Detecting non linear dynamics in cardiovascular control: the surrogate data approach

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Introduction

Biological systems are characterized by interacting subsystems, self-sustained oscillators and feedback loops reacting to internal and external inputs

All these structures are characterized by important non linearities

However, due to massive integration among control mechanisms non linear patterns might be hardly observable from time course of a physiological variable

Aim

to review a non linear approach capable of detecting non linearities in short-term cardiovascular variability series

Outline

1) Operational definition of non linear dynamics

2) Hypothesis testing procedure helpful to detect non linear dynamics in an univariate process

3) List of discriminating parameters helpful to detect non linearities in one biological series

4) Applications to short-term heart period variability

5) Hypothesis testing procedure to helpful detect non linear relationships in a bivariate process

6) List of discriminating parameters helpful to detect non linear relationships between two biological series

7) Applications to short-term interactions between heart period and systolic arterial pressure variabilities

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Operative definition of linear dynamics

A process y(t) is linear if it is completely described in terms of first and second order statistics (i.e. mean and autocorrelation function in the time domain or power spectrum in the frequency domain)

Given the Fourier transformation of y(t)

$$X(f)=F[y(t)]=A(f)\cdot e^{j\varphi(f)}$$

where A(f) is the amplitude spectrum ($A^2(f)$ is the power spectrum)
$\varphi(f)$ is the phase spectrum

y(t) is a linear process if A(f) retains all the information about y(t)

$\Downarrow$

$\varphi(f)$ is random sequence between 0 and 2π

Toward a test for the detection of non linear dynamics

Given a process $y(t)$ and its Fourier transformation

$$X(f)=F[y(t)]=A(f)\cdot e^{j\varphi(f)}$$

If $y(t)$ is linear, the substitution of the original phase spectrum, $\varphi(f)$, with a random sequence between 0 and 2π, $\tilde{\varphi}(f)$, preserves all the relevant information contained in $y(t)$

This means that, given

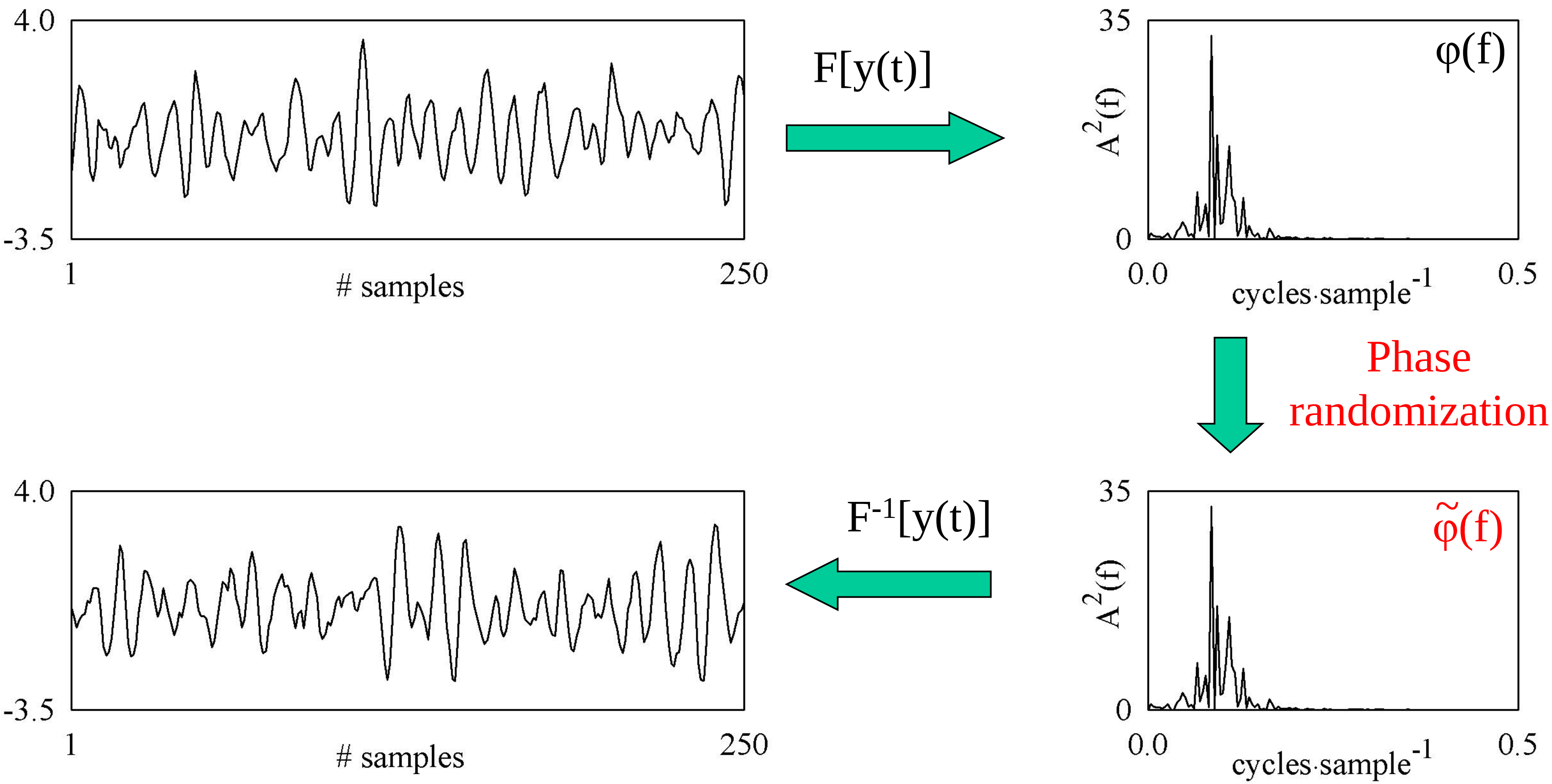
$$\tilde{y}(t)=F^{-1}[A(f)\cdot e^{j\tilde{\varphi}(f)}]$$

$\tilde{y}(t)$ is indistinguishable from $y(t)$ in a statistical sense

An example of linear dynamics: the autoregressive process

$$x(t)=2\cdot\rho\cdot\cos\varphi\cdot x(t-1)-\rho^{2}\cdot x(t-2)+w(t)$$

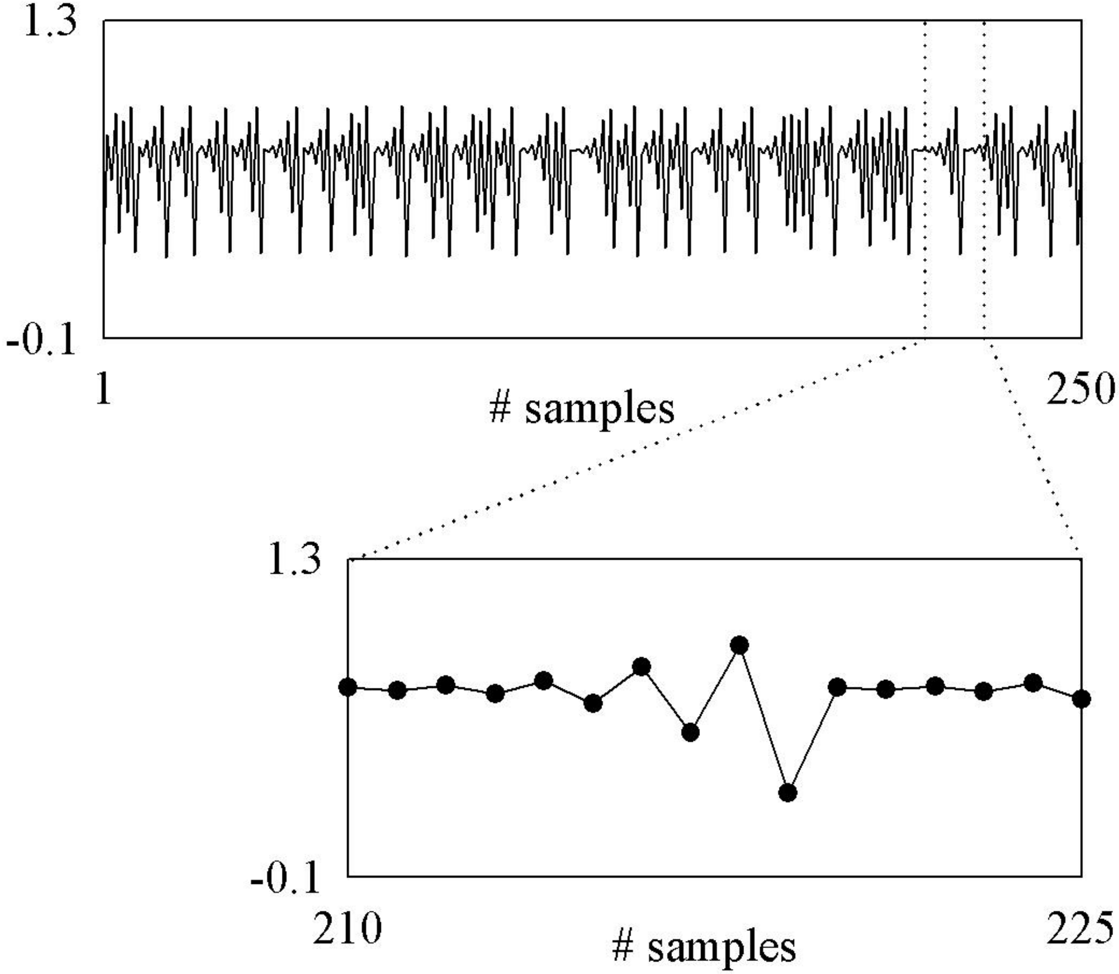
AR(2) process with
$\rho=0.9$, $\varphi=\pi/5$ and $w(t)=WGN(0,\lambda^2)$



An example of non linear dynamics: the logistic map

$x(t)=k\cdot x(t-1)-k\cdot x^2(t-1)$

logistic map with k=3.7



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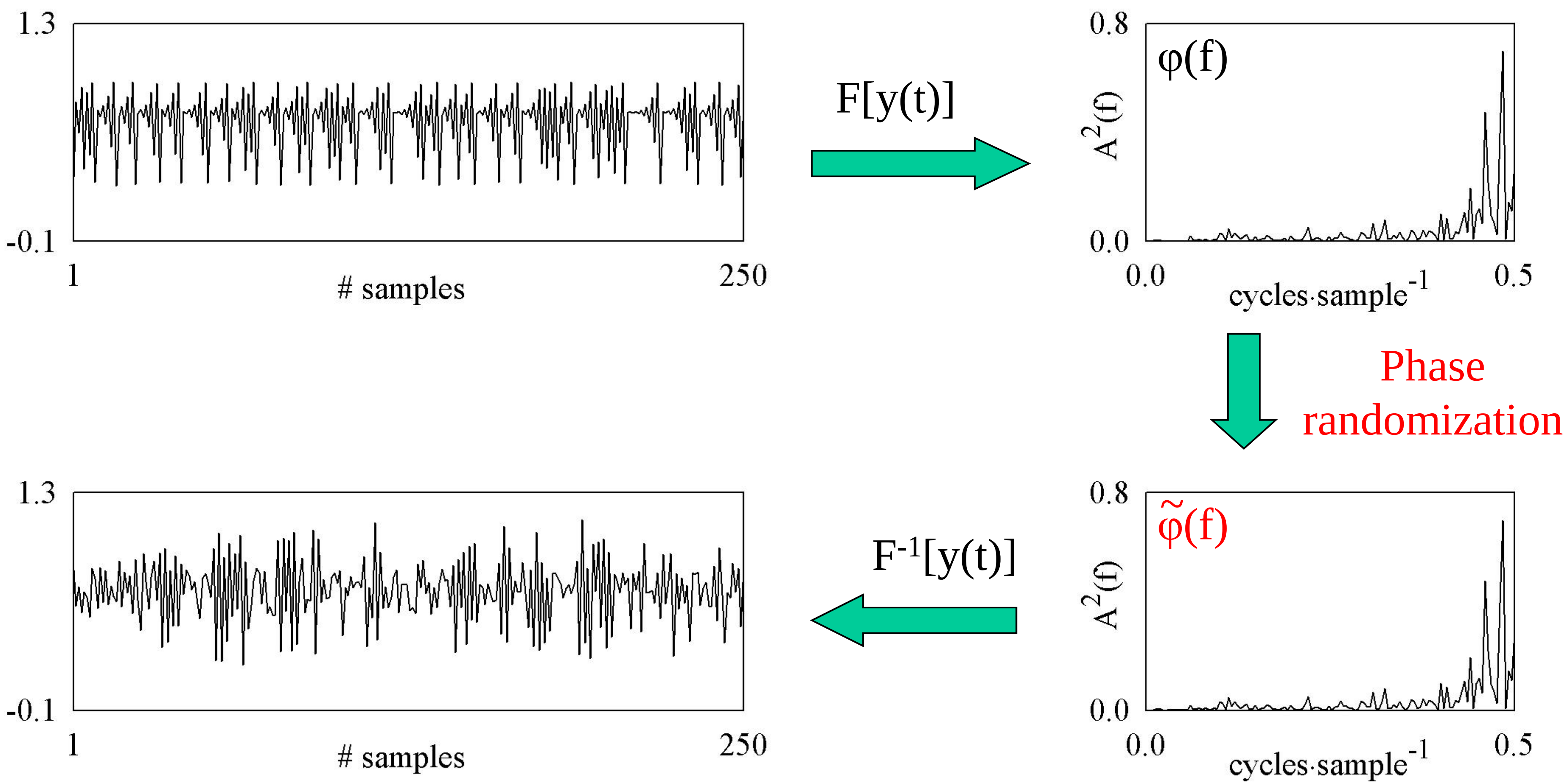

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Univariate process: hypothesis testing procedure

The procedure is based on:

1) an hypothesis (the Null Hypothesis) to be rejected

2) the construction of a series referred to as surrogate series according to the null hypothesis

3) a discriminating parameter

4) a statistical test on the discriminating parameter

Theiler J et al, Physica D, 58:77-94, 1992

Univariate process: Null hypotheses

1) Type-0 Null Hypothesis: the series is completely explained by a white noise

2) Type-1 Null Hypothesis: the series is completely explained by a Gaussian linear process

3) Type-2 Null Hypothesis: the series is completely explained by a Gaussian linear process eventually transformed through a non linear static invertible transformation

Univariate process: surrogate data

Surrogate series are realizations derived from the original series and consistent with the Null Hypothesis

Surrogate data for testing Type-0 Null Hypothesis:

white noises shaped to have the same distribution as the original series

Surrogate data for testing Type-1 Null Hypothesis:

linear Gaussian processes shaped to have the same power spectrum as the original series

Surrogate data for testing Type-2 Null Hypothesis:

linear processes shaped to have the same distribution and power spectrum as the original series

Univariate process: surrogate data

Surrogate data for Type-0 Null Hypothesis:

1) shuffled surrogate

Theiler J et al, Physica D, 58:77-94, 1992

Surrogate data for Type-1 Null Hypothesis:

1) Fourier transform based (FT) surrogate

Theiler J et al, Physica D, 58:77-94, 1992

Surrogate data for Type-2 Null Hypothesis:

1) Amplitude-adjusted FT (AAFT) surrogate

Theiler J et al, Physica D, 58:77-94, 1992

2) Iteratively-refined AAFT (IAAFT) surrogate preserving
   - distribution (IAAFT-1)

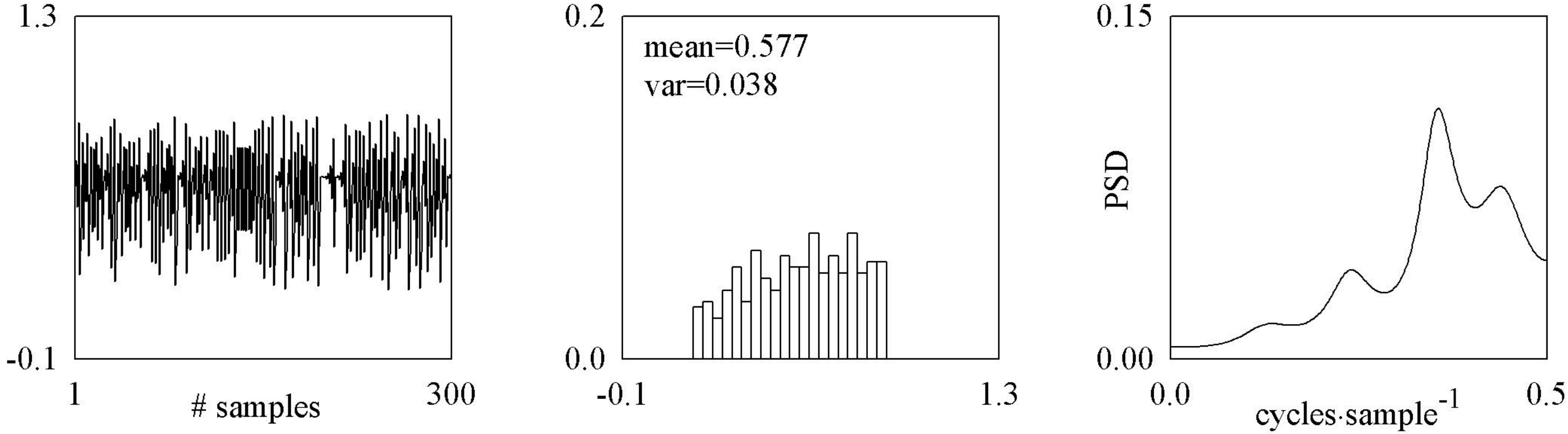
   Schreiber T and Schmitz A, Phys Rev Lett, 4: 635-638, 1996

   - power spectrum (IAAFT-2)

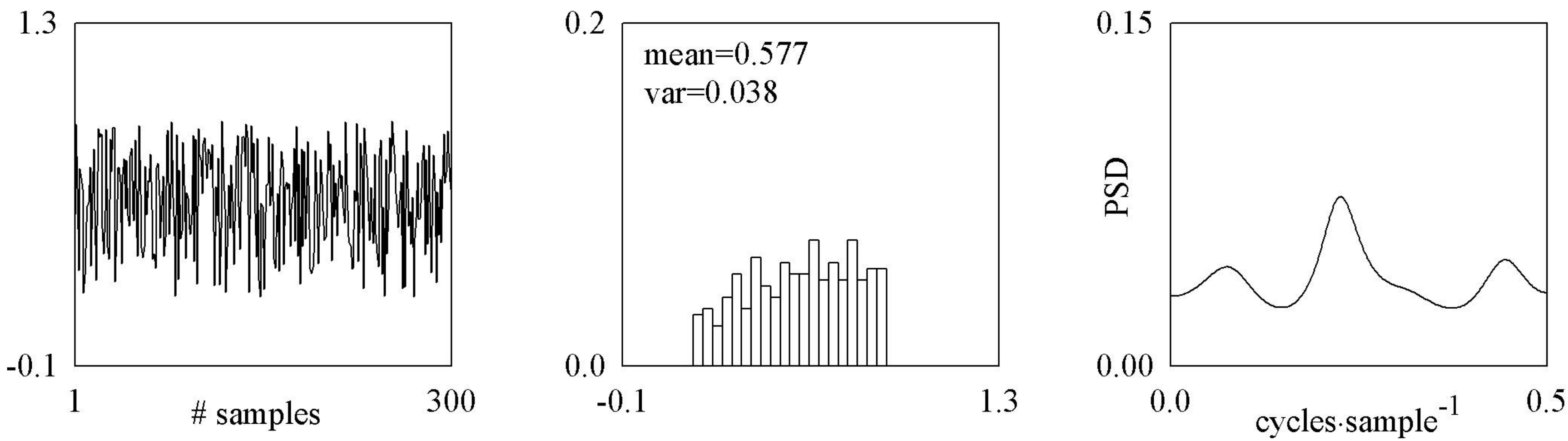
   Kugiumtzis D, Phys Rev E, 60:2808-2816, 1999

Shuffled surrogate

Tent map: original realization

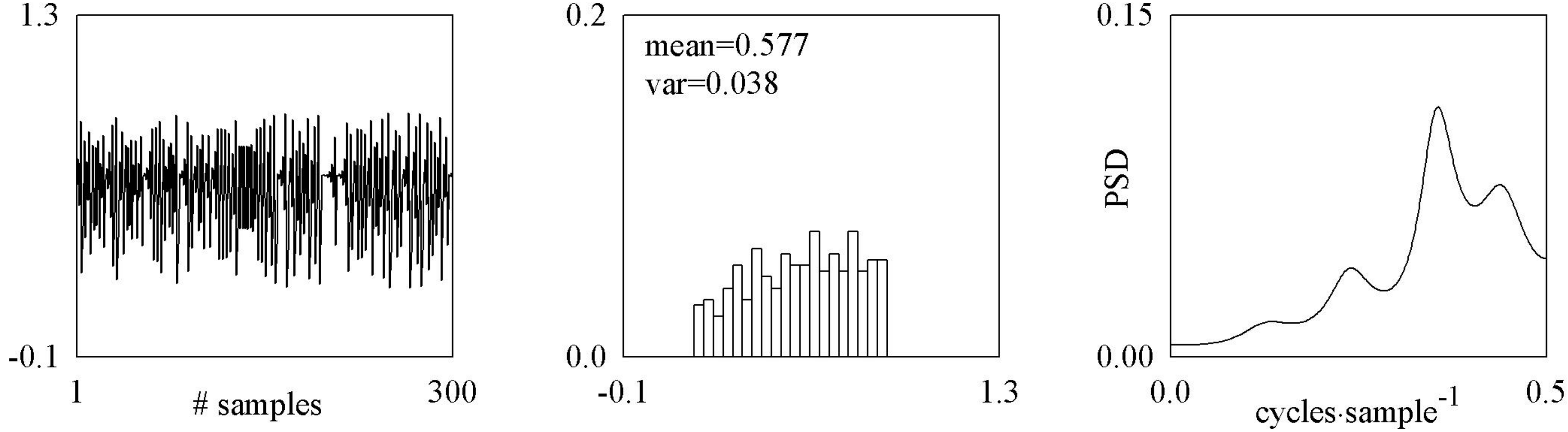


Tent map: shuffled surrogate

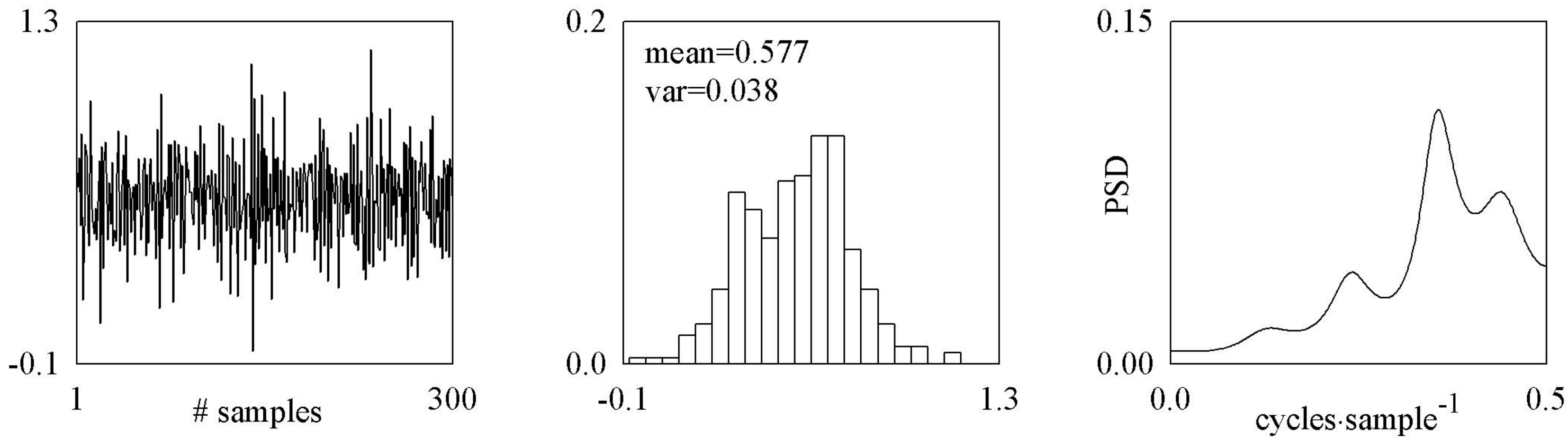


Fourier transform (FT) surrogate

Tent map: original realization

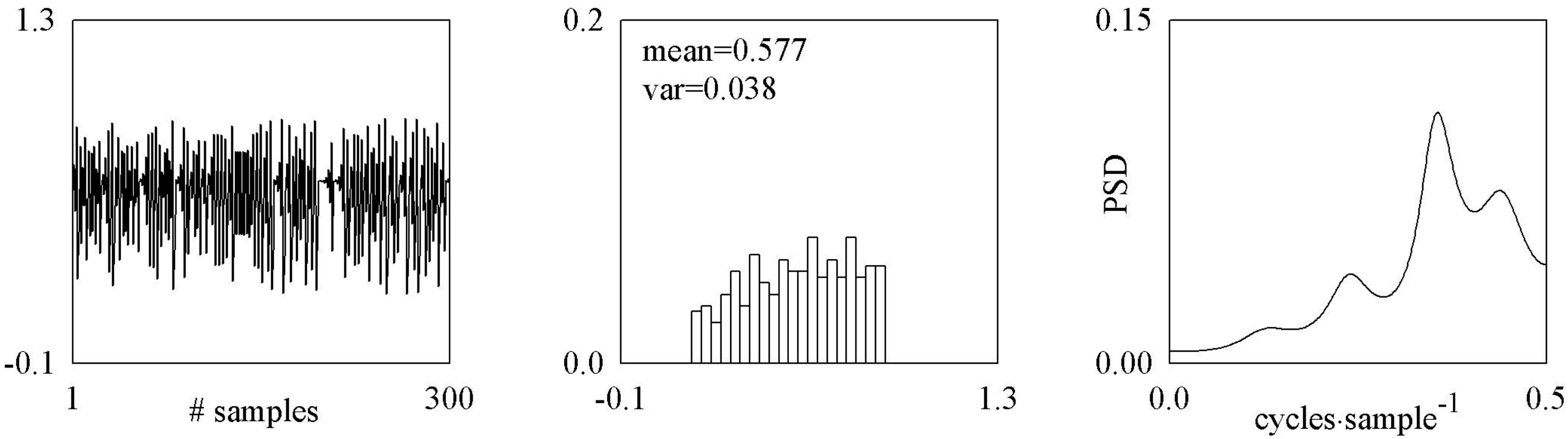


Tent map: FT surrogate

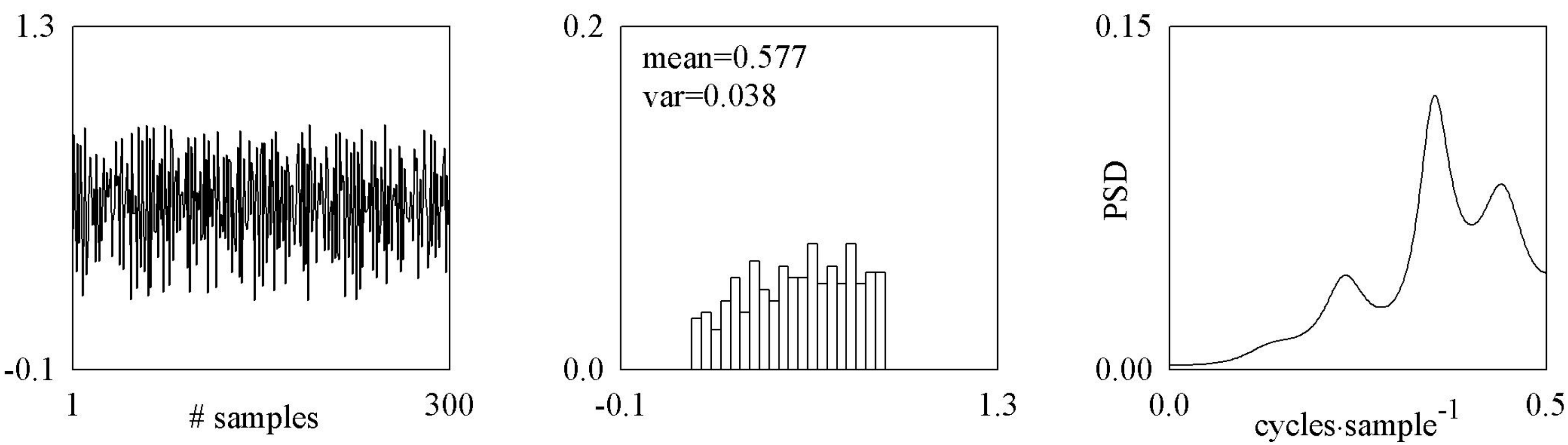


Amplitude-adjusted Fourier transform (AAFT) surrogate

Tent map: original realization

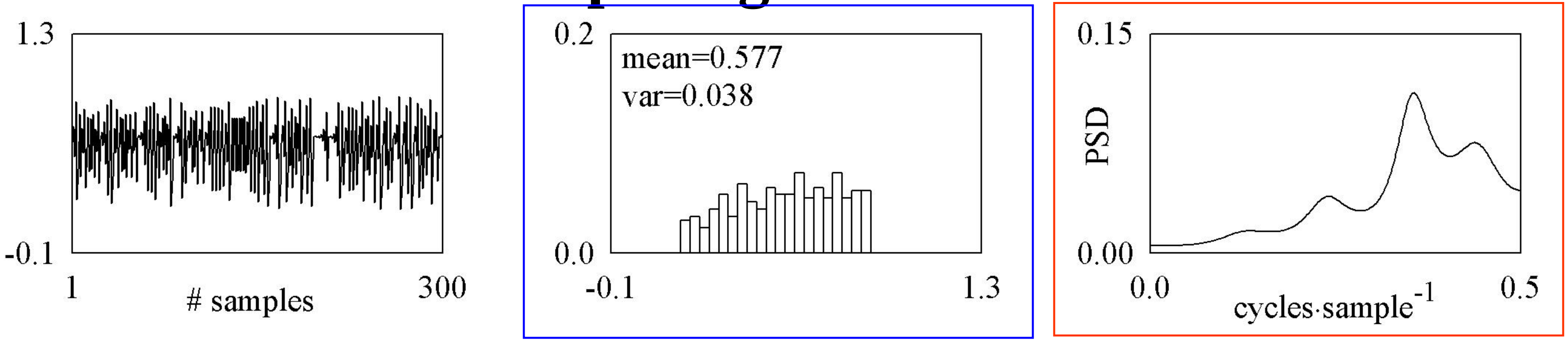


Tent map: AAFT surrogate

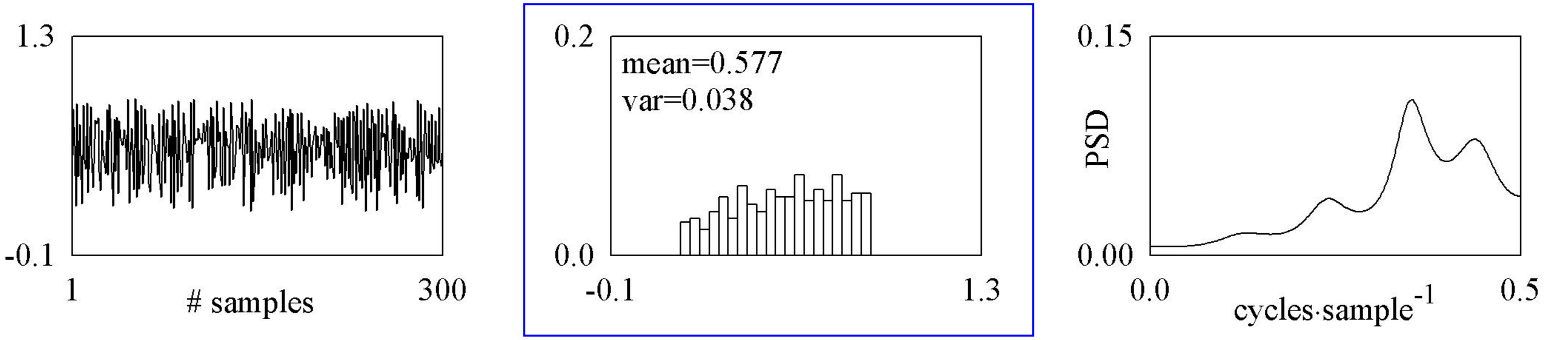


Iteratively-refined amplitude-adjusted Fourier transform (IAAFT) surrogate

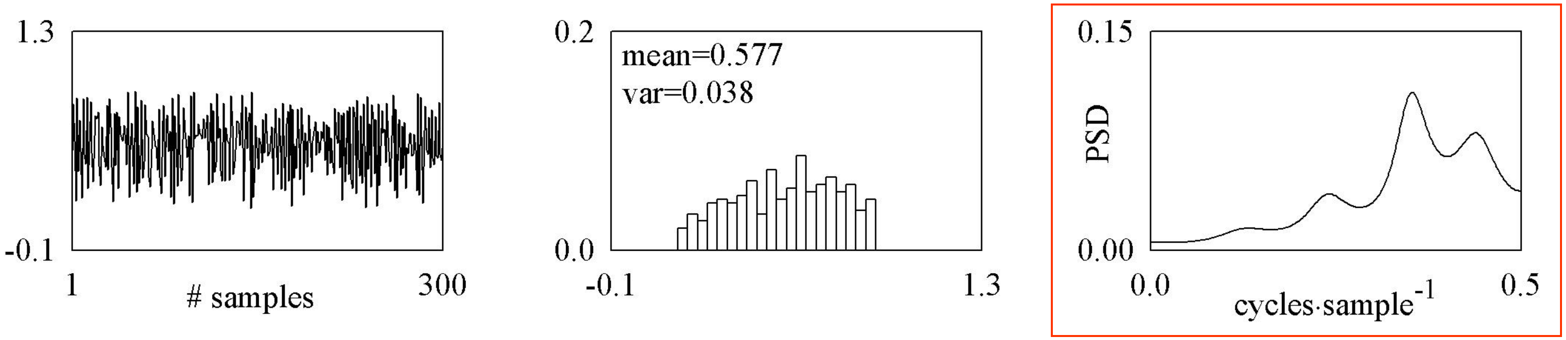
Tent map: original realization



Tent map: IAAFT-1 surrogate



Tent map: IAAFT-2 surrogate



Univariate process: the discriminating parameter (DP)

Features of the discriminating parameter:

- capable to account for non linear dynamics
- reliable over short data segments (~300 samples)
- describing a meaningful patho-physiological quantity to which nonlinearities might contribute

Indexes based on local non linear predictability or conditional entropy fulfill all these criteria

Examples

DP=UPI or NUPI
DP=CI or NCI

Statistical test on the discriminating parameter (DP)

DP_o= DP calculated over the original series
DP_s= DP calculated over the surrogate series

We generated 100 surrogates according to the null hypothesis

$DP_{s,0.025}$ = 2.5th percentile of DP_s
$DP_{s,0.975}$ = 97.5th percentile of DP_s

If $DP_o < DP_{s,0.025}$ or $DP_o > DP_{s,0.975}$ then the Null Hypothesis is rejected, otherwise it is accepted

Univariate process: practical meaning of the rejection of the Null Hypotheses

Rejection of Type-0 Null Hypothesis

It suggests the presence of a significant correlation among samples

Rejection of Type-1 Null Hypothesis

It suggests the presence of static and/or dynamical non linearities

Rejection of Type-2 Null Hypothesis

It suggests the presence of dynamical non linearities

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Univariate process: discriminating parameters derived from entropy

Corrected approximate entropy (CApEn)

Pincus SM et al, Chaos, 5:110-117, 1995

Porta A et al, J Appl Physiol, 103:1143-1149, 2007

Corrected conditional entropy (CCE)

Porta A et al, Biol Cybern, 78:71-78, 1998

Sample entropy (SampEn)

Richman JS and Moorman JR, Am J Physiol, 278:H2039-2049, 2000

Permutation entropy (PE)

Brandt C and Pompe B, Phys Rev Lett, 88:174102, 2002

Univariate process: discriminating parameters derived from local non linear predictability

Approach based on an uniform quantization over q bins

Porta A et al, IEEE Trans Biomed Eng, 47:1555-1564, 2000

Approach based on k nearest neighbors

Farmer JD and Sidorowich JJ, Phys Rev Lett, 59:845-848, 1987

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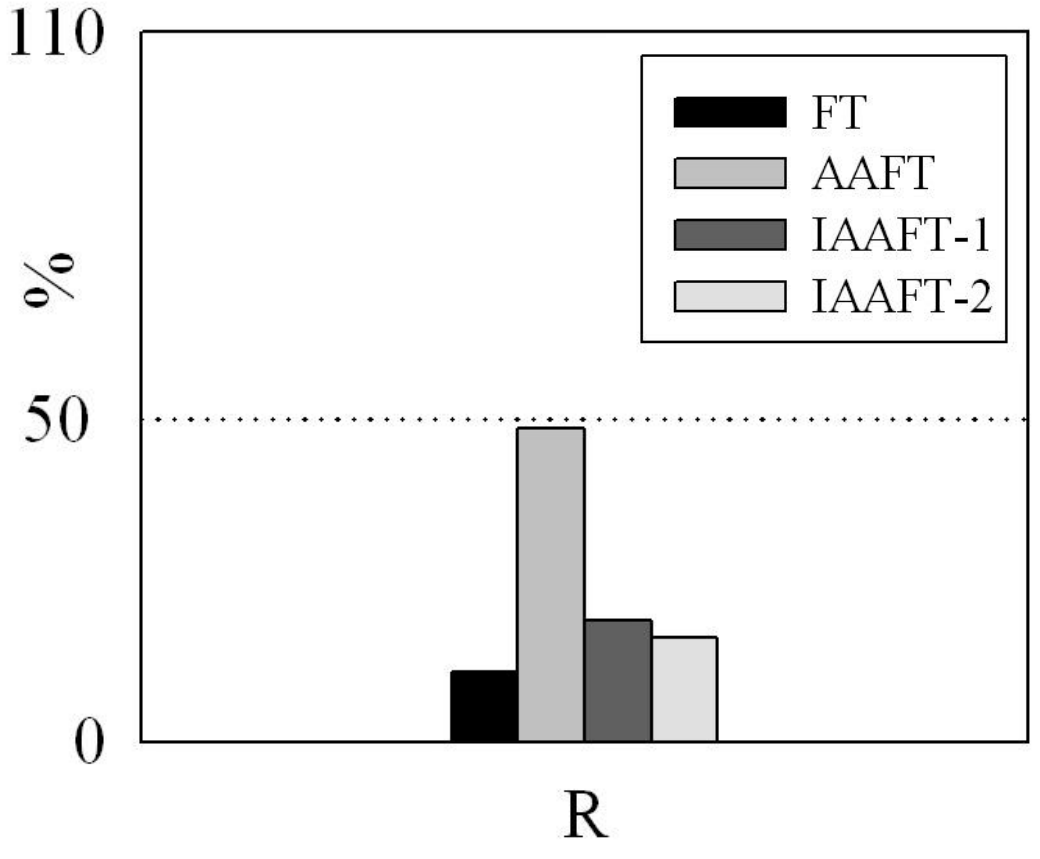
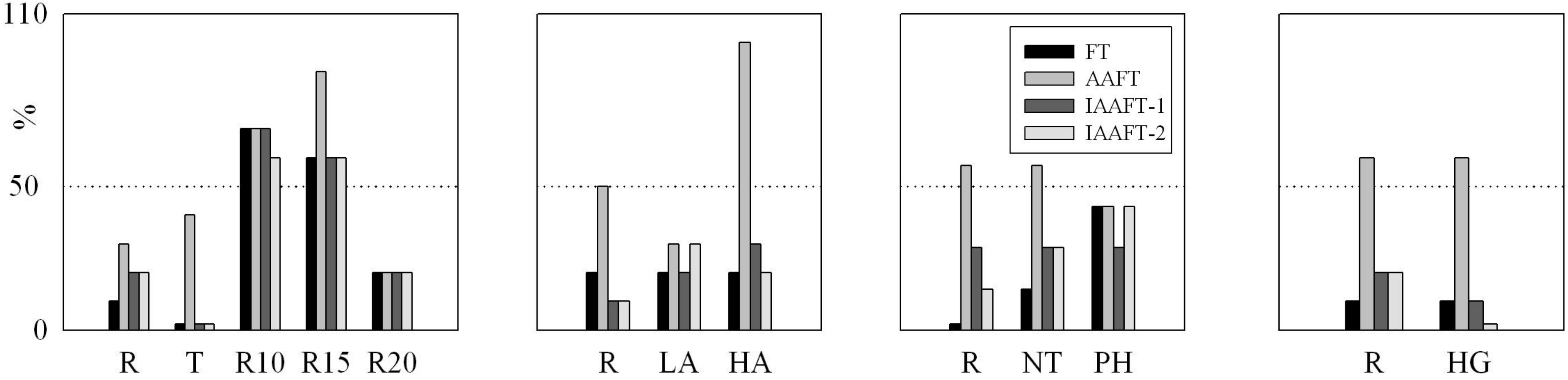
Non linear dynamics in short-term heart period variability in healthy humans at rest



Non linear dynamics in short-term heart period variability in healthy humans



Porta A et al, IEEE Trans Biomed Eng, 54:94-106, 2007

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4) a statistical test on the discriminating parameter

Theiler J et al, Physica D, 58:77-94, 1992

Bivariate process: Null Hypotheses

1) Type-0 Null Hypothesis: the two series are completely explained by a pair of white noises with no interactions

2) Type-1 Null Hypothesis: the two series are completely explained by a pair of Gaussian linear processes with no interactions

3) Type-2 Null Hypothesis: the two series are completely explained by a pair of Gaussian linear processes linearly cross-correlated each other

Bivariate process: surrogate data

Surrogate data for testing Type-0 Null Hypothesis:

two white noises shaped to have the same distribution as the original series and independent each other

Surrogate data for testing Type-1 Null Hypothesis:

two linear Gaussian processes shaped to have the same power spectrum as the original series and independent each other

Surrogate data for testing Type-2 Null Hypothesis:

two linear Gaussian processes shaped to have the same power spectrum and cross-correlation as the original series

Bivariate process: surrogate data

Surrogate data for Type-0 Null Hypothesis:

1) Shuffled series with independent random permutation

Surrogate data for Type-1 Null Hypothesis:

1) IAAFT surrogates with independent seeds

Prichard D and Theiler J, *Phys Rev Lett*, 73: 951-954, 1994

Palus M, Phys Lett A, 213: 138-147, 1996

Surrogate data for Type-2 Null Hypothesis:

1) IAAFT surrogates preserving phase difference of the original series

Prichard D and Theiler J, *Phys Rev Lett*, 73: 951-954, 1994

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Selection of the discriminating parameter:

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Bivariate process: practical meaning of the rejection of the Null Hypotheses

Rejection of Type-0 Null Hypothesis:

It suggests the presence of a link (linear and/or non linear) between two noises

Rejection of Type-1 Null Hypothesis:

It suggests the presence of a link (linear and/or non linear) between the two linear dynamics

Rejection of Type-2 Null Hypothesis:

It suggests the presence of a non linear relationship between the two linear dynamics

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Bivariate process: discriminating parameters based on cross-entropy

Normalized corrected cross-conditional entropy (NCCCE)

Porta A et al, Biol Cybern, 81:119-129, 1999

Cross-approximate entropy (Cross-ApEn)

Pincus SM and Singer W, Proc Natl Acad Sci, 93:2083-2088, 1996

Mutual information

Palus M, Phys Lett, 235:341-351, 1997

Bivariate process: discriminating parameters based on local non linear cross-predictability

Approach based on a uniform quantization

Approach based on k nearest neighbors

Abarbanel HDI et al, Phys Rev E, 49:1840-1853, 1994

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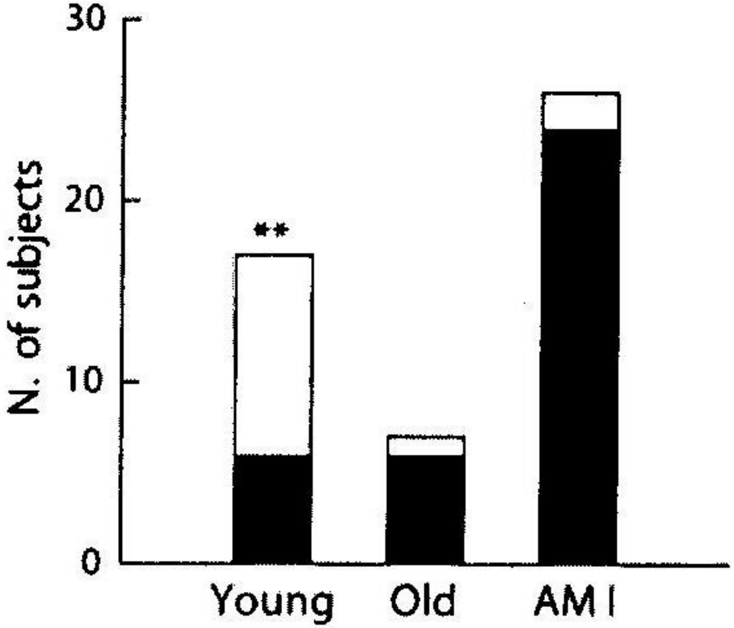
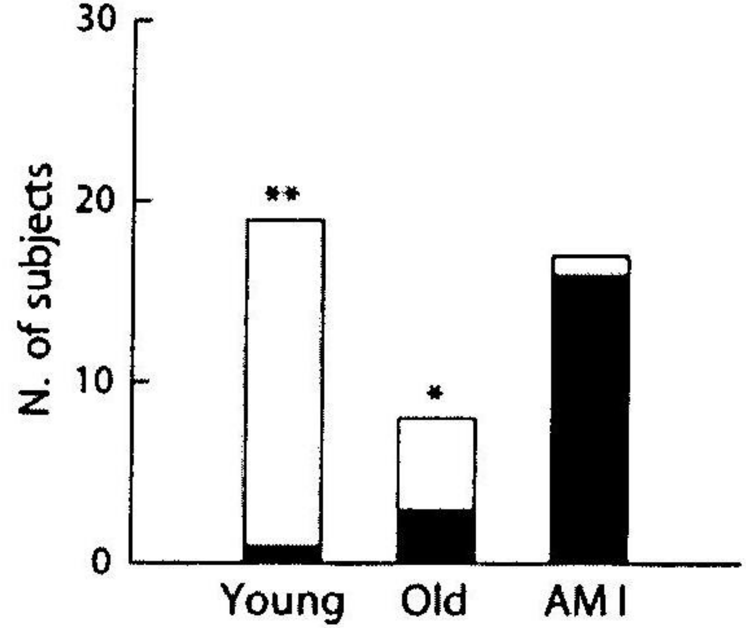
HP-SAP non linear interactions

Rest



Head-up tilt



linear coupling
non linear coupling

Nollo et al, Am J Physiol, 283:H1200-H1207, 2002

Conclusions

Hypothesis testing procedure is a valuable approach to detect non linearities in both univariate and bivariate processes

Non linear dynamics are not ubiquitous in heart period variability series

Non linear interactions are not an ubiquitous feature characterizing heart period - systolic arterial pressure variability relationship

The presence of non linear dynamics and non linear interactions are helpful to distinguish experimental conditions and to separate pathological subjects from healthy patients

There is a need to develop null hypothesis testing strategies for more complex situations including assessment of causal interactions along predefined pathways in multivariate processes