

The cardiac electrical activity

From the cells to organ

O. Meste

Biomed Team-I3S lab, Université Nice Côte d'Azur, France

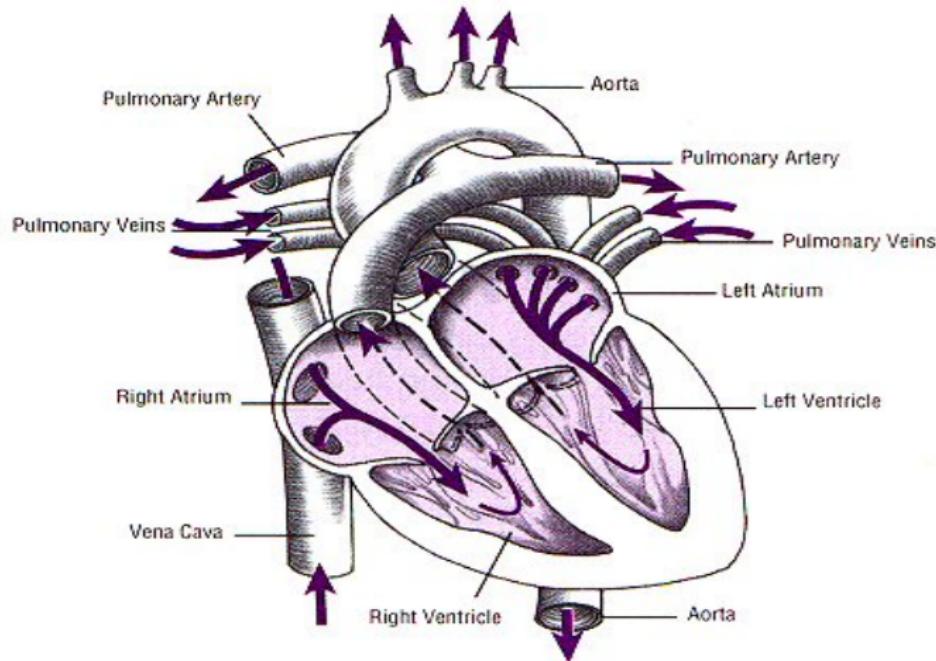
2024

Role of the heart

Main properties :

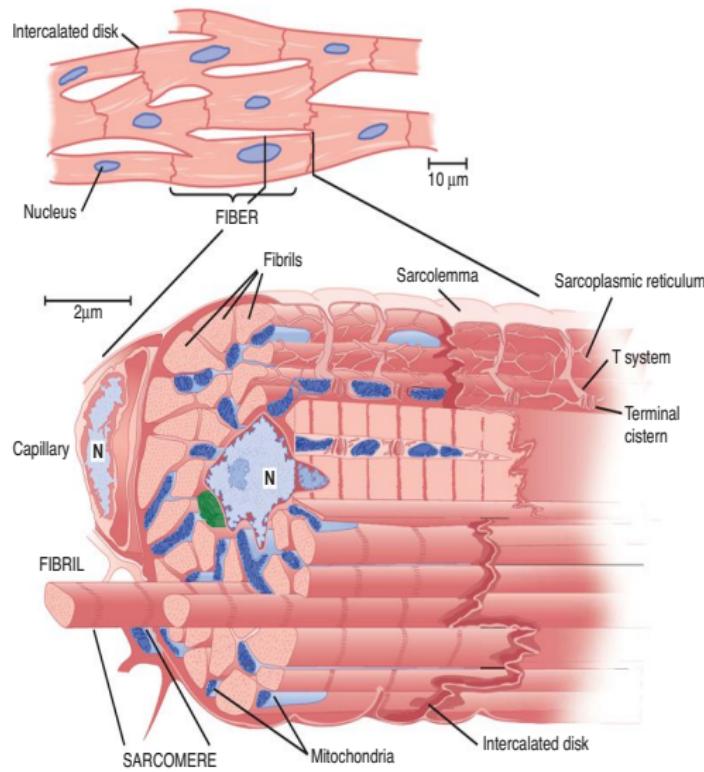
- Irrigates organs with oxygenated blood (itself)
- Mirror of successive activated regions
- Four chambers autonomous pump
- The Autonomous Nervous System (ANS) modulates the heart rhythm
(sympathetic ↗ and parasympathetic ↘ activity)

Blood Flow



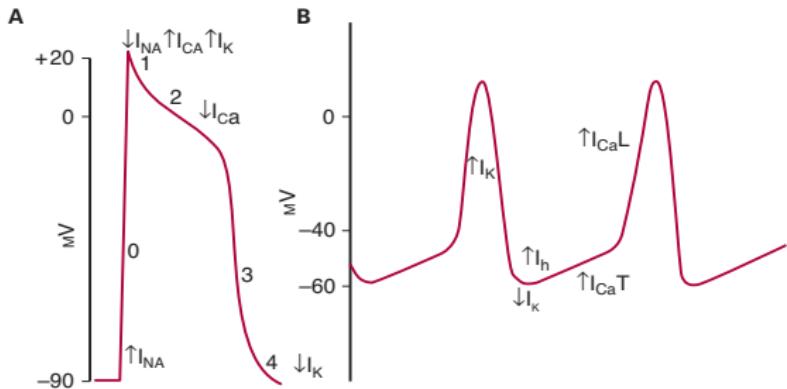
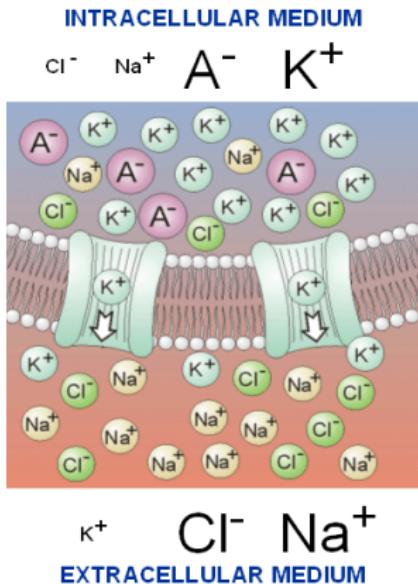
- Left Ventricle bigger than right
- More connections in the left auricle

Cardiac cells : cardiomyocytes and nodal tissues



- The cell type depends on the location in the heart
- Cardiac muscle and nodal tissue
- The cells are interconnected to a large extent (myocytes)
- The cells contract (myocytes) and spread electrical wavefront from one cell to another in any direction
- Different than skeletal myocytes (spindle)

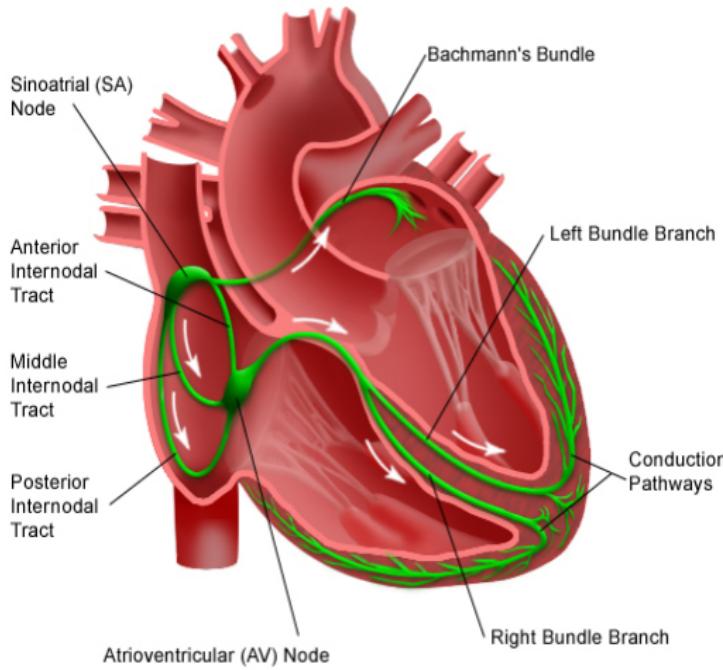
Focus on the electrical behavior of the cardiac cells



- The transmembrane voltage ($V_i - V_o$) changes with time : inflow (sodium) and outflow (potassium) of ions
- Depolarize and repolarize : Action Potential (AP)
- Contract and propagate information to adjacent cells
- Different AP profiles for cardiomyocytes (left) and nodal tissue (right)
- Possible automaticity (nodal) → depolarizes interconnected cells
- "Blind" (refractory) during the repolarization

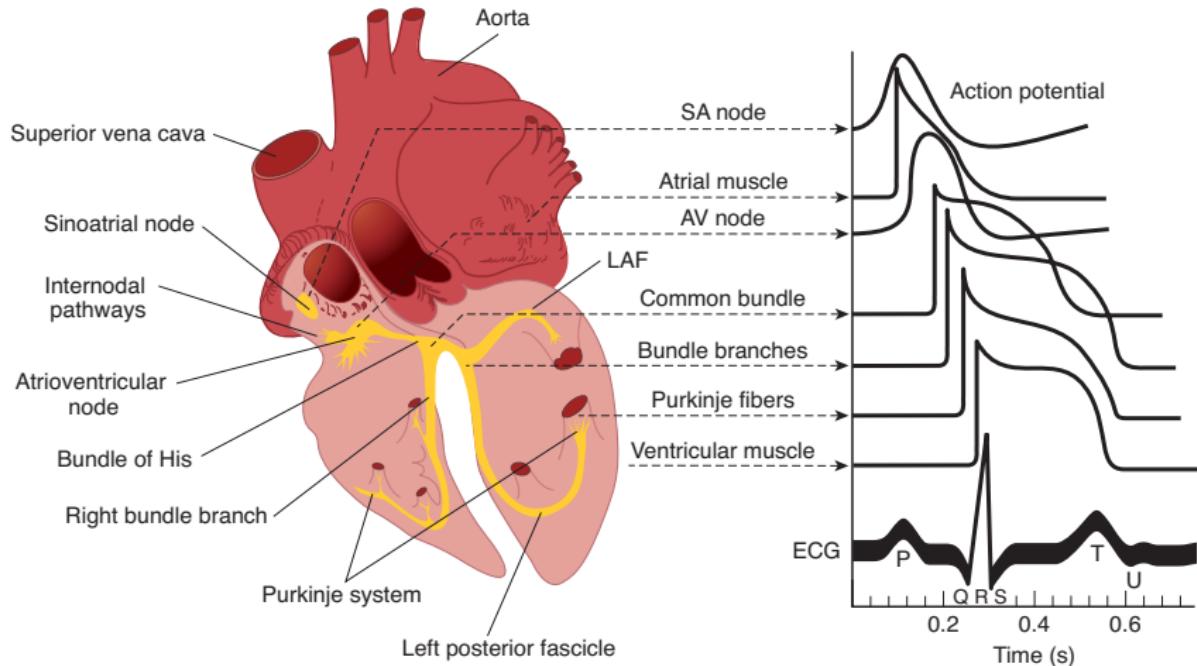
Dépolarization -> Contraction -> pumping

Electrical System of the Heart



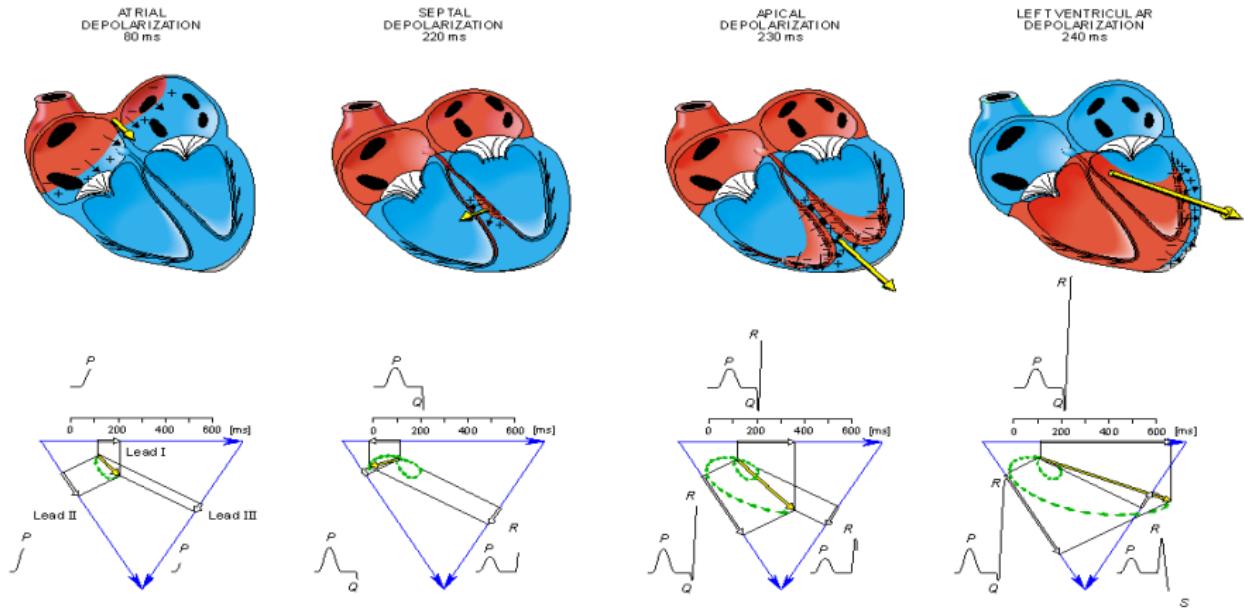
- At rest, the cells are repolarized
- The SA cells are spontaneously depolarized (alone 120 beats/sec)
- The depolarization wavefront covers the auricles
- The wavefront reaches the AV node that delays and blocks the stimulus
- The stimulus travels within the bundle branch (low velocity !)
- The ventricles are depolarized in sequence
- A wavefront raises a single dipole (approx.)
- The Refractory Period imposes a unidirectional wavefront
- The AV node protects the ventricles from frequent depolarization
- This cycle produces the heart beat, and so forth ...

ECG and depolarization/repolarization sequence

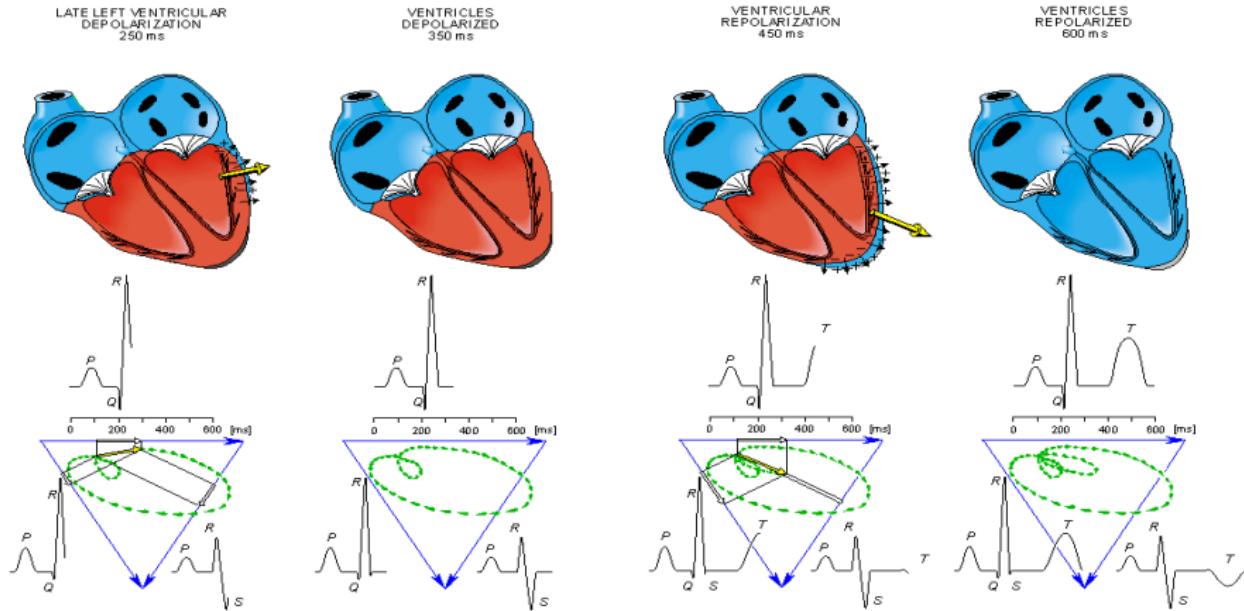


- ECG is recorded on the surface of the Body (**Easy**)
- ECG is not at all simply explained by the Action Potentials
- ECG reflects the sequence of Depolarization/Repolarization (**R-R, P-R, Q-T**), the Electrical pathway geometry, the volume conductor (Forward problem). (**Difficult**)

Heart cycles : The dipole changes explain the ECG (1/2)



Heart cycles : The dipole changes explain the ECG (2/2)



ECG acquisition

Main properties :

- Muirhead (1872), Einthoven (1901), Wilson (1944)
- Essentially on the body surface
- 12-leads standard ECG
- V5, aVF, V2 \approx X, Y, Z (vectorcardiography) or use the Dower transform
- Frank leads = X, Y, Z orthogonal leads system
- > 64 leads (BSPM)
- 12 bits-1KHz
- High dynamics : $1\mu\text{V}$ to 1V (baseline)

ECG leads

Note : for the unipolar leads the reference is $(V_{la}+V_{ra}+V_{ll})/3$

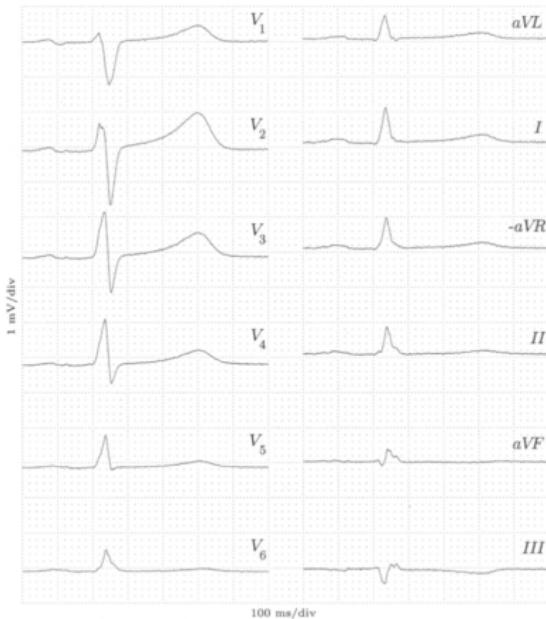


Figure 6.5: The standard 12-lead ECG with bipolar limb leads (I, II , and III), augmented unipolar limb leads (aVF, aVL , and $-aVR$), and unipolar precordial leads (V_1, \dots, V_6). The ECG was recorded from a healthy subject.

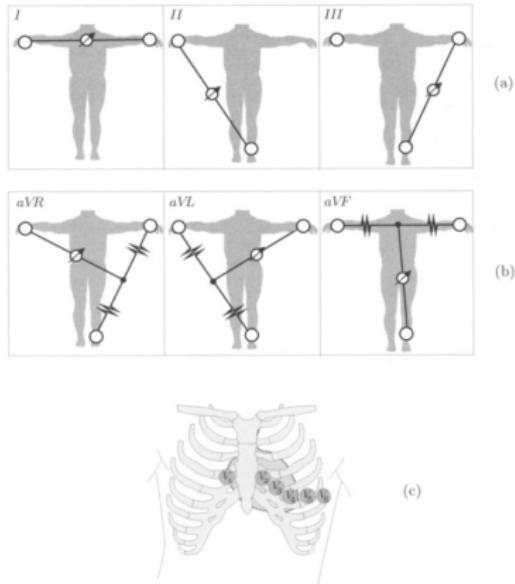
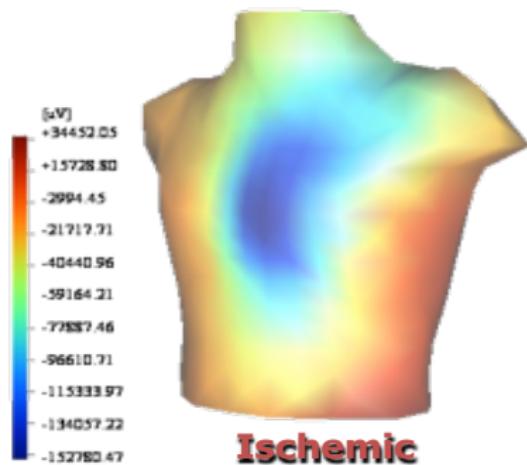
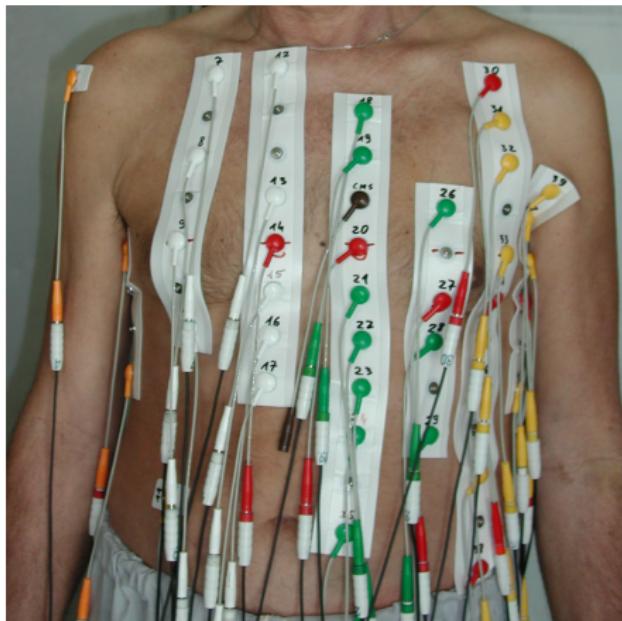


Figure 6.6: Electrode positions for recording (a) the bipolar limb leads I, II , and III (together these three leads define Einthoven's triangle), (b) the augmented unipolar limb leads aVR, aVL , and aVF (the output signal is measured between the two resistors), and (c) the precordial leads V_1, \dots, V_6 .

ECG leads : BSPM 64 leads



Mapping of the T wave surface

Vectorcardiography

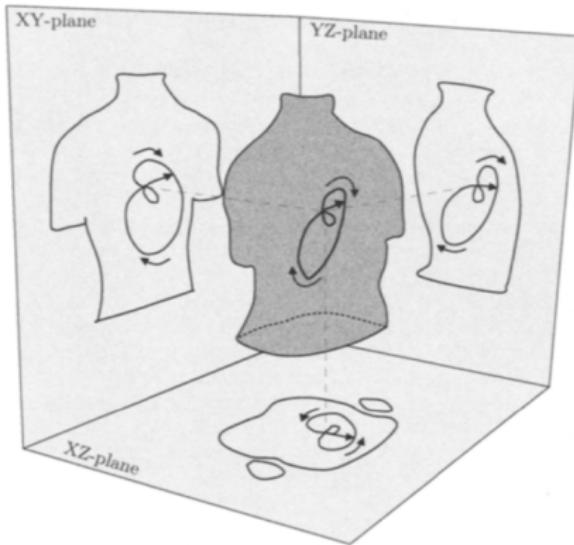
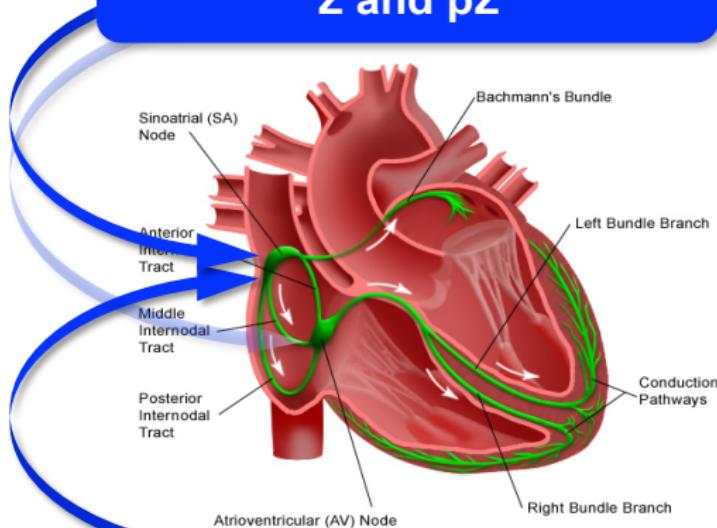


Figure 6.8: A vectorcardiographic loop and its projection onto the three orthogonal planes. The two arrows outside each loop indicate the direction in which the loop evolves.

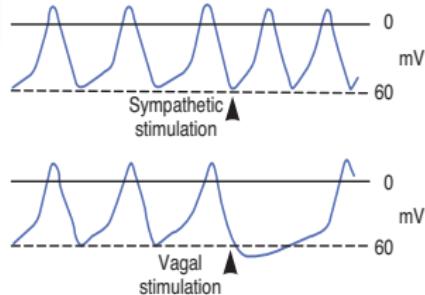
- Presence of loops
- Spatial representation of the dipole

Depolarization sequences influenced by Autonomous Nervous System

NEURAL influences Σ and $p\Sigma$

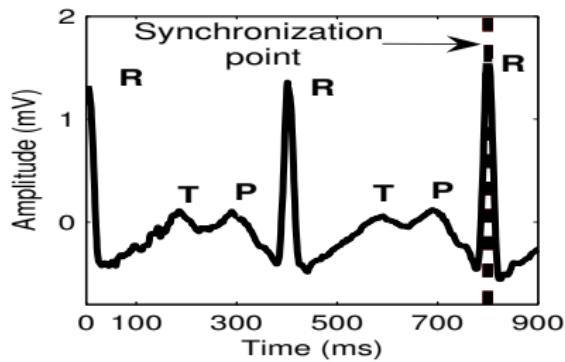
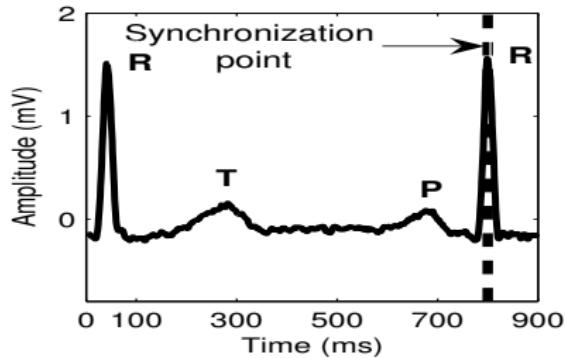


NON NEURAL influences Hormones / Mechan. stretch



- ANS : sympathetic (slow) and parasympathetic (fast) nerves
- Beating initiates at the SA node.
- Nodes are subject to ANS influence
- SA node affected by stretching
- ANS (Σ and $P\Sigma$) has a key role
- Depolarizations follow a sequence

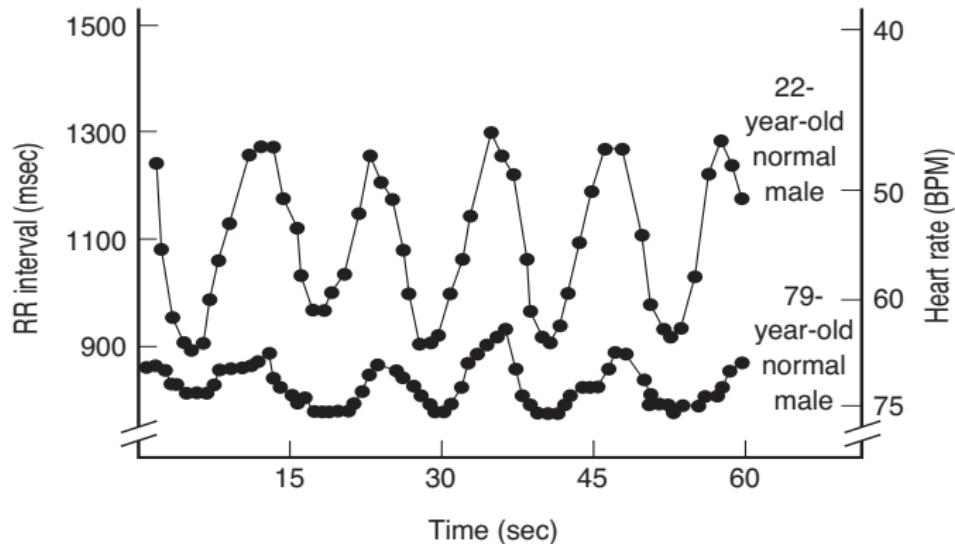
Stress test example



During exercise :

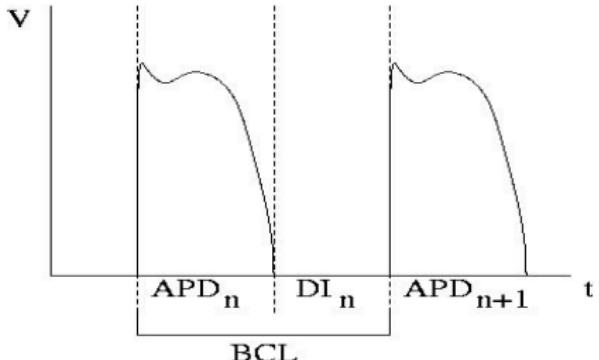
- Body demand changes
- ANS adapts to the demand
- (Symp.) $\Sigma \nearrow$ and (Vagal) $P\Sigma \searrow$
- RR, PR, RT (QT) \searrow (Adaptation)
- But also subtle **variability** of the intervals : RSA, MSA, ...

Respiratory Sinus Arrhythmia (RSA)

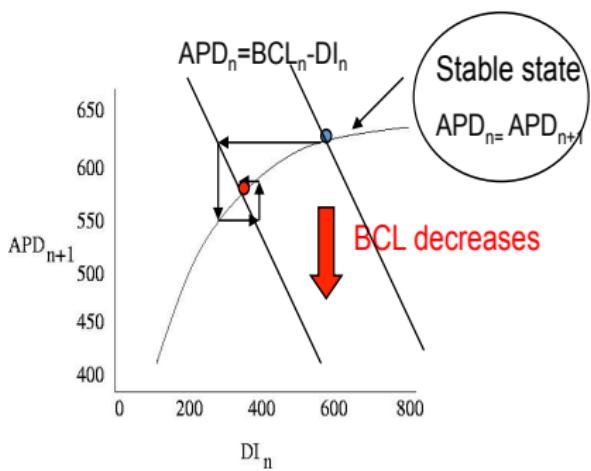


- Primarily due to the stretch receptors in the lungs connected to ANS
- The ANS Vagal-(PΣ) slightly modulates the Heart rate to benefit from the full lungs (oxygen)
- If the PΣ withdraws then the RSA is canceled

Dynamic of the AP & Restitution Curve



- The APD mostly represents the repolarization phase (T wave)
- $DI=diastole$
- $BCL=APD+DI=ECG\ RR\ interval$
- $APD(n+1)$ is function of previous $DI(n)$: **restitution curve**
- APD dynamically adapts



- RR changes : straight line moves
- Instability may occur !**
- T wave alternans

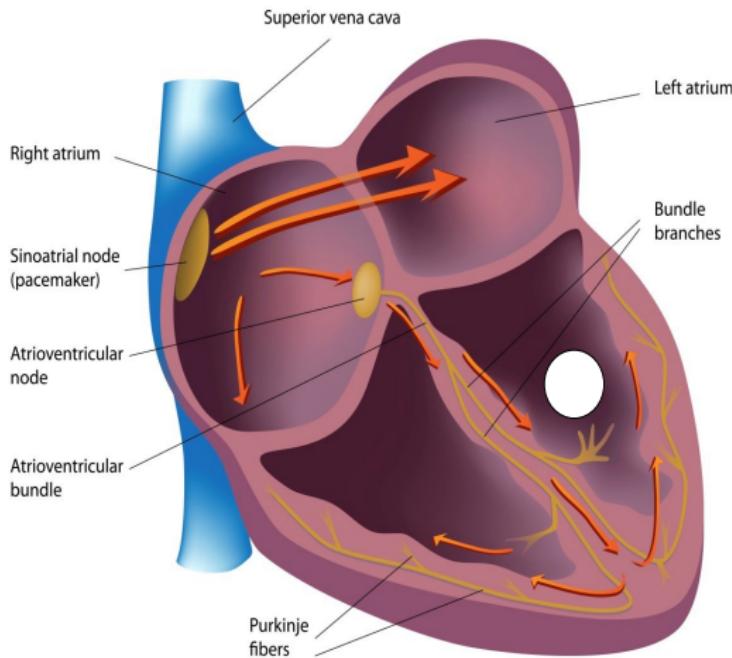
From cell to the organ

Aim of this talk : Illustrate how the electrophysiological knowledge improves the modeling and the processing of the ECG signals :

- Physiological and pathological cases
- Focus on different heart compartments
- Nodal or myocyte properties

I-Focus on the Ventricular Cardiomyocytes (Mice)-Harvard Med. Sch.

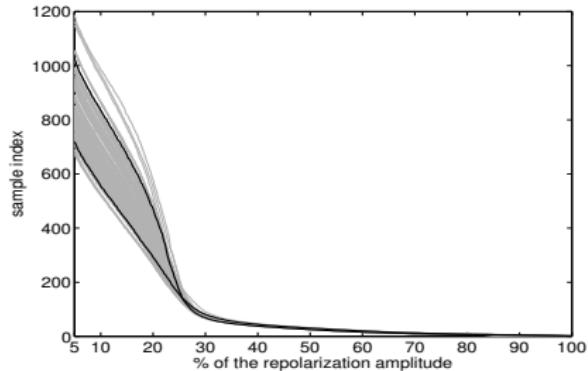
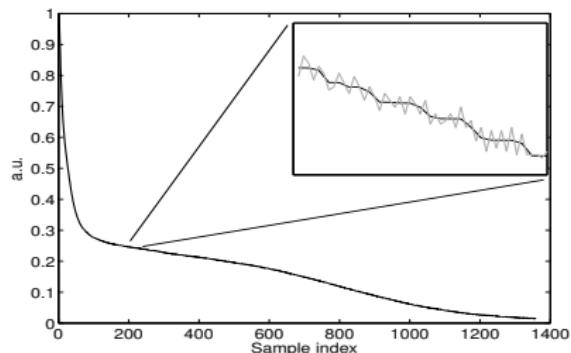
The Cardiac Conduction System



Compare the control and diabetic cells :

- Only repolarization periods
- Sequentially stimulated (2Hz)
- Automatic analysis
- Analyse the dynamics

Processing and Results

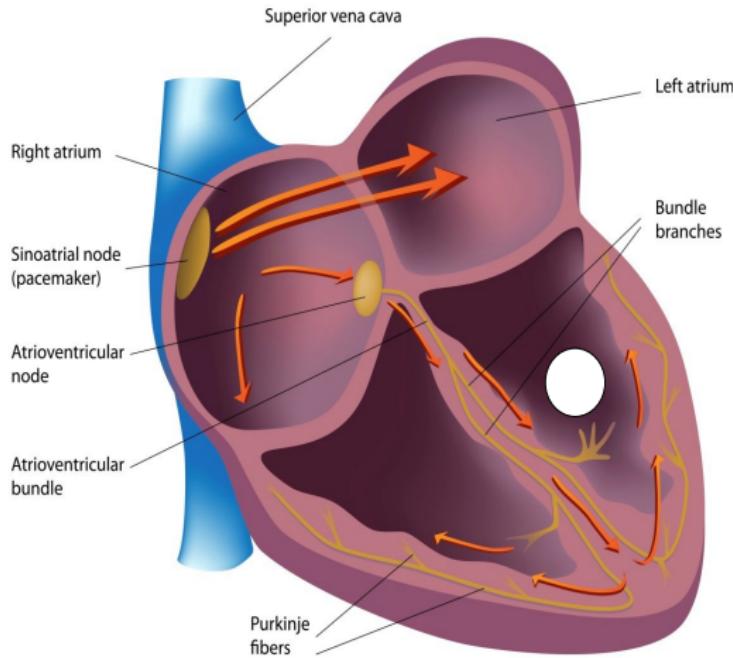


- The APs are smoothed with monotonicity constraints
- \Rightarrow the inverses of the functions are computed
- The width dynamics is assessed with Shape analysis methods
- Diabetic group significantly shortens (**some prolongate!**) the late repolarization phase
- The variability is very large (Cont. and Diab.) : **random behavior**

II-Focus on T waves duration-EPFL

→ Impact of the Restitution Curve properties (oscillation) over the Ventricular Repolarization

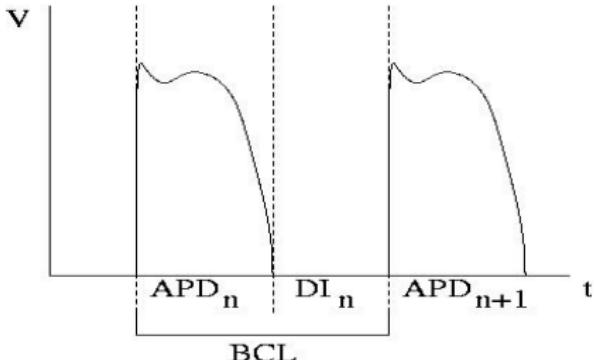
The Cardiac Conduction System



Explain the QT/RR adaptation based on the AP restitution curve :

- The macro level (organ) should reflect the micro level (cell)
- Assessment of repolarization disturbances (Ischemia)

Approximation and modeling



- The sum of all the Ventricular Cells AP almost explains the QT duration.
- The APD is mostly composed by the repolarization
- The BCL is similar to the Heart period (R-R)
- For a given BCL, the curve can be approximated by an affine function

We get for the fast adaptation :

$$APD(n+1) = aAPD(n) + aBCL(n) + b \quad (1)$$

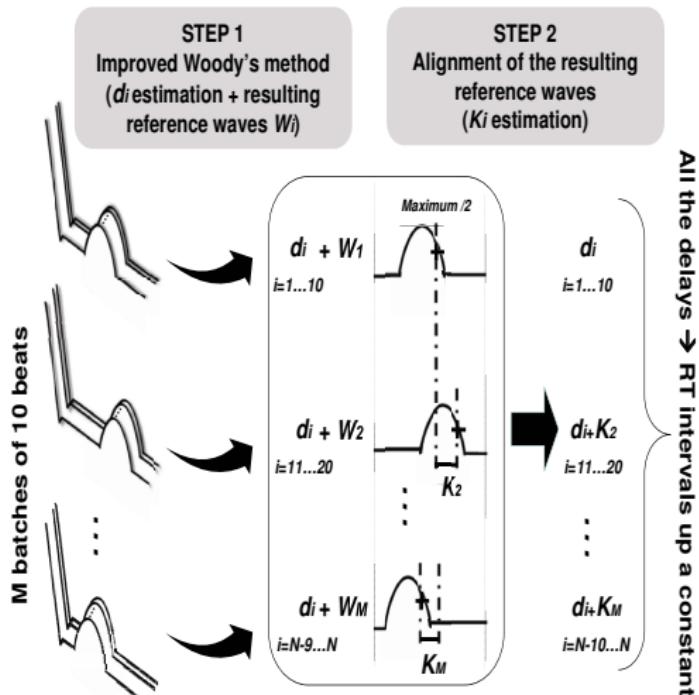
or

$$QT_F(n+1) = aQT_F(n) + aRR(n) + b \quad (2)$$

and for the slow (not explained by the Restitution Curve)

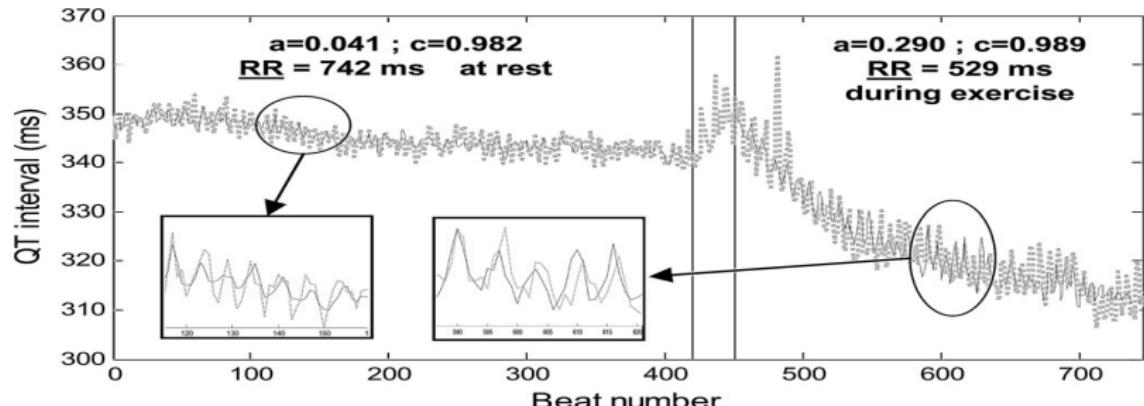
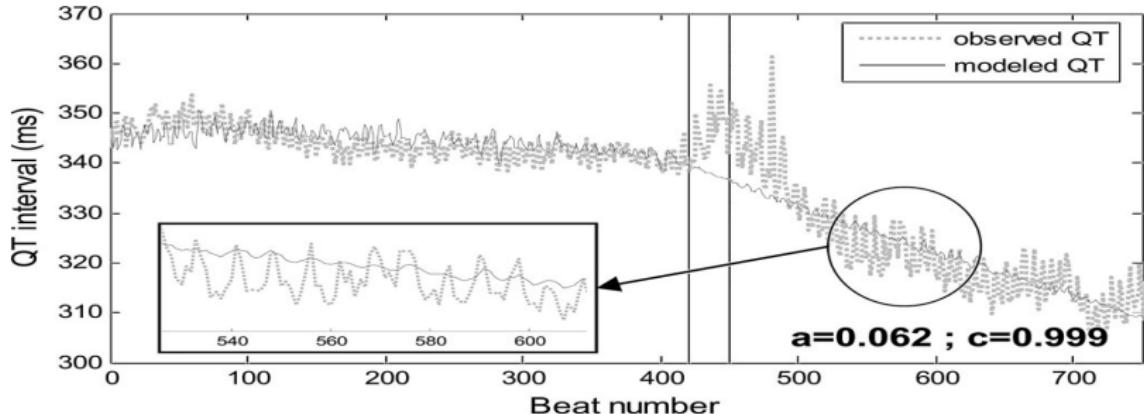
$$QT_S(n+1) = cQT_S(n) + RR(n) \quad (3)$$

QT(n) and (a,b,c) parameters Estimation



- We consider blocks of 10 waves for shape adaptation
- The QT(n) are estimated by using an original and optimal method
- The (a,b,c) are estimated by using alternated Least Square algo.

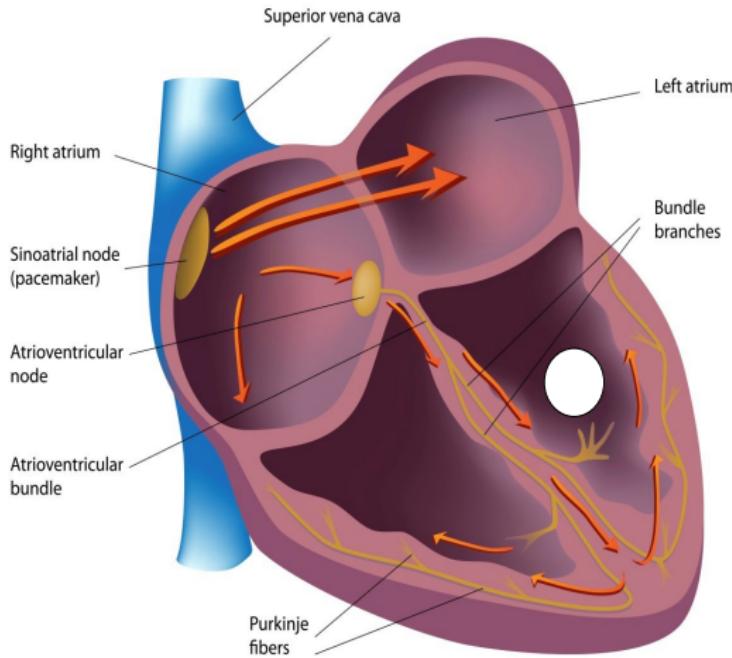
Example : exercise test (variable R-R)



III-Focus on T waves amplitudes-Acad. Sciences Poland

→ Impact of the Restitution Curve properties (oscillation) and AP randomness over T wave magnitudes

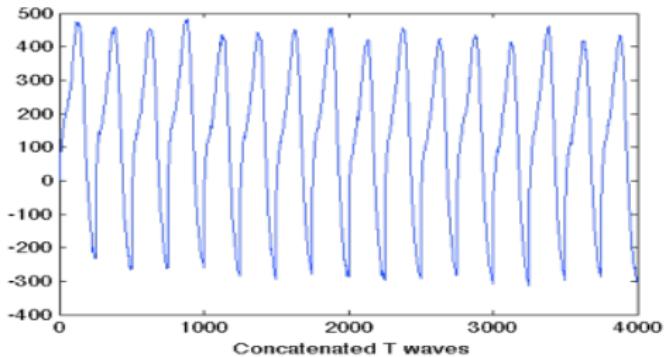
The Cardiac Conduction System



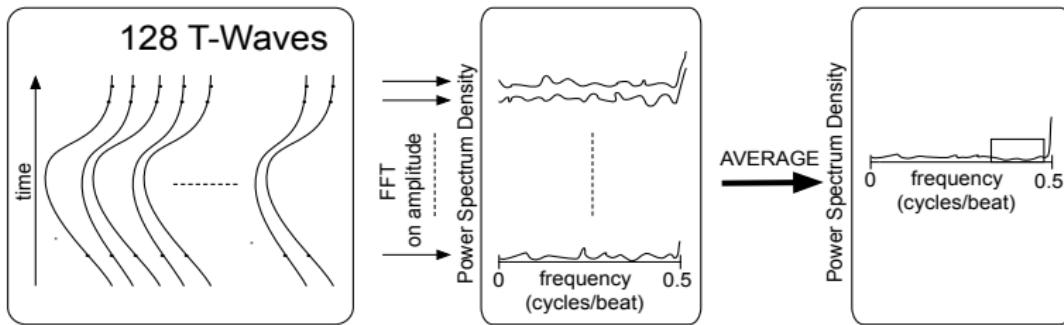
Compare the T waves magnitudes from Coronary Artery disease (CAD), Ventricular Tachy/Fib (VT/VF), Myocardial Infarction (MI), etc ...

- Segmentation of the T waves
- Apply typical TWA detectors
- Develop new robust detectors
- Set the detectors parameters with simulations

Example and typical method



- T waves are processed by blocks
- The typical detector is frequency based
- Alternative detectors are statistics based (t-test etc ...)



Detectors

$$SM = \frac{\bar{F}\{0.5\} - mean(\bar{F}\{[0.35, 0.45]\})}{std(\bar{F}\{[0.35, 0.45]\})} \quad (4)$$

$$Amp_i = \frac{1}{N} \sum_{n=1}^N (\bar{T}_{odd,i}(n) - \bar{T}_{even,i}(n))^2 \quad (5)$$

$$pttest = t_{test}(seq_{odd} - seq_{even}, 0) \quad (6)$$

$$ttest = t_{test}(seq_{odd}, seq_{even}) \quad (7)$$

To add robustness, new methods :

$$SMM = \frac{F\{0.5\}}{median(F\{[0, 0.5]\})} \quad (8)$$

$$MMPT = \frac{1}{K} \sum_{k=0}^{K-1} t_{test}(seq_{odd} - circ(seq_{even}, k), 0) \quad (9)$$

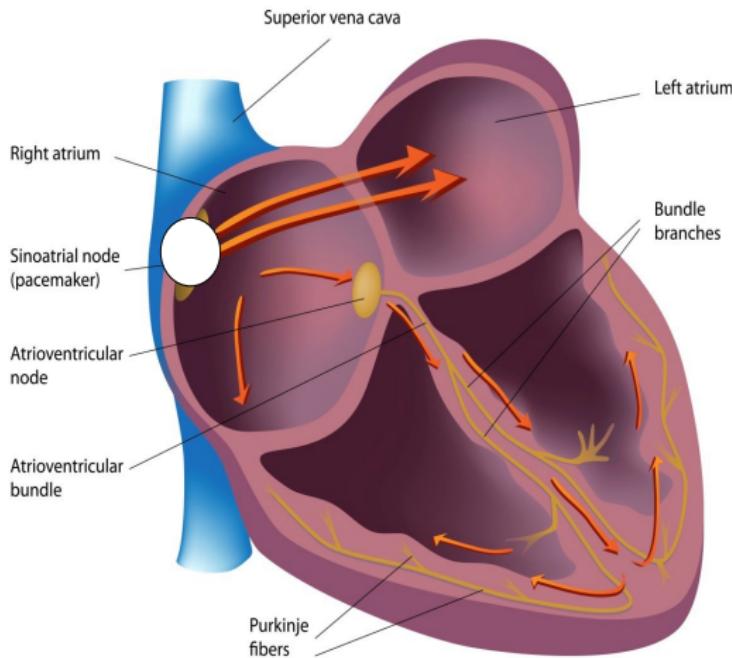
Results

Table – AUC values for all the methods considering separately VT/VF, CAD, MI status and their intersection \cap . Left and right values correspond to M and S transformations, respectively. Bold face type is applied when ranksum test for means comparison is < 0.05

Method	VT/VF	CAD	MI	\cap
<i>MMPT</i>	0.64 0.52	0.75 0.69	0.68 0.65	0.73 0.63
<i>SMM</i>	0.62 0.63	0.70 0.73	0.64 0.67	0.71 0.71
<i>ESM</i>	0.54 0.50	0.72 0.72	0.67 0.67	0.64 0.58
<i>ttest</i>	0.60 0.50	0.75 0.65	0.68 0.62	0.67 0.58
<i>pttest</i>	0.52 0.57	0.59 0.62	0.52 0.59	0.57 0.62
<i>glrt</i>	0.54 0.50	0.59 0.50	0.56 0.5	0.54 0.5
<i>SM</i>	0.45	0.58	0.60	0.6
<i>A_X</i>	0.65	0.61	0.60	0.73
<i>A_{min}</i>	0.71	0.51	0.53	0.72

IV-Focus on the Modulation of the Heart Rhythm/Period- Zaragoza

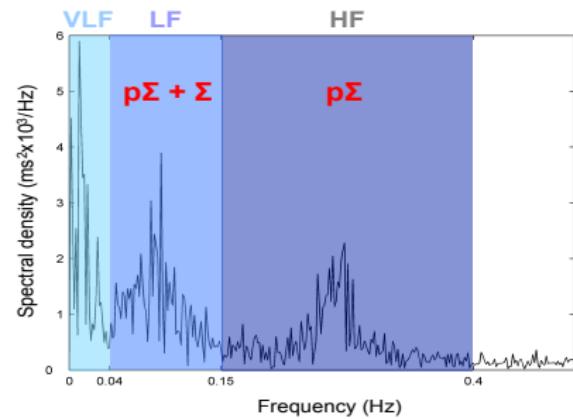
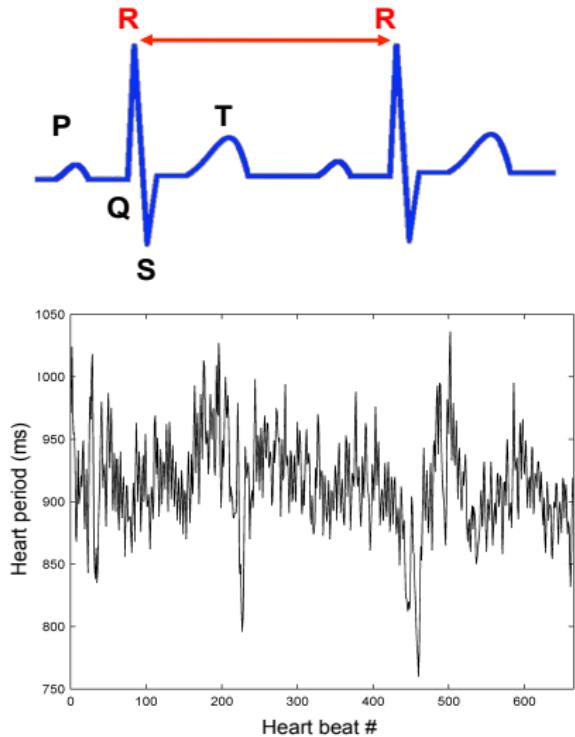
The Cardiac Conduction System



Heart is a not blind pump :

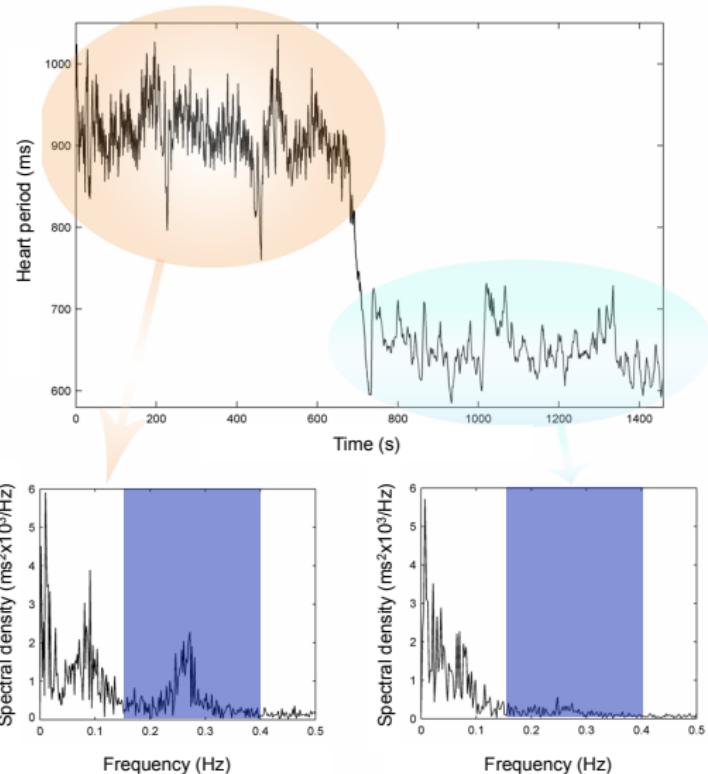
- Neural and Non neural affect the SA node
- ↘ or ↗ the PP (RR) and PR intervals
- Adaptation to body demands

HRV frequency analysis (steady)



- RR instead of PP
- Σ (slow) and $p\Sigma$ (fast)
- HF mostly respiration (RSA)
- baroreflex mechanism evidence

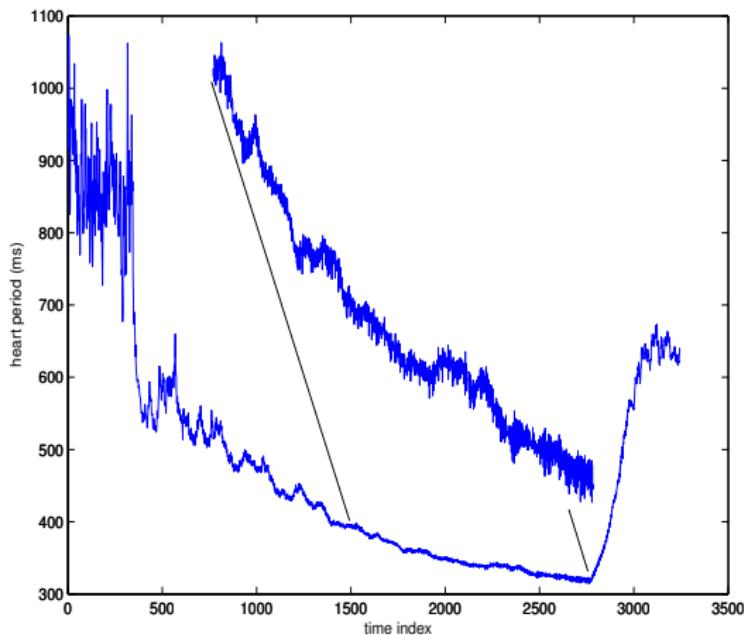
HRV frequency analysis (two steady states : tilt table test)



During tilt test table :

- Supine \Rightarrow Upright position
- Blood pressure regulation
- \nearrow heart rate or \searrow heart period
- $p\Sigma$ (vagal) \searrow
- quantification

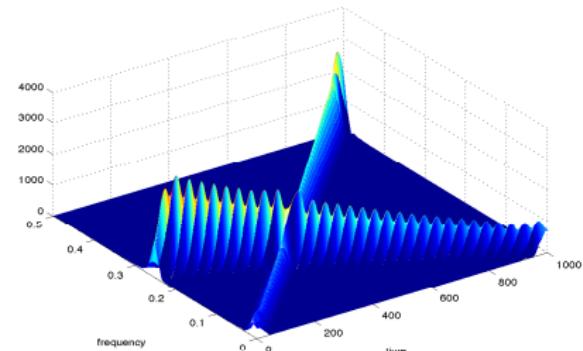
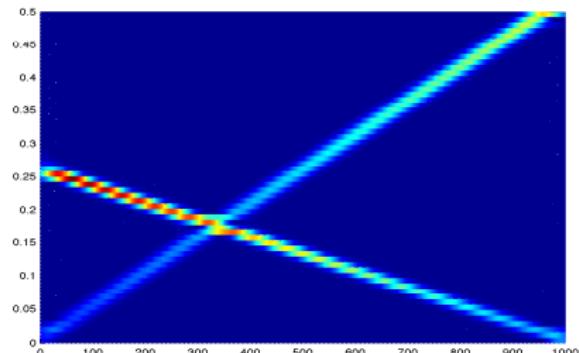
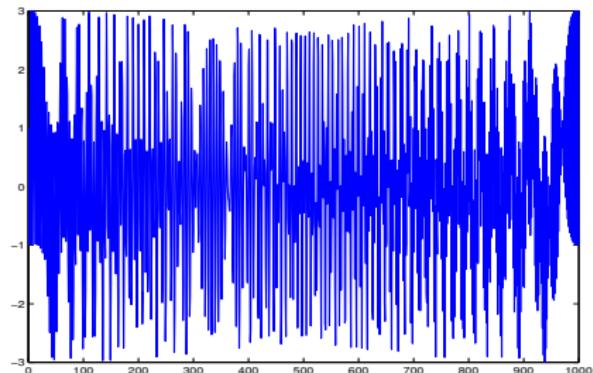
A more complex example



During stress test protocol (cycling) :

- The mean heart rate ↗
- The variability (Low-High) ↘
- The RSA ↘ (??)
- Mechanical influences ?
- Observation model ?
(self sampled signal !)
- Non-stationnary ?
(frequencies & amplitudes)
- Qualitative/Quantitative analysis ?
(local or global analysis)

Spectrogram for the non-stationarity



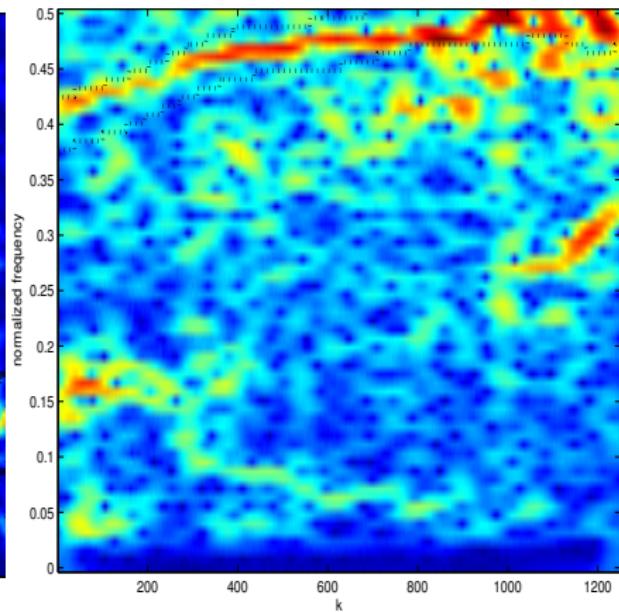
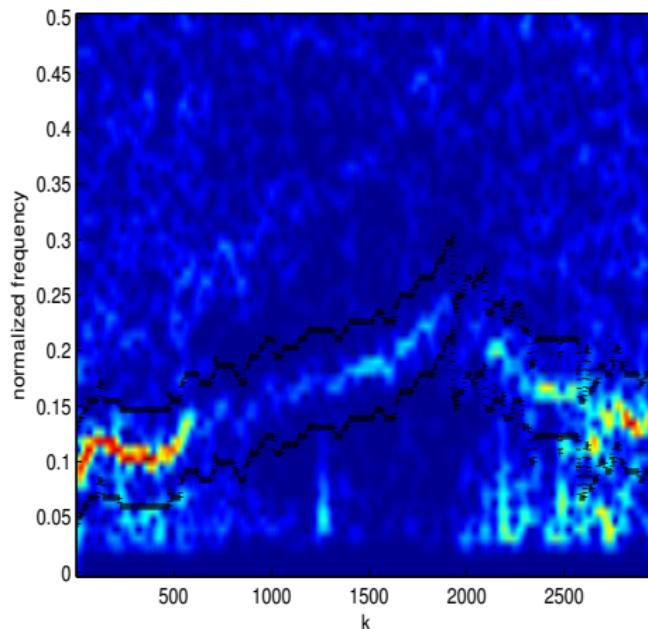
Defined by

$$S(t,f) = \left| \int m(s) h^*(s-t) e^{-i2\pi fs} ds \right|^2$$

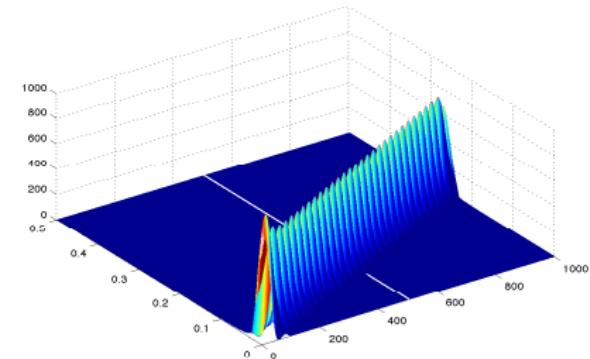
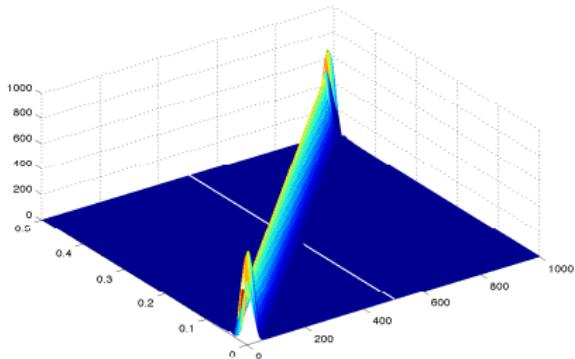
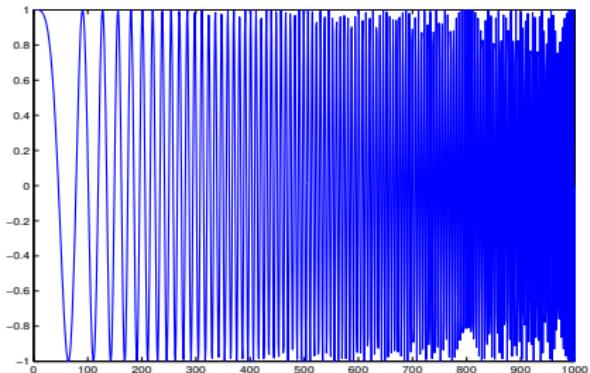
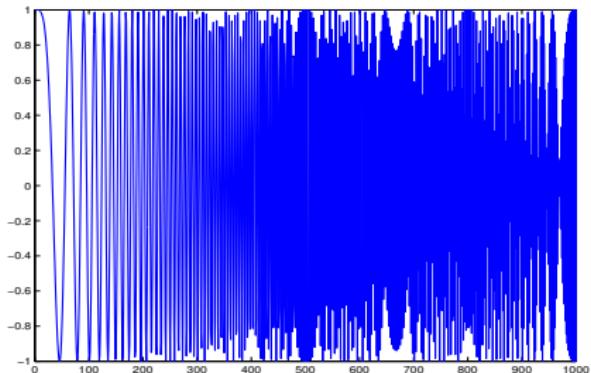
- Quadratic TFR (Cohen's class)
- Bad TF resolution
- But well located cross-terms !
- Closely related to the STFT (linear)

Spectrogram for the non-stationarity

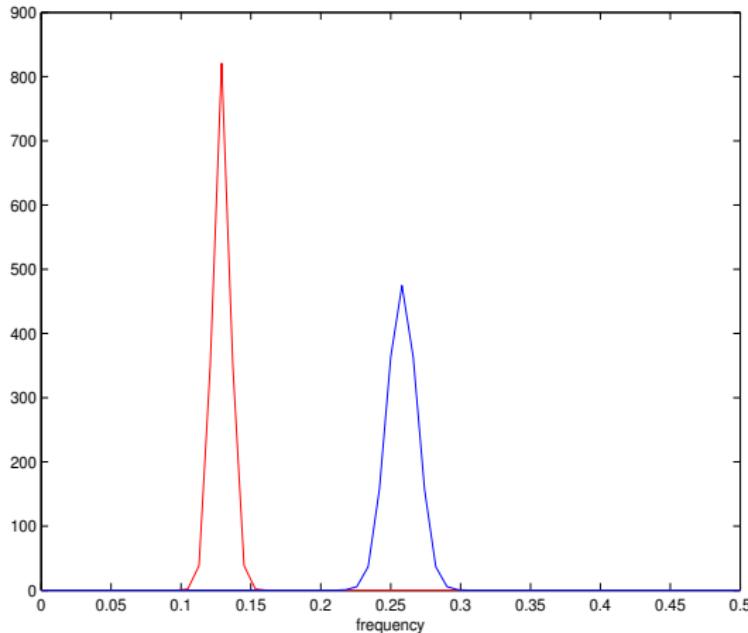
Needs quantitative assessment : not so easy with real data (noisy, multicomponent, ...) !



Chirp signals : different modulation rates, same amplitudes



Magnitude extracted from the TF plane ?



For a given t_0 (white line) :

- Different widths
- Different amplitudes
- Integrals are equal

⇒ OK for visual inspection but not for quantification !

TF processing (not developed here)

I) Magnitude of the modulation directly computed from the TF plane

$$R(k) = \sqrt{\frac{1}{K} \sum_{f=f_{obs}(k)-\delta}^{f_{obs}(k)+\delta} |M(k,f)|^2}$$

with $f_{obs}(k)$ the time-varying frequency of interest. $M(k,f)$ is the STFT of the R-R intervals variability.

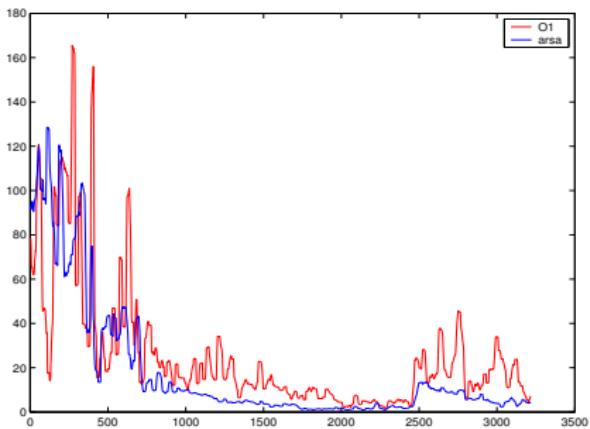
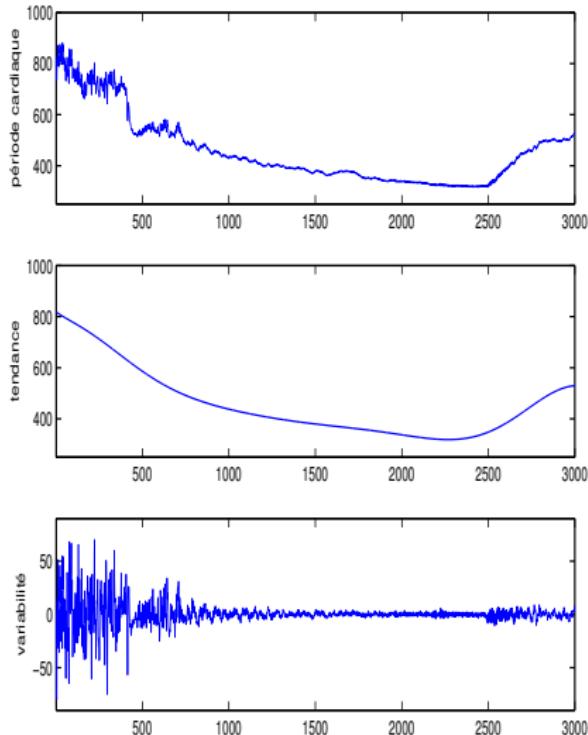
$$M(k,f) = \sum_u m(u) h(u-k) e^{-j2\pi \frac{\ell}{K} u}$$

with $-K/2 \leq \ell \leq K/2 - 1$ integer and $f = \ell/K$

The analysis window $h(u)$ is energy normalized.

⇒ Integrate over the given frequency range (the two black lines) !

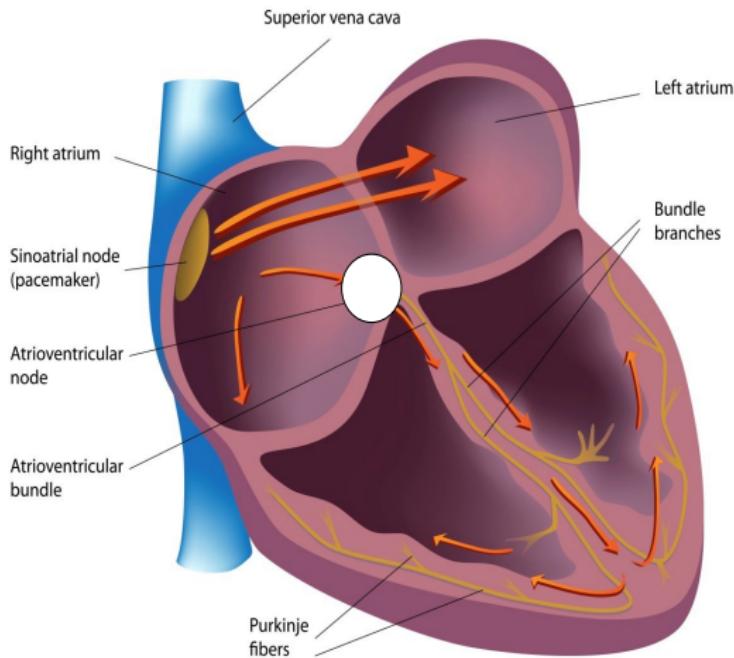
Simple example-ANS modulation of the SA node



- From the Heart periods series :
 - ▶ the trend $T(t)$
 - ▶ the variability (TF processed)
- Clear vagal withdrawal
- Strong vagal return

V-Focus on the Effect of the ANS on the AV Velocity Conduction

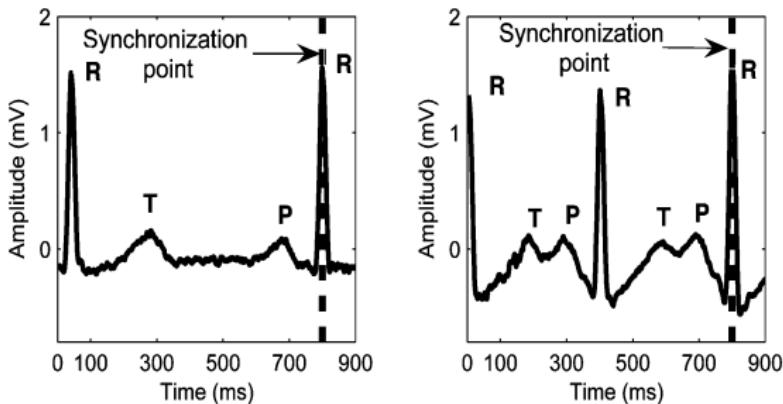
The Cardiac Conduction System



Strong vagal return visible in the Heart Rate Variability (SA node)

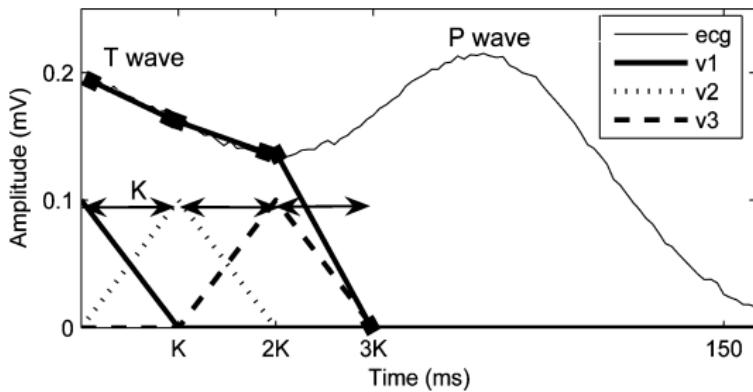
- Visible in the PR (includes AV node conduction)?
- Adapted to subject status (elite/sedentary) ?

PR intervals analysis-Observations modeling



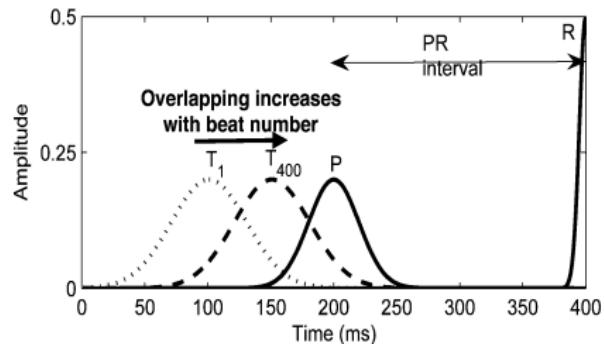
- ECG recorded during maximal exercise tests (cycling)
- Segmentation of RR windows
- P waves, delays, factors are unknown & T waves overlaps P waves
- The model is $x_i(n) = \alpha_i s_{d_i}(n) + f(n; \theta_i) + e_i(n)$ but $i = 1 \dots I$

PR intervals analysis-T wave modeling

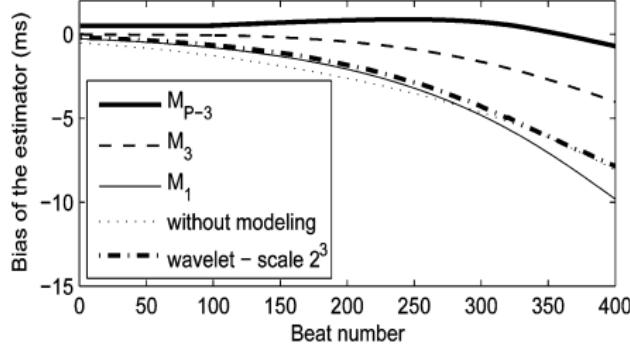


- T waves are modeled with sum of piecewise affine functions
- Monotonicity is imposed
- MLE : iterative LS problem with linear inequality constraint (LSI problem)

PR intervals analysis- Simulations

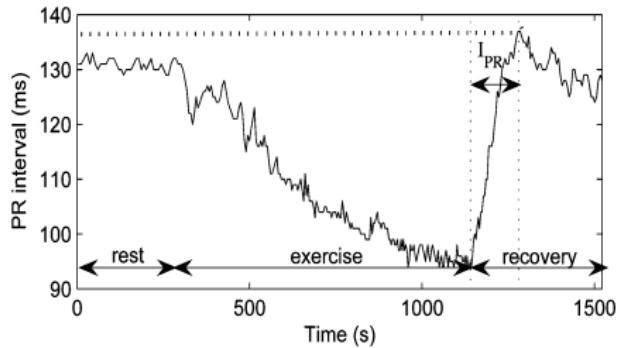


- Constant PR
- 400 overlapping T waves

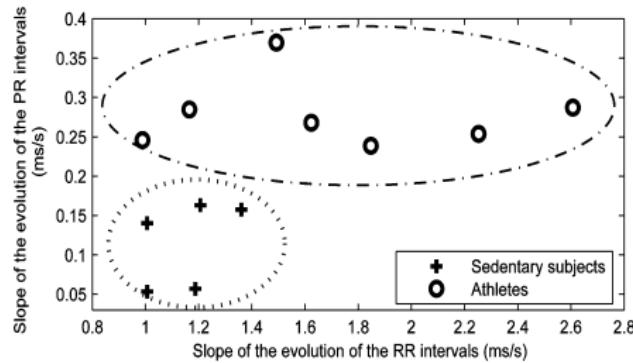


- Small bias
- Bias almost removed
- Justified by weak PR variations (real)

PR intervals analysis- Results slopes

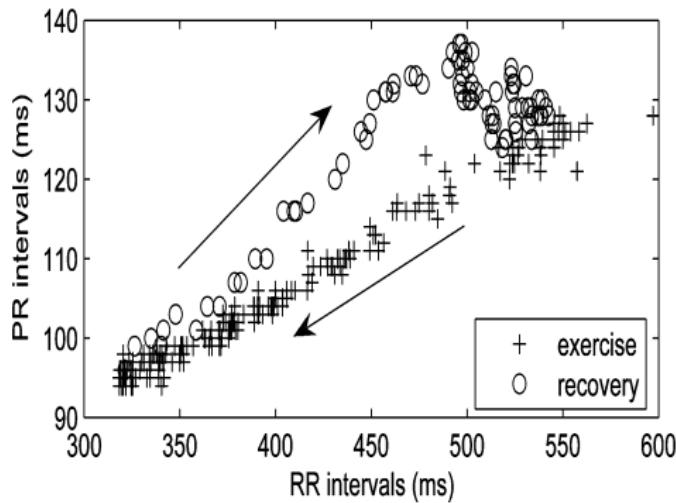


- Clear variation
- Overshoot during recovery
- focus on the slopes



- Athletes (professionals) & sedentaries
- Better clustering with PR slope

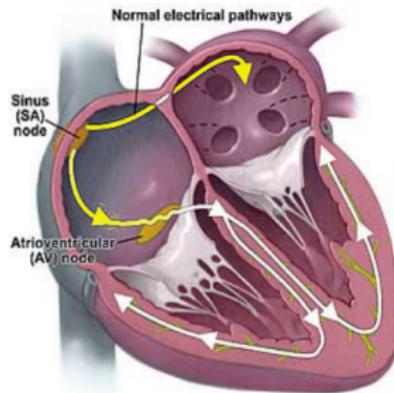
PR intervals analysis- Results hysteresis



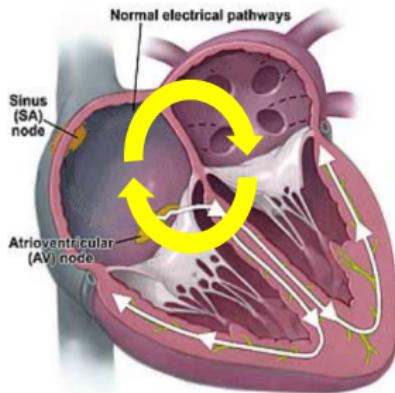
- Similar to overshoot
- Computed Hysteresis Area
- Original results
- Strong return of the vagal

T-wave model	SED	ATH
M_{P-3}	7.84 ± 2.52	13.49 ± 3.64
M_3	6.33 ± 4.32	13.35 ± 2.58
M_1	7.05 ± 3.12	9.70 ± 8.74

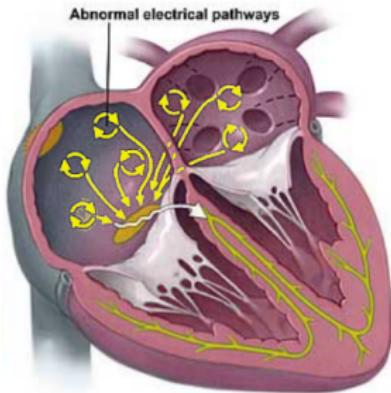
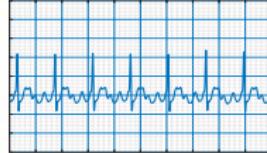
V-Supra ventricular Arrhythmias



Normal sinus rhythm



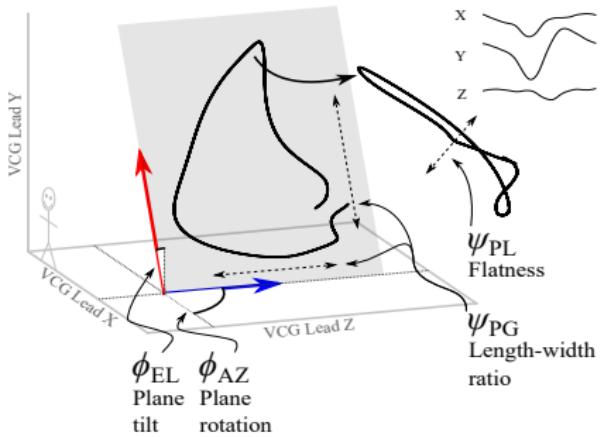
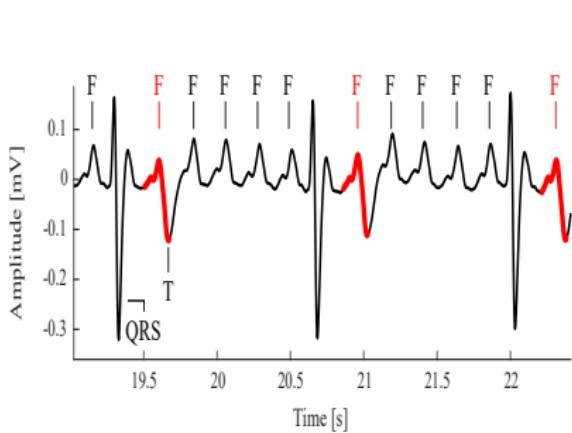
Flutter



Atrial fibrillation

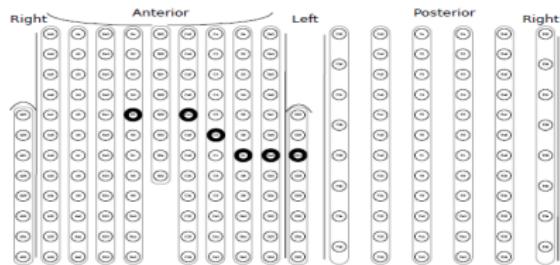


Flutter Characterization and classif. (L/R) - UniKL, Monaco

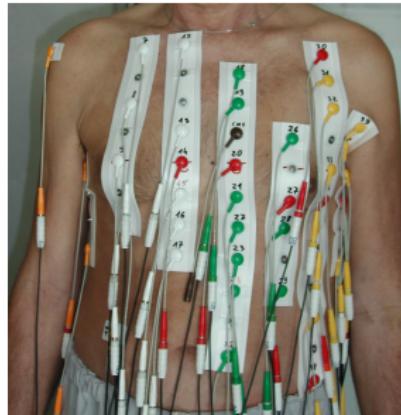


- High Heart Rate (75-150 beats/min at rest, single P waves replaced by F waves)
- Should be stopped → Sinus rhythm
- Stopped : cardioversion, medication, RF ablation
- **Detected** F waves loops can be geometrically characterized by using mean F waves (needs realignment) → **static** or by using each individual F wave → **variability**
- Machine learning methods and respiration cancellation → 0.95 Acc (L or R) with 8 Features

Analysis of Short-term Atrial Activity (PerAF), Maastricht



Theoretically



The real life !

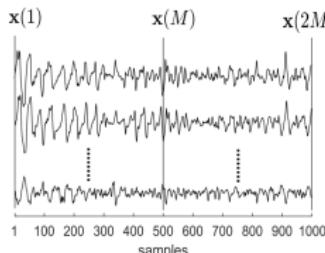
- 12-Leads system may not suffice (non homogeneous volume conductor)
- AF needs High-Resolution spatial/temporal (ECGi) —> 184 electrodes

A novel BSPM approach to capture short term atrial activity dynamics during AF :

- Based on recurrence spatial descriptor
- Capture more spatial/temporal details about AF
- Discriminate among patients characterized by very similar AF substrate complexity.

Recurrence spatial descriptor

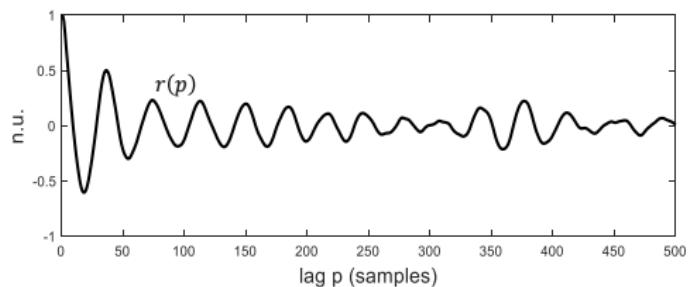
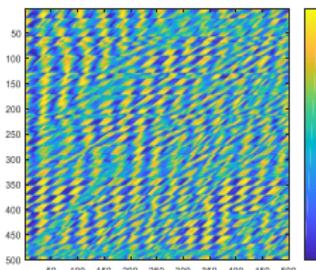
$$M = 500$$



$$p = \begin{matrix} 0 \\ 1 \\ \dots \\ M-1 \end{matrix}$$

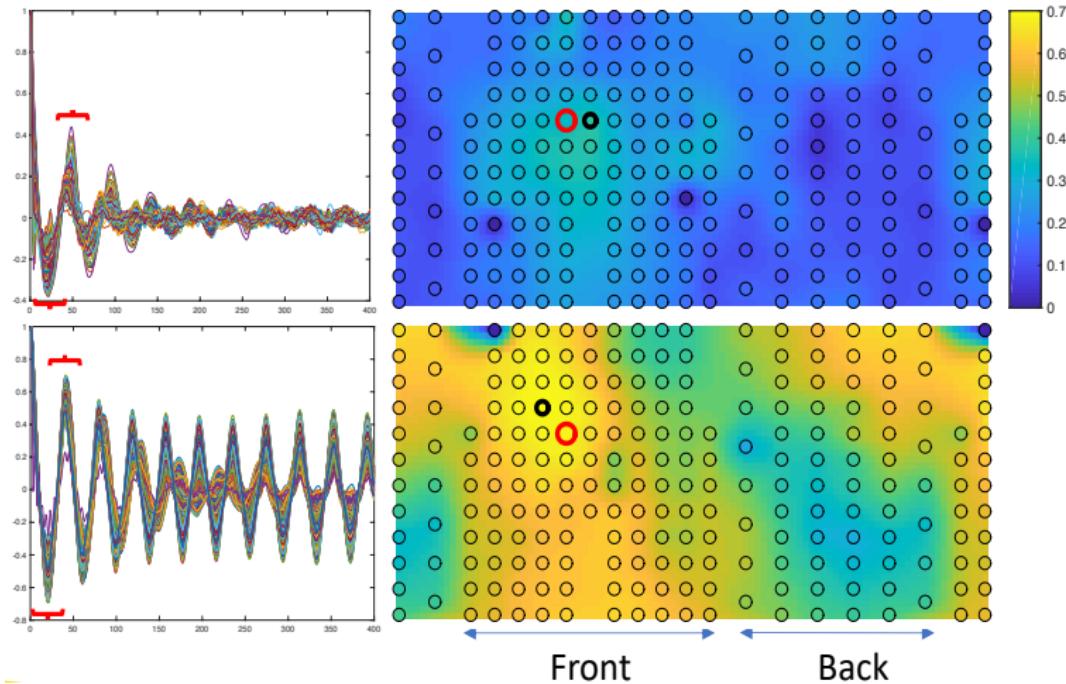
$$R = \begin{pmatrix} \cos(x(1), x(1)) & \cos(x(1), x(2)) & \dots & \cos(x(1), x(M)) \\ \cos(x(2), x(2)) & \cos(x(2), x(3)) & \dots & \cos(x(2), x(M+1)) \\ \vdots & \vdots & \ddots & \vdots \\ \cos(x(M), x(M)) & \cos(x(M), x(M+1)) & \dots & \cos(x(M), x(2M-1)) \end{pmatrix}$$

$$r(p) = \left(\frac{1}{M} \sum_{i=1}^M R_{i,1}, \frac{1}{M} \sum_{i=1}^M R_{i,2}, \dots, \frac{1}{M} \sum_{i=1}^M R_{i,M} \right)$$



- Needs ventricular (QRST) contribution removal (PCA, ICA, ...)
- The early MIN and MAX values are : Stable, relevant, inform globally

Two Examples (recurrent AF & non-recurrent AF after Elec. Card.)



- Correlation function for each electrode & first $|Min|$ Map
- Red circle : V1 ; bold circle : the max value.
- → the most discriminant electrodes for classification

Still many things to present

This type of topic :

- Needs strong collaborations with clinicians
- Needs large background knowledge
- Provides research topics for Computer Science (IBM very active in the simulation field), Biology (Pharmacological Companies), Engineering (Pacemakers, Defibrillators) etc ...
- Questions ?