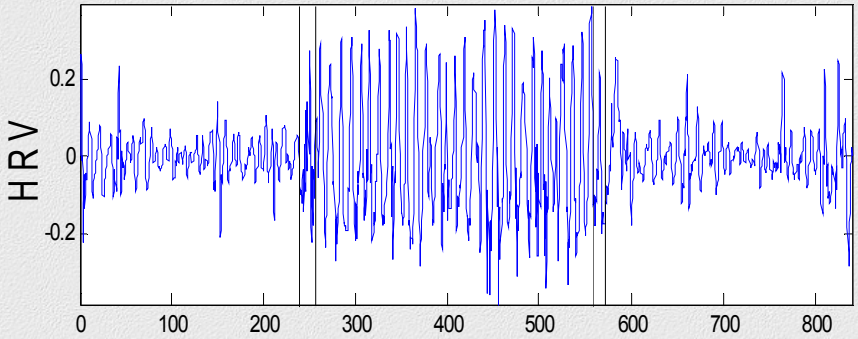
Multimodal analysis of cardiovascular variability in non stationary conditions

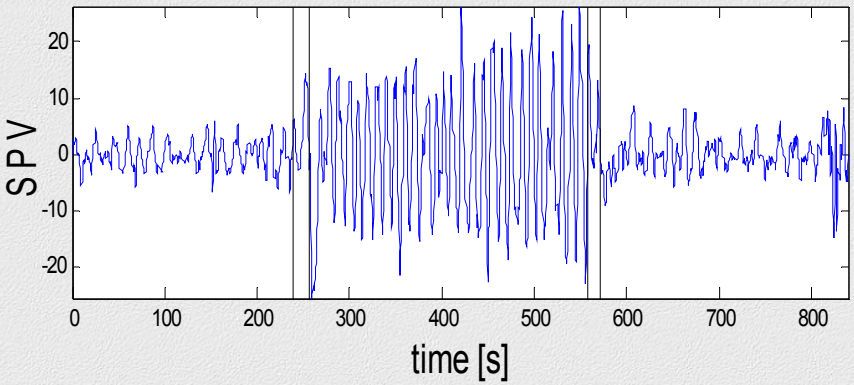
- Tilt Test data (14 min approx.)

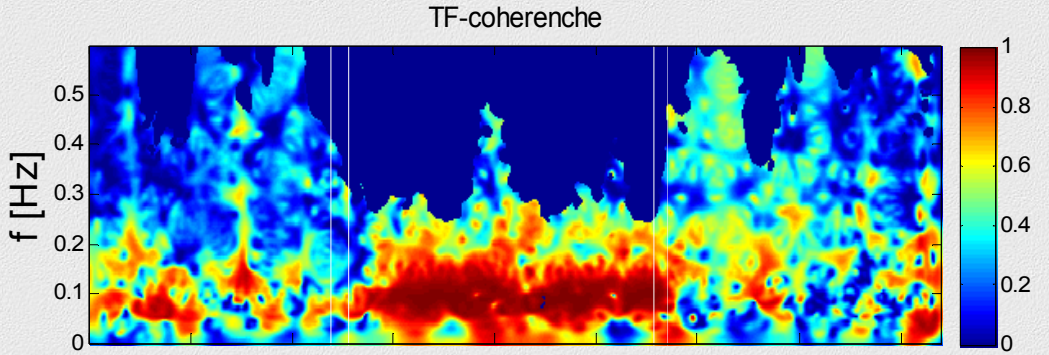
Supine 4m – T1	Standing 70º 5m – T2	Supine 4m- T3

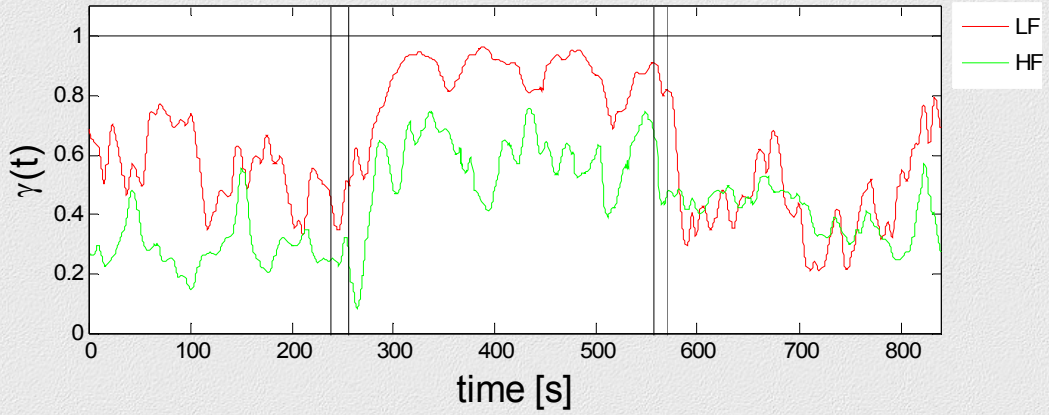


T1 T2 T3 T1 T2 T3

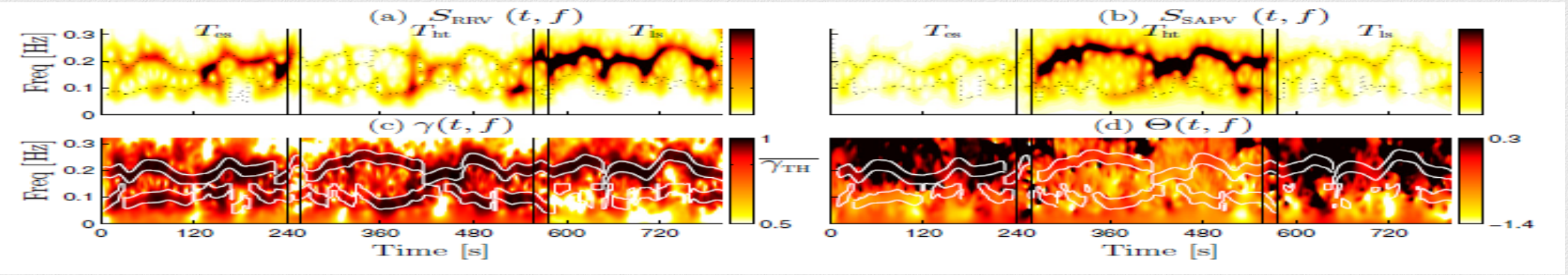


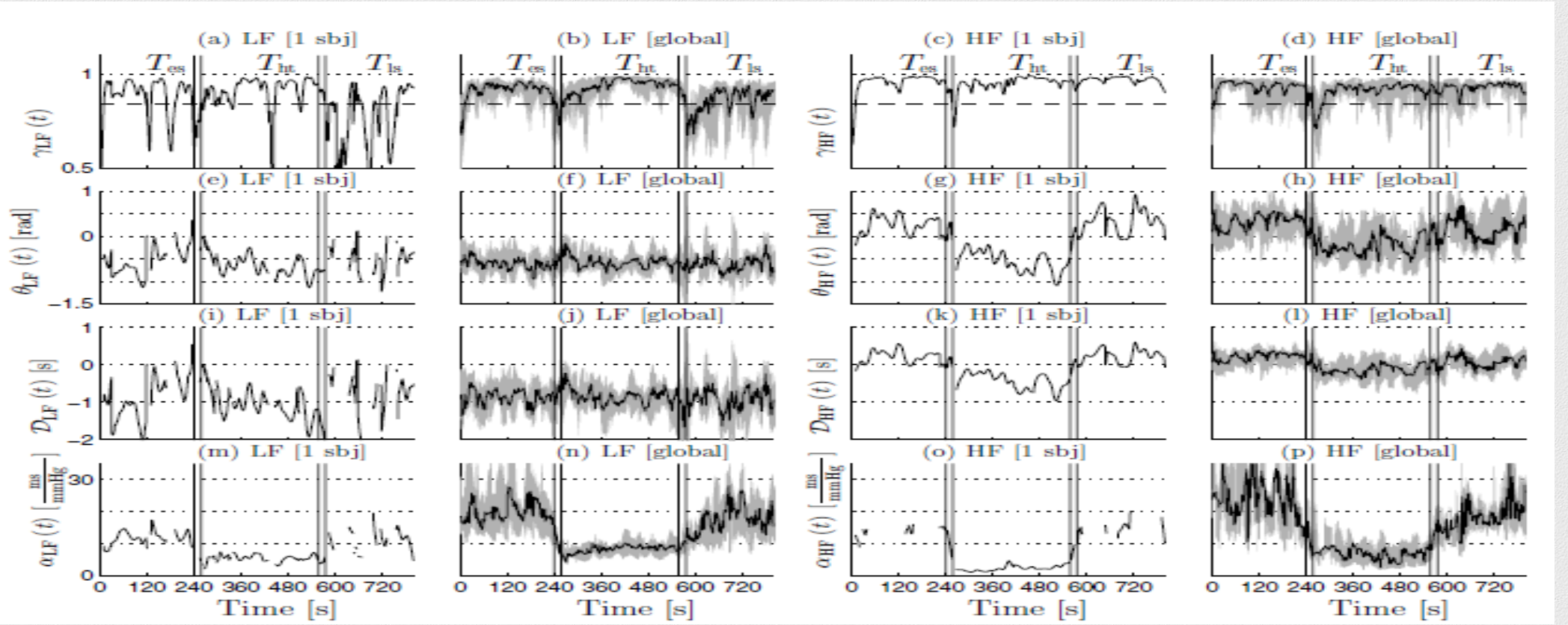






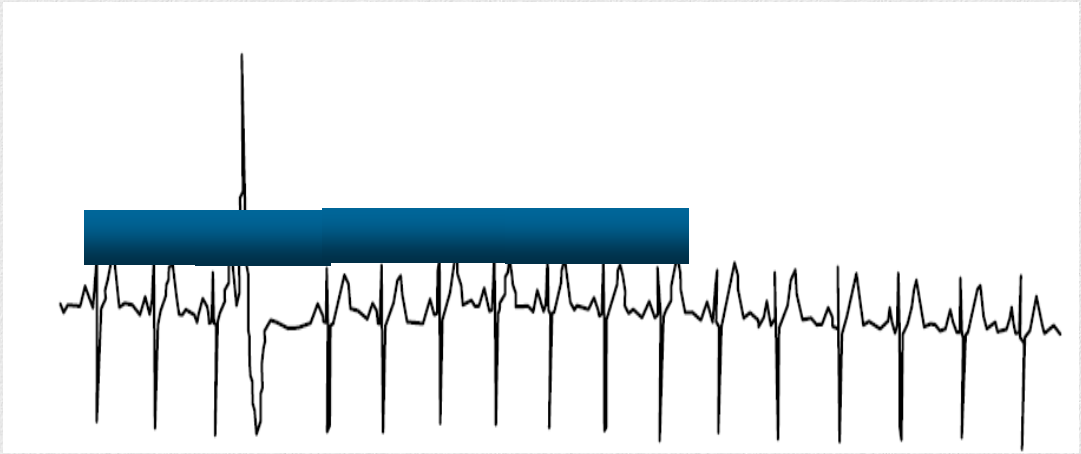
Dynamic iteration between RR and SBP



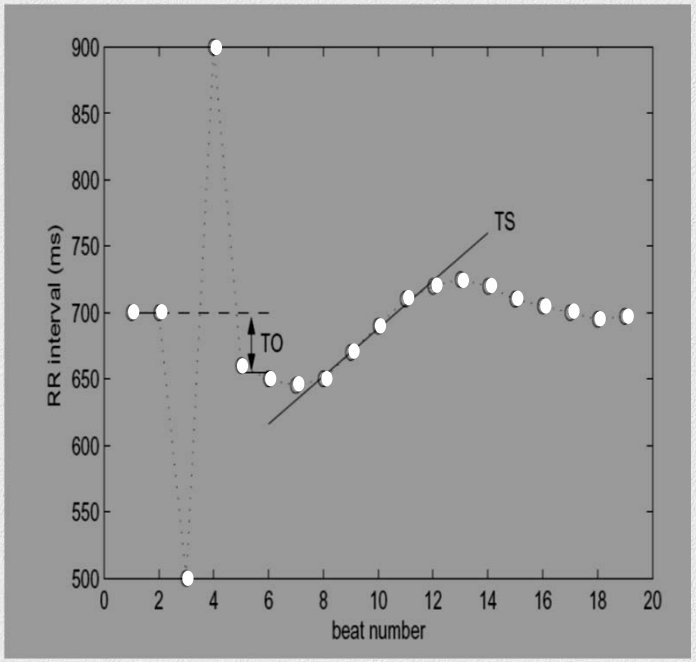


Heart Rate Turbulence

- Heart Rate Turbulence (HRT) is a pattern of response to a VPB in the instantaneous heart rate.
- Early heart rate acceleration phase followed by heart rate deceleration.

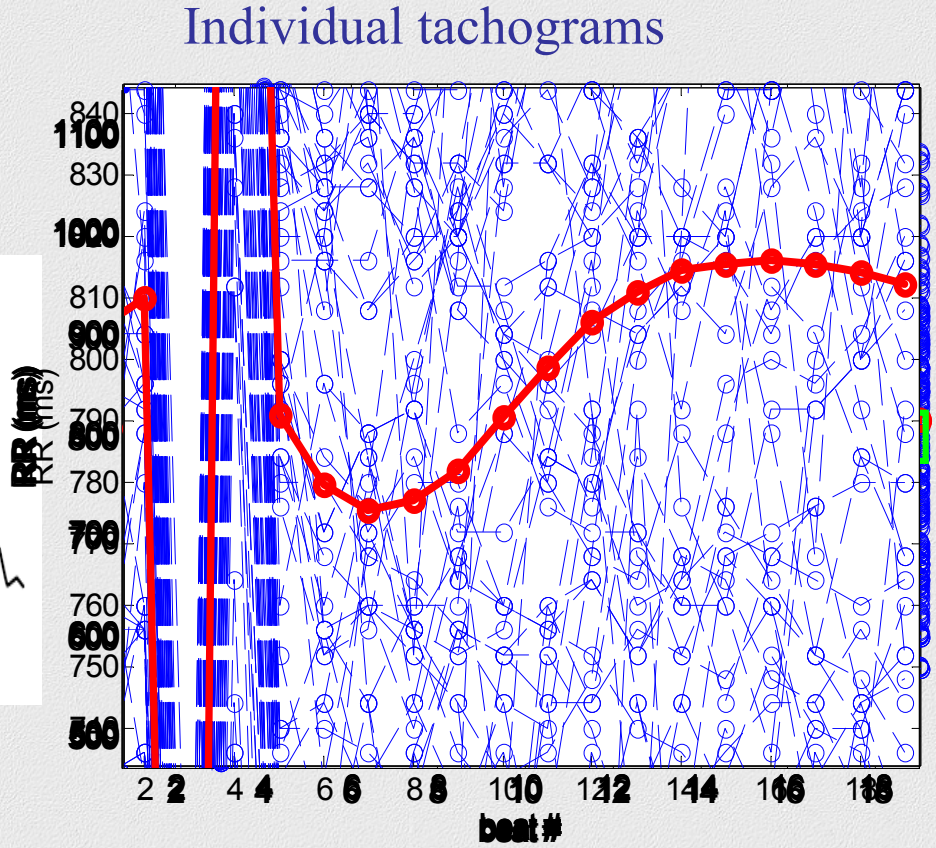


Averaged tachogram (RR series)



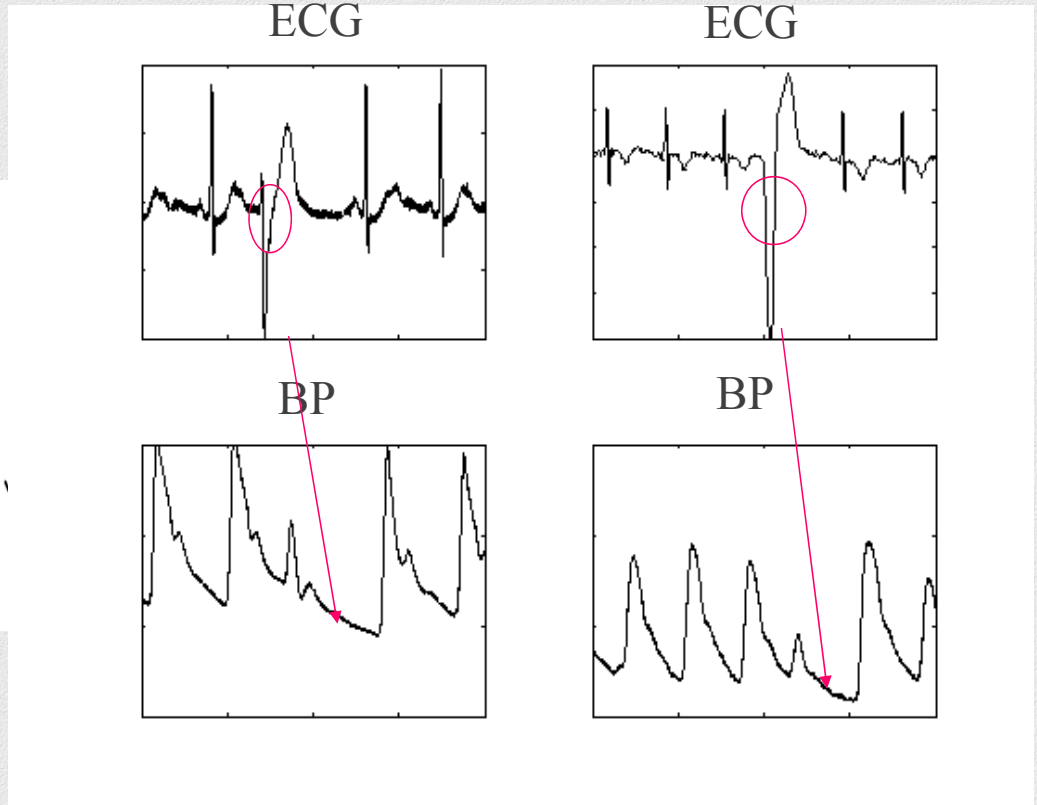
Introduction

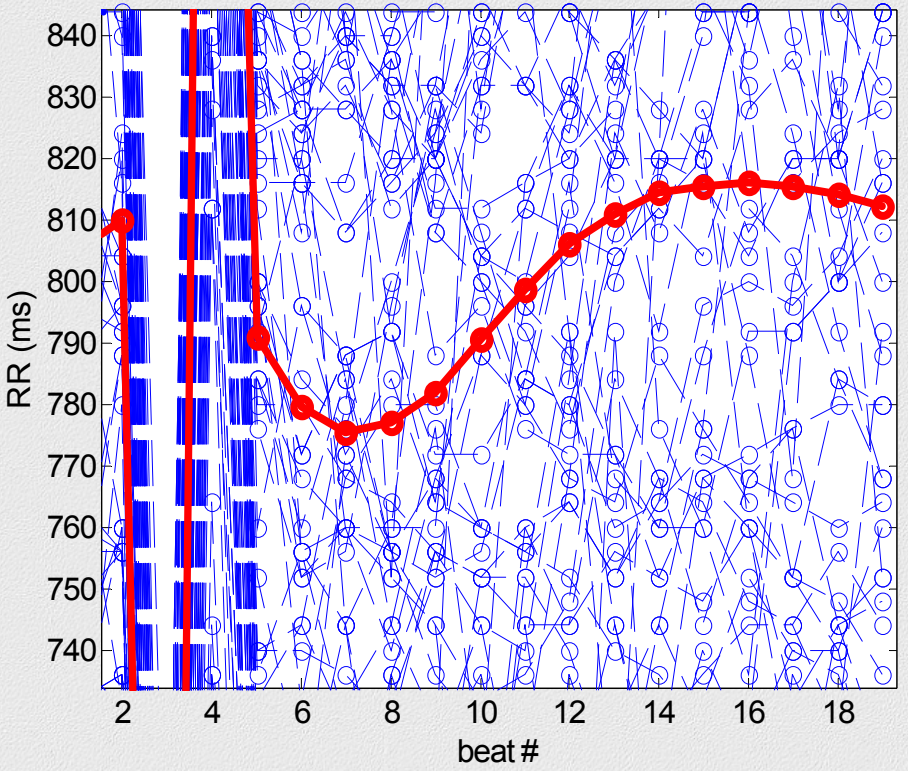
- Heart Rate Turbulence (HRT) is a pattern of response to a VPB in the instantaneous heart rate.
- Early heart rate acceleration phase followed by heart rate deceleration.



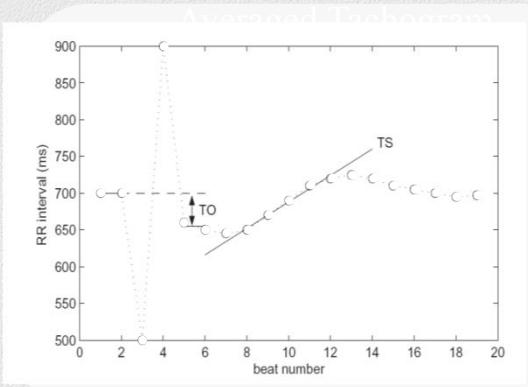
Introducción

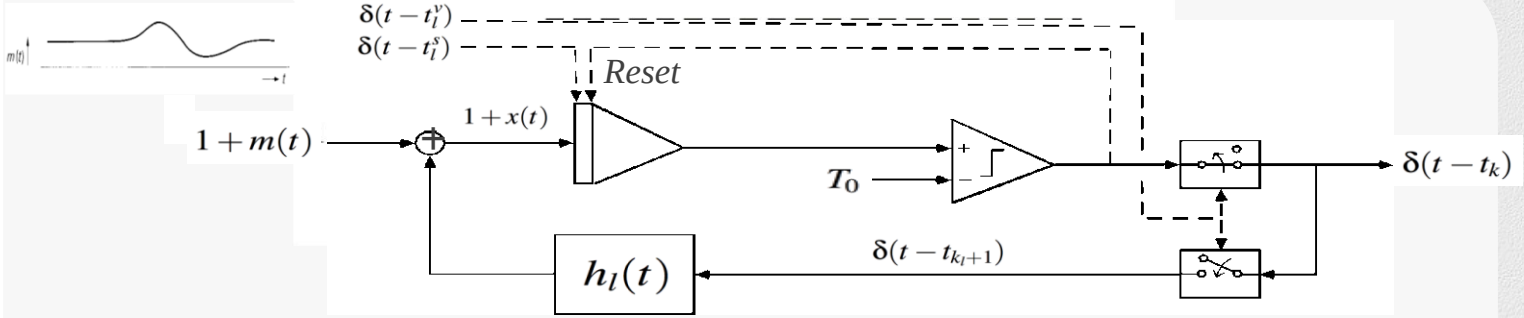
- Baroreflex phenomenon triggered by the BP decrease due to the VPB.
- Main role played by parasympathetic branch of ANS

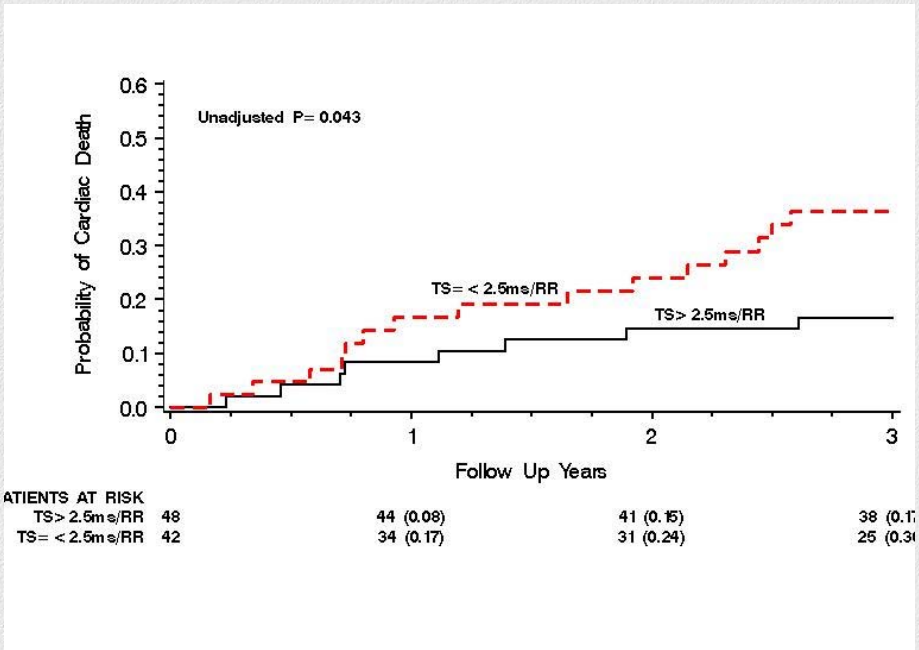


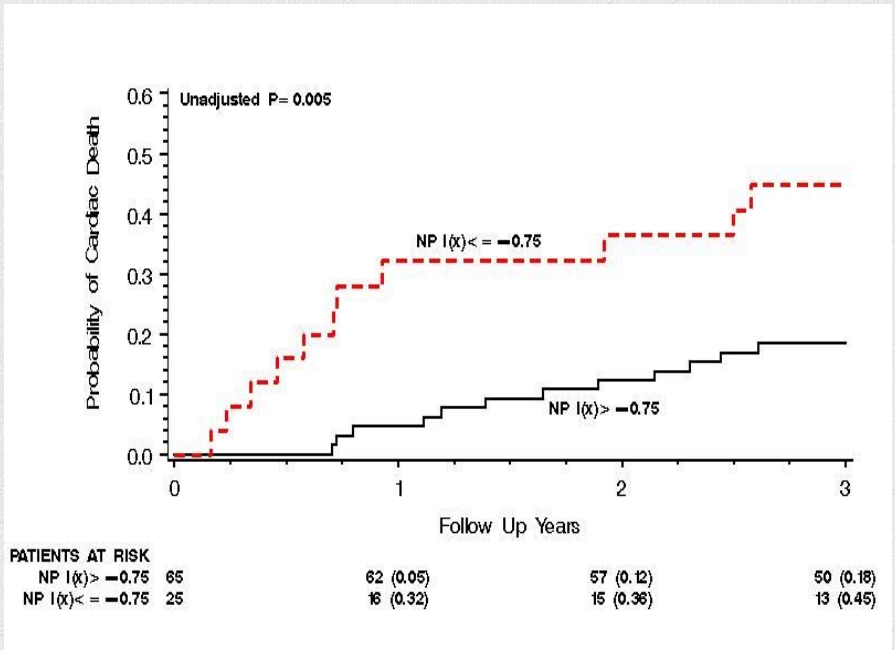


Heart Rate Turbulence

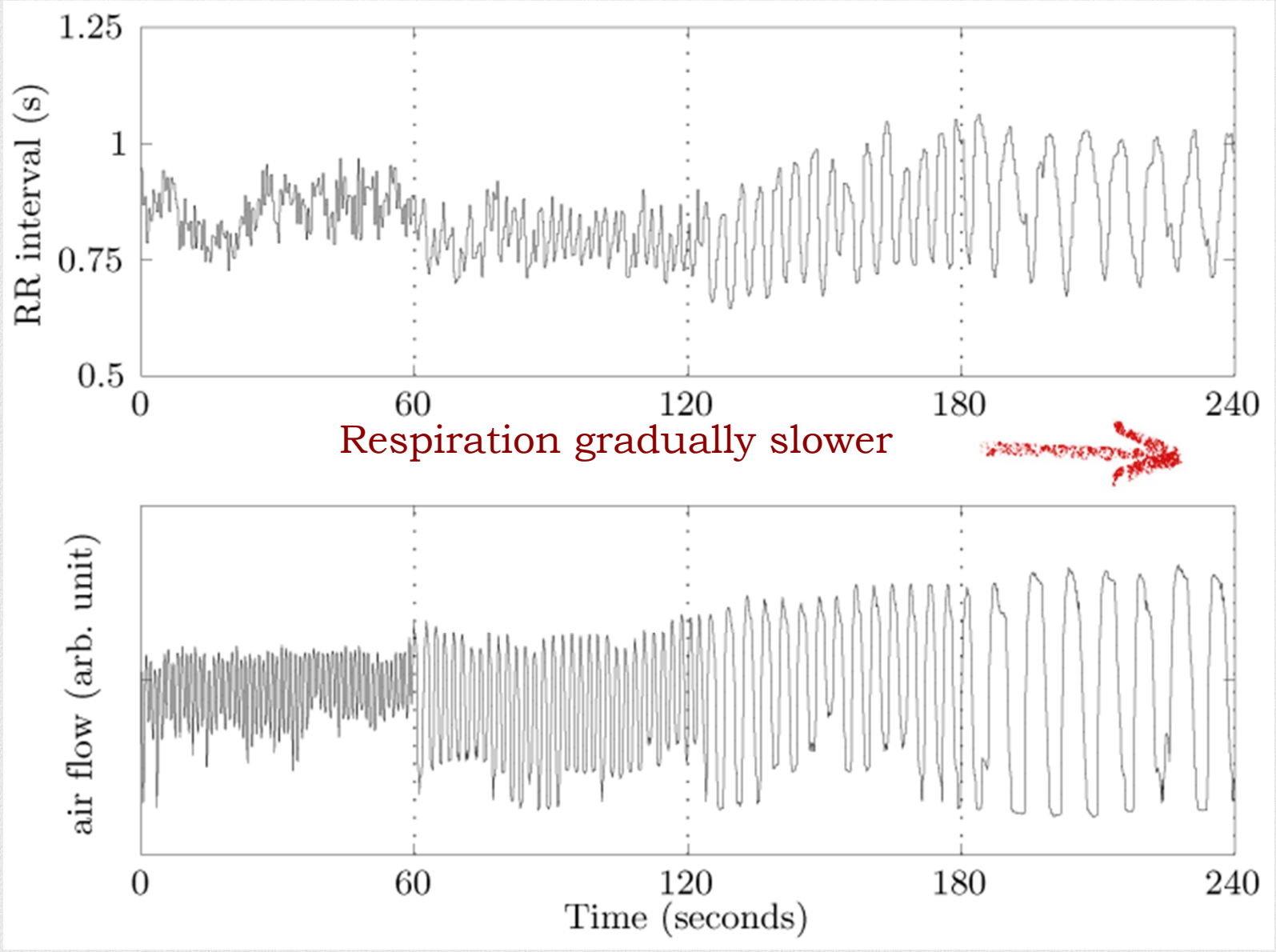




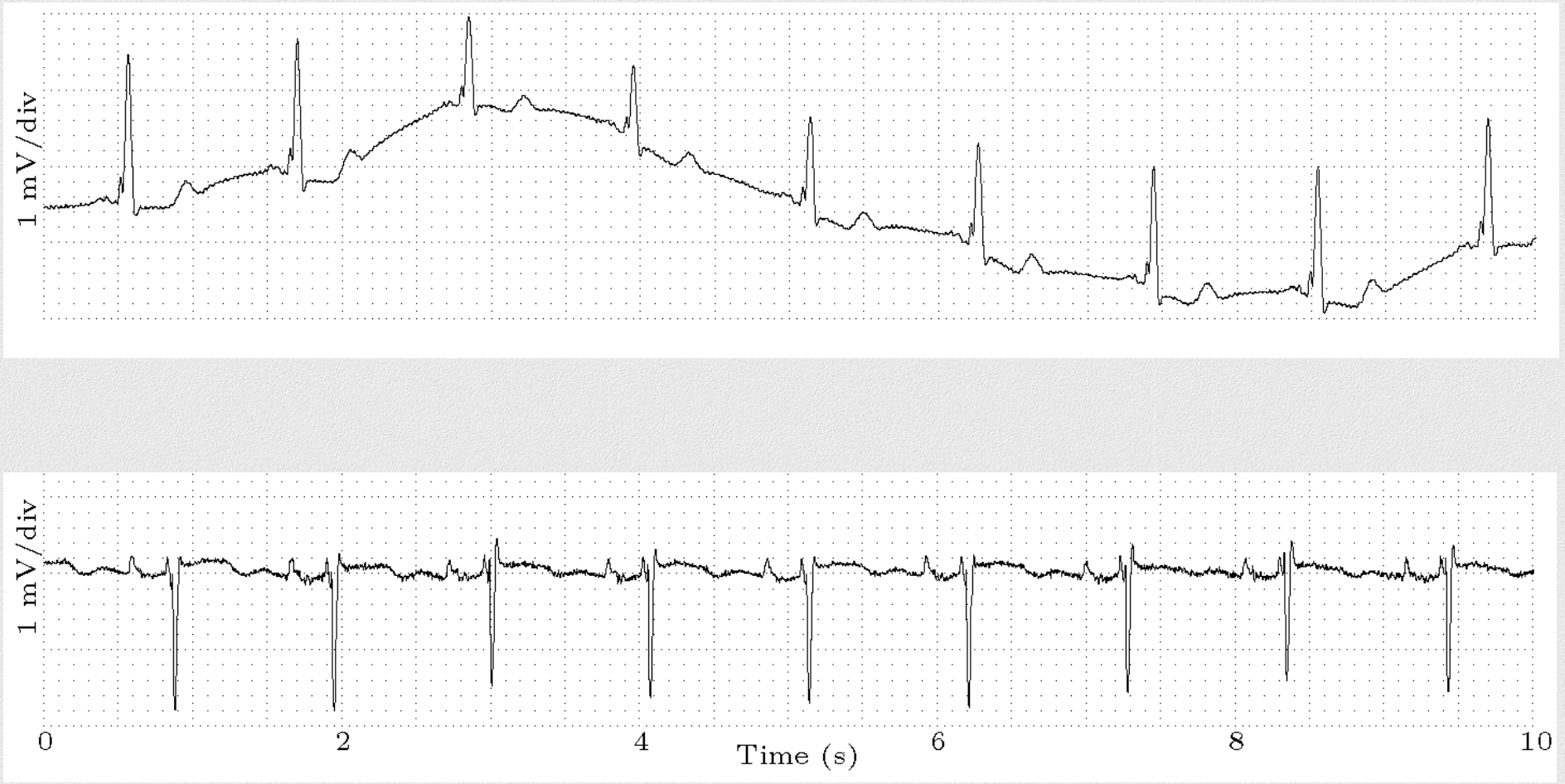




Respiratory information derived from ECG (rhythm)

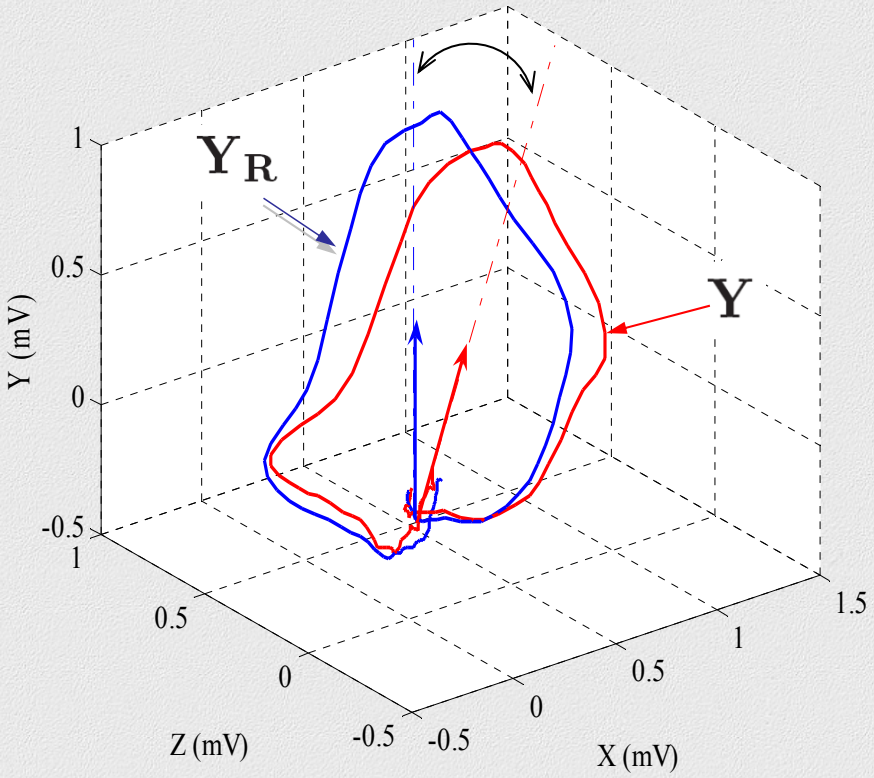


Respiratory information derived from ECG (Amplitude/Slopes)



Respiratory information derived from VCG (loop)

- **EDR signal: QRS-VCG loop alignment**



- QRS-VCG loop rotation

$$\varepsilon_{min} = \min_{\varrho,\tau,\mathbf{Q}} \frac{\|\mathbf{Y_R} - \varrho\mathbf{J}_\tau\mathbf{Y}\mathbf{Q}\|_F^2}{\|\varrho\mathbf{J}_\tau\mathbf{Y}\mathbf{Q}\|_F^2}$$

$$\mathbf{Z}_\tau = \mathbf{Y}_\mathbf{R}^T\mathbf{J}_\tau\mathbf{Y}$$

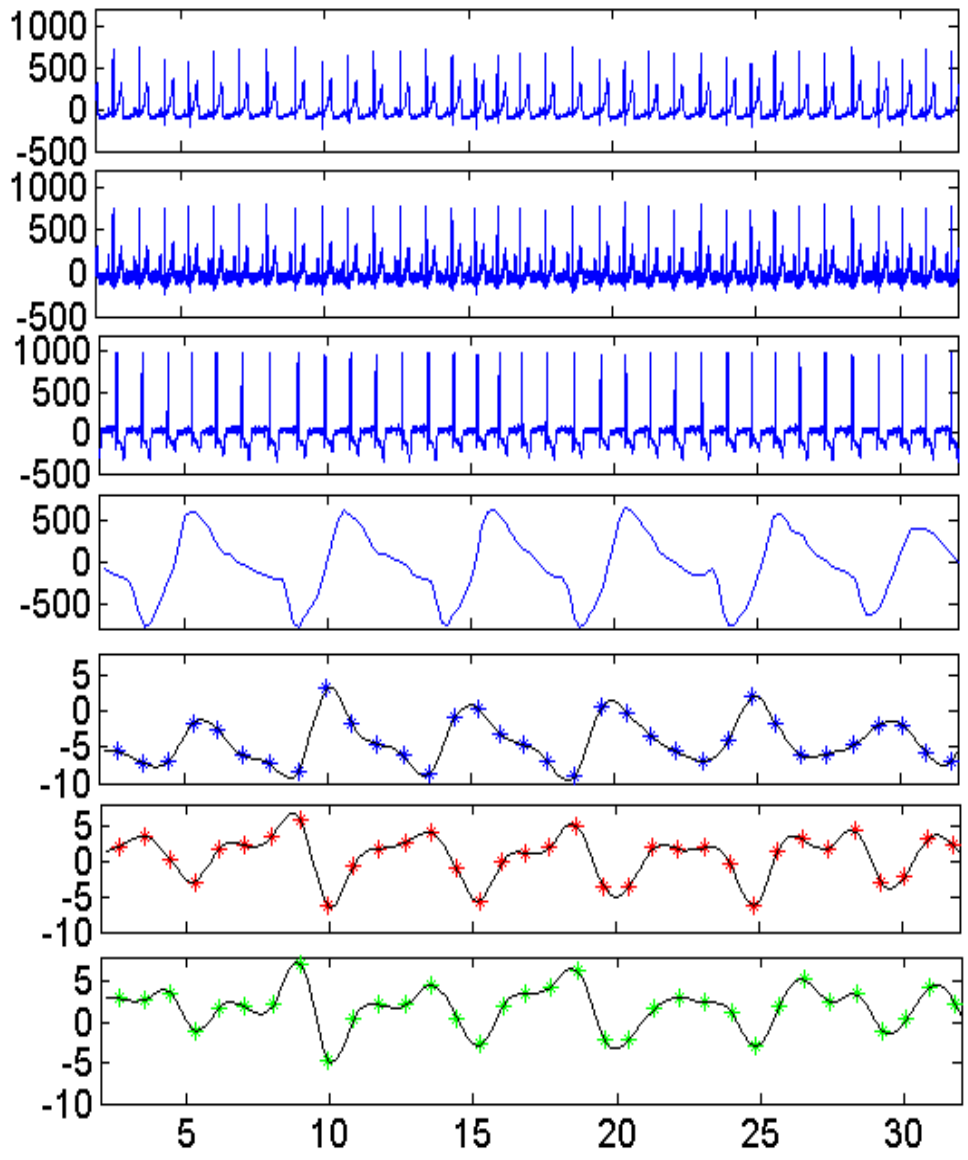
selection of τ for minimum ε
rotation matrix

Respiratory information derived from ECG

ECG

Air volume

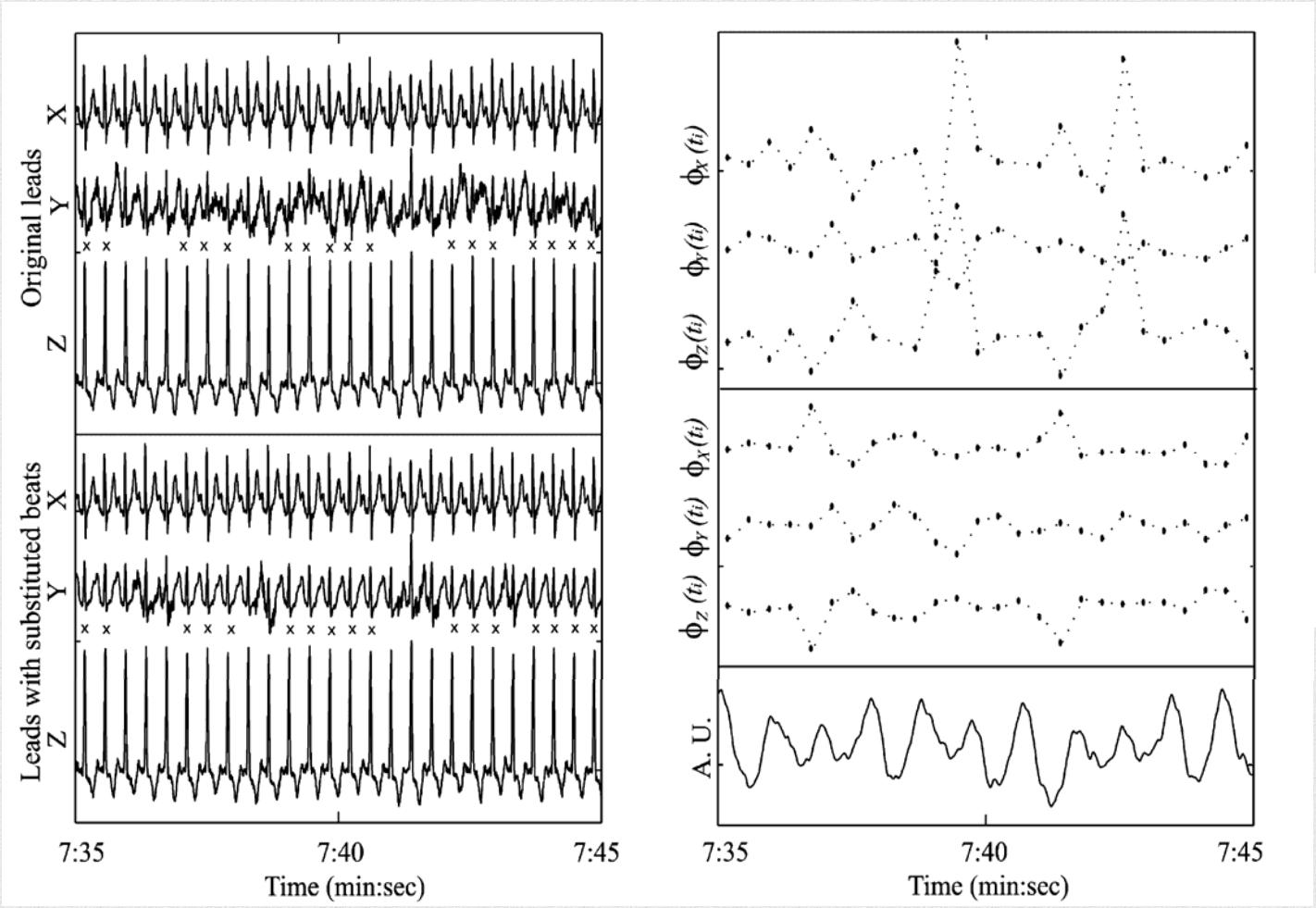
angles

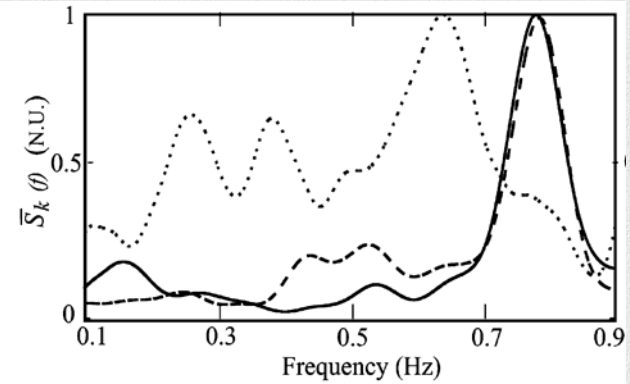


Rotation angles are the basis for respiratory signal estimation.

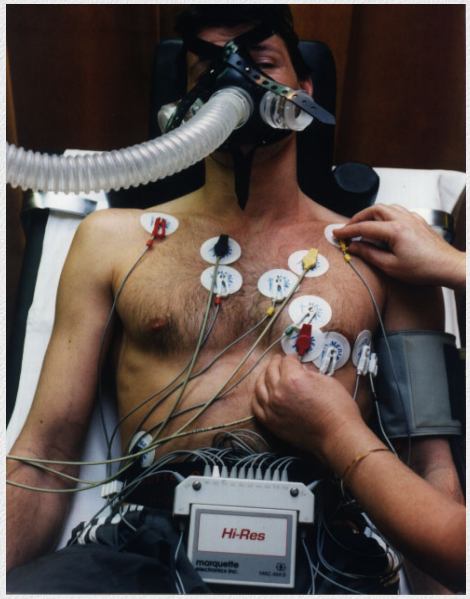
ECG derived respiratory frequency

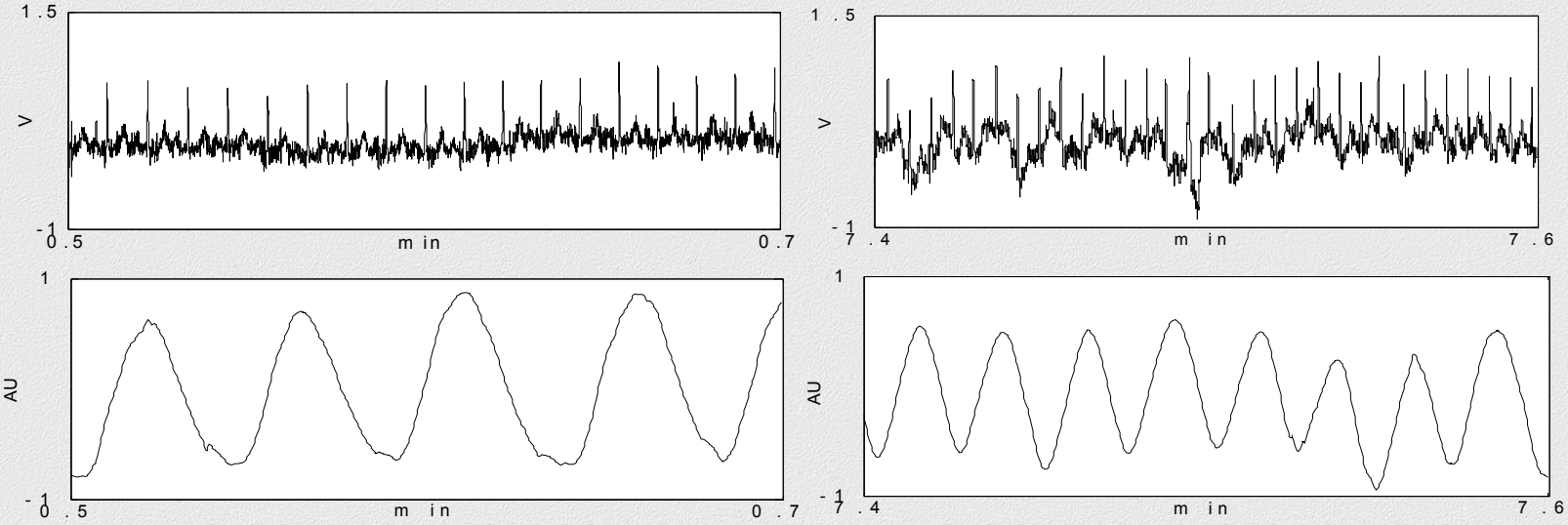
- **Beat substitution in low SNR leads**

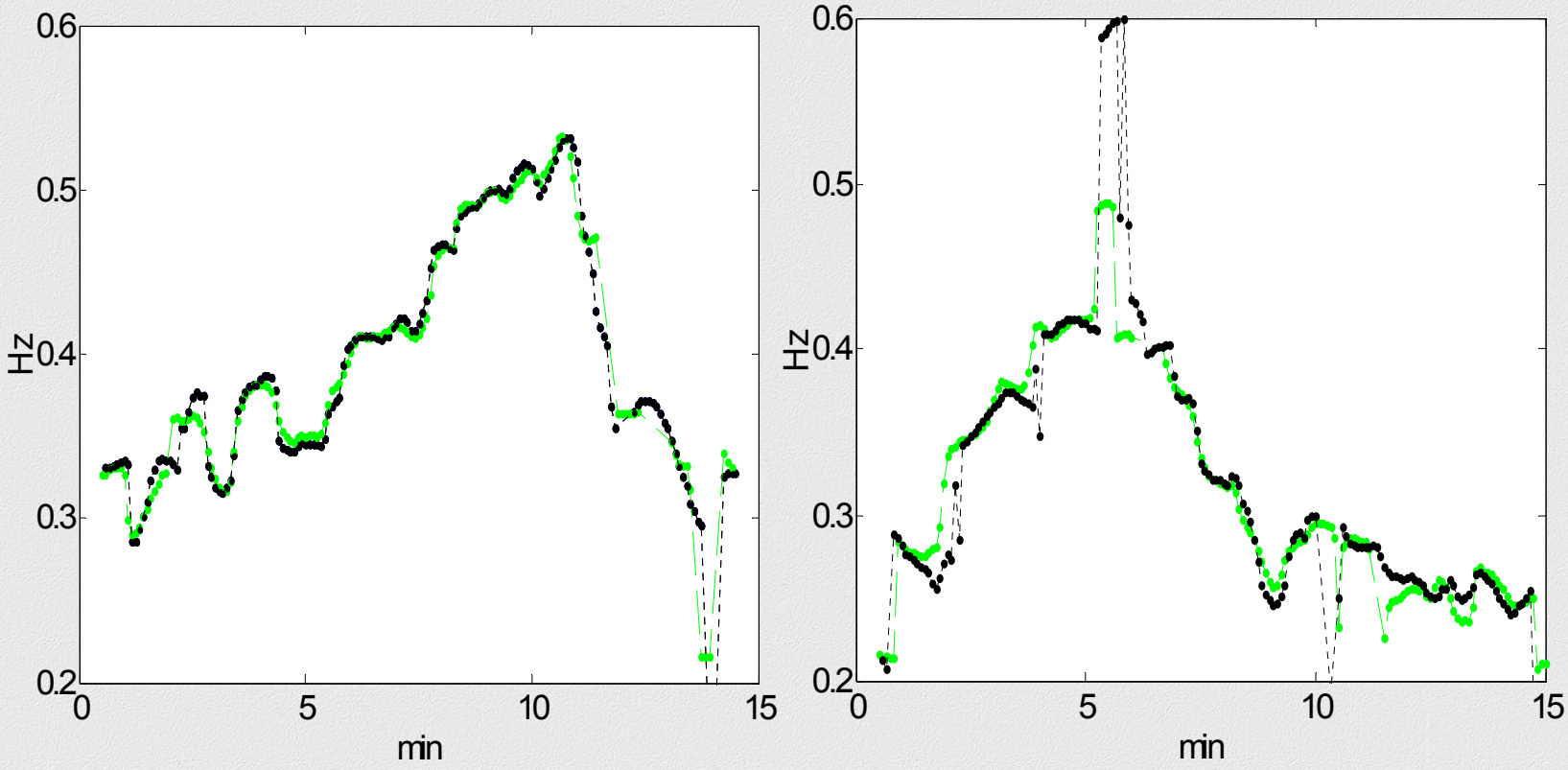




EDR Results


Hi-Res

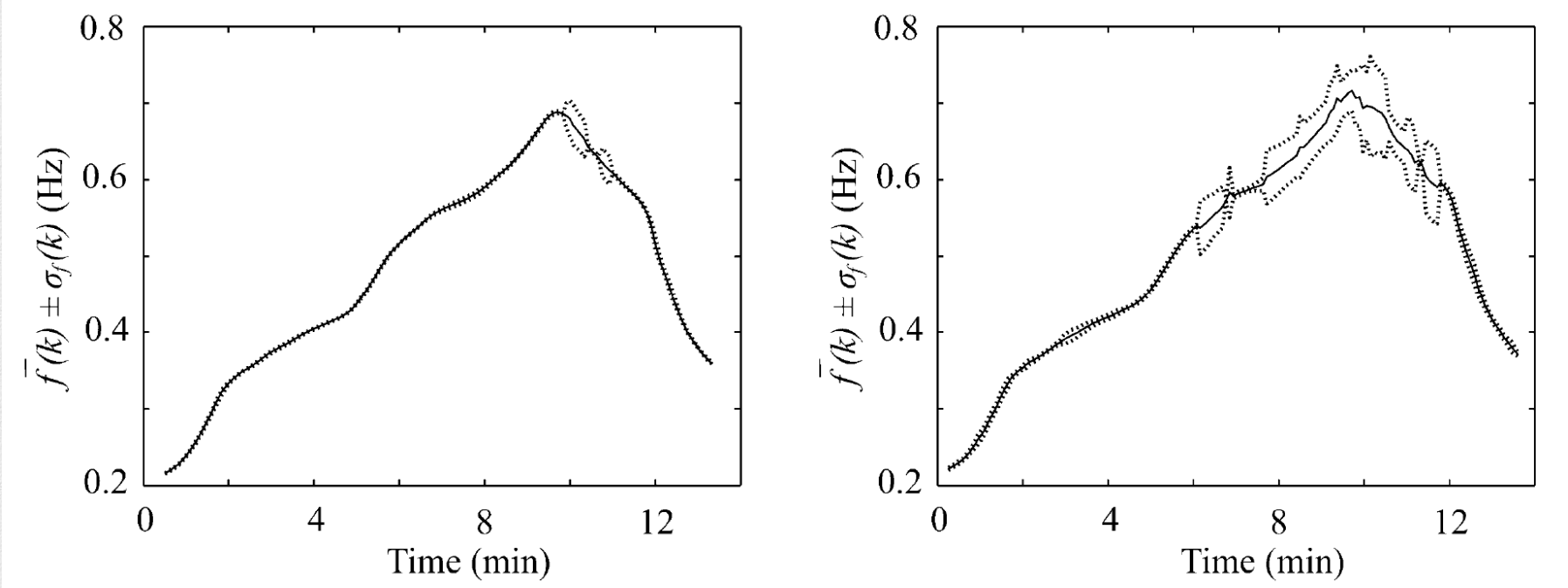

1.5
V
-1
0.5
min
0.7
1.5
V
-1
7.4
min
7.6
1
AU
-1
0.5
min
0.7
1
AU
-1
7.4
min
7.6


0.6
0.5
0.4
0.3
0.2
Hz
0
5
10
15
min
0.6
0.5
0.4
0.3
0.2
Hz
0
5
10
15
min

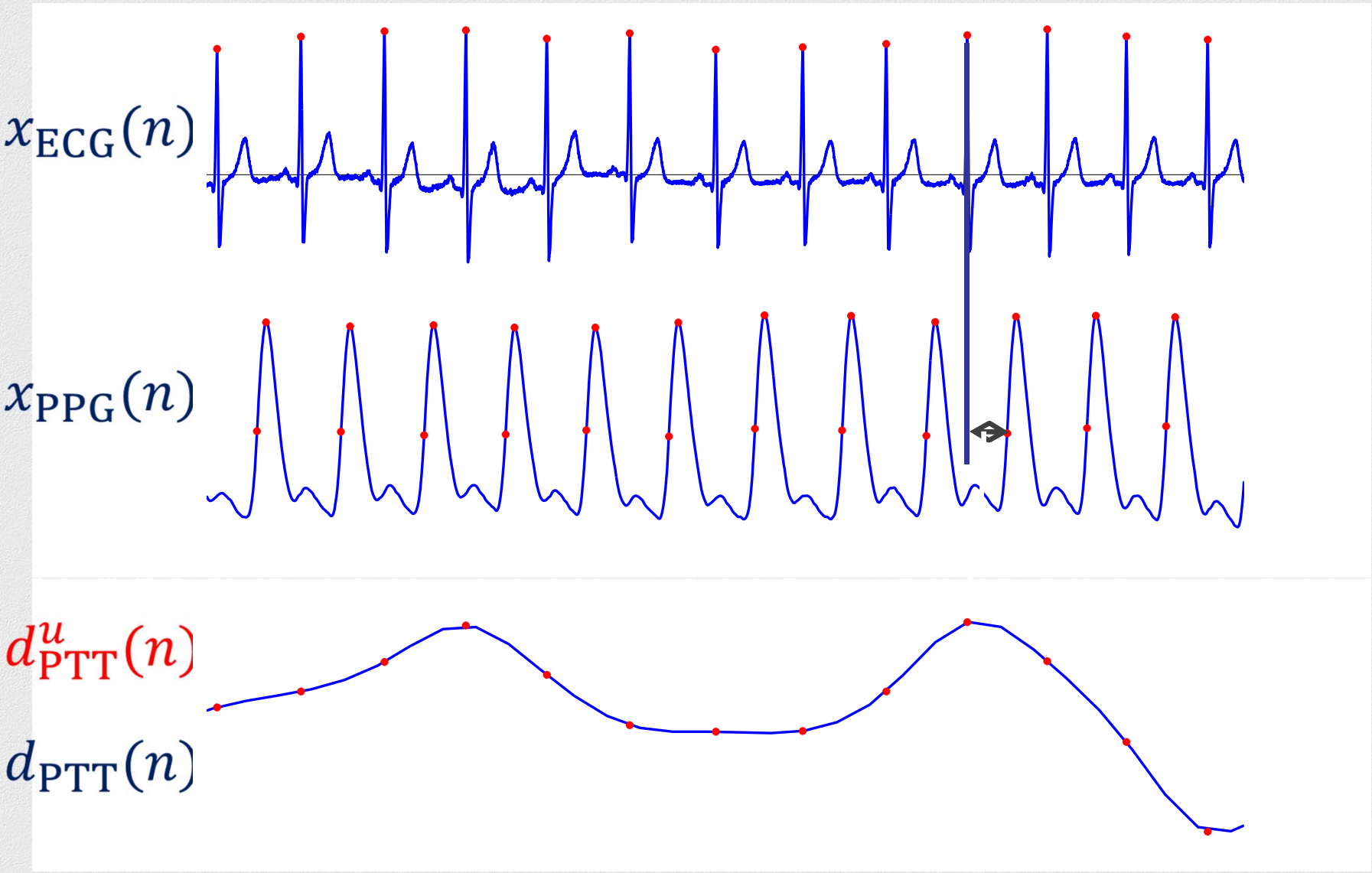
ECG derived respiratory frequency

- **Simulation study**

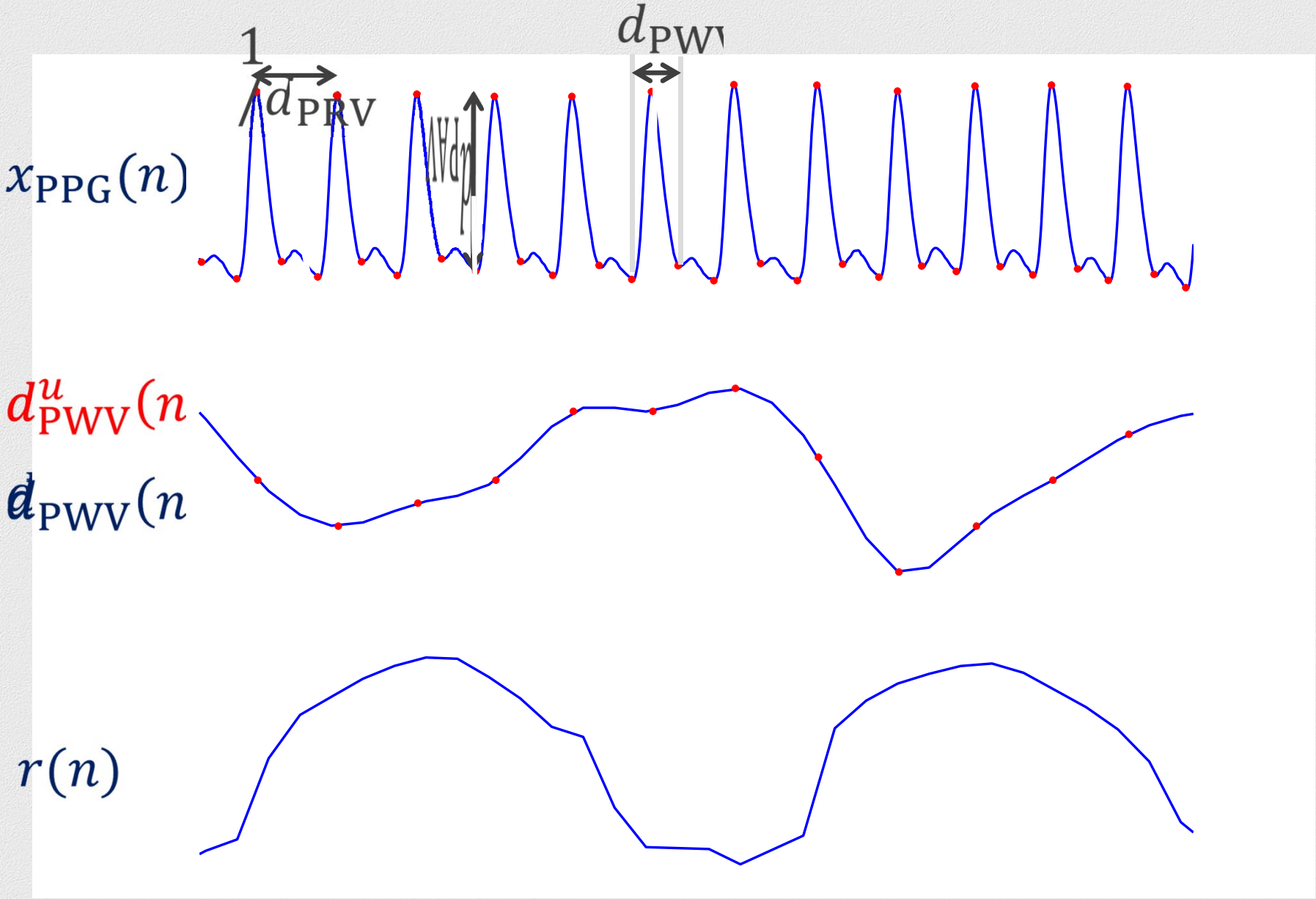
	QRS-VCG loop		Multi-lead QRS area	
	μ	σ	μ	σ
Hz	0.002 ± 0.001	0.003 ± 0.004	0.005 ± 0.004	0.009 ± 0.012
%	0.5 ± 0.2	0.7 ± 0.8	1.0 ± 0.7	1.7 ± 2.0
T%	96±2		95±3	



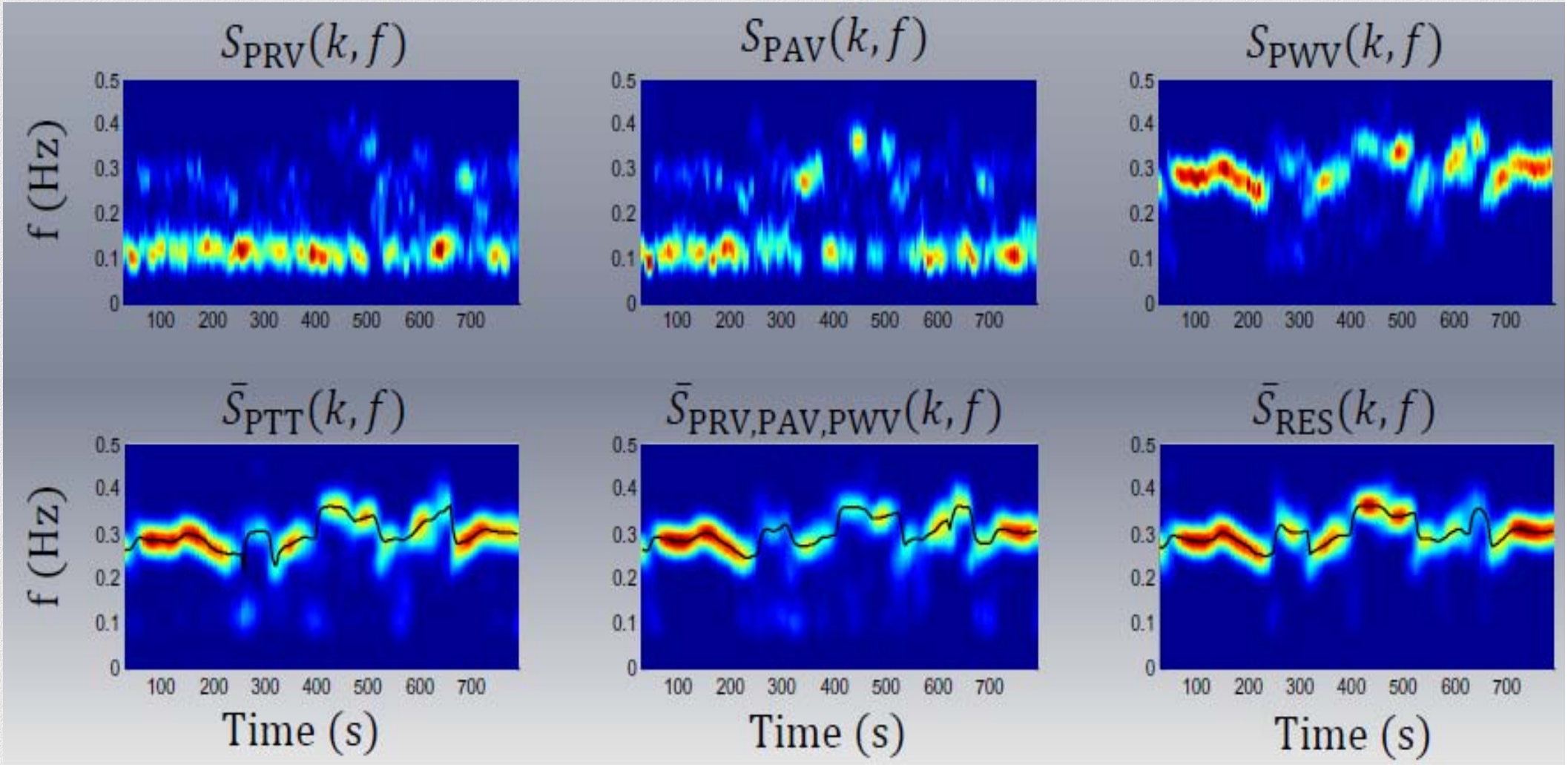
Deriving Respiration from the Pulse PPG Signal



Deriving Respiration from the Pulse PPG Signal



Deriving Respiration from the PPG Signal



	PWV		PAV		PRV		P_{COMB}		PTT		Φ_{COMB}	
	mean	std	mean	std	mean	std	mean	std	mean	std	mean	std
$\hat{f}_{RES} \geq 0.15\ Hz$	-1.03%	6.79%	-25.19%	19.63%	-22.87%	16.58%	-1.19%	5.40%	-3.37%	9.14%	0.71%	5.00%
$\hat{f}_{RES} < 0.15\ Hz$	5.21%	14.28%	2.33%	17.13%	4.92%	13.07%	1.45%	10.79%	6.71%	15.80%	3.55%	11.89%
All	1.17%	9.44%	-15.45%	18.75%	-13.07%	15.34%	-0.26%	7.30%	0.19%	11.49%	1.72%	7.43%

Conclusions

- **Physiology-oriented** processing allows **better extracting the information** hidden in the biomedical signal
- **Multimodal, Multiscale, Multidisciplinary** signal processing may add in diagnosis, therapy and follow-up of diseases
- No general solutions, **contextualization** is always required
- Biosignal analysis, usually not optimum, but still suitable for massive scrutiny and monitoring so making sense **go for the most**

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Thanks for your attention!