Time irreversibility analysis: a tool to detect non linear dynamics in short-term heart period variability

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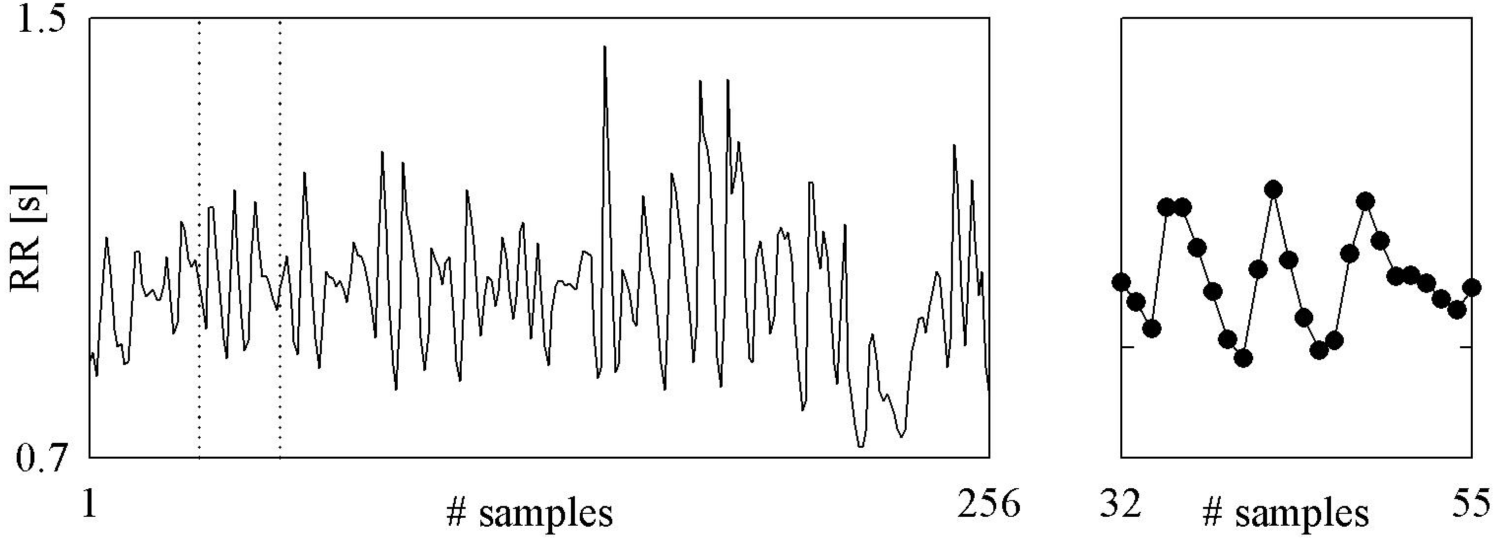
Introduction

There is a need to better characterize temporal features responsible for non linear dynamics of heart period variability

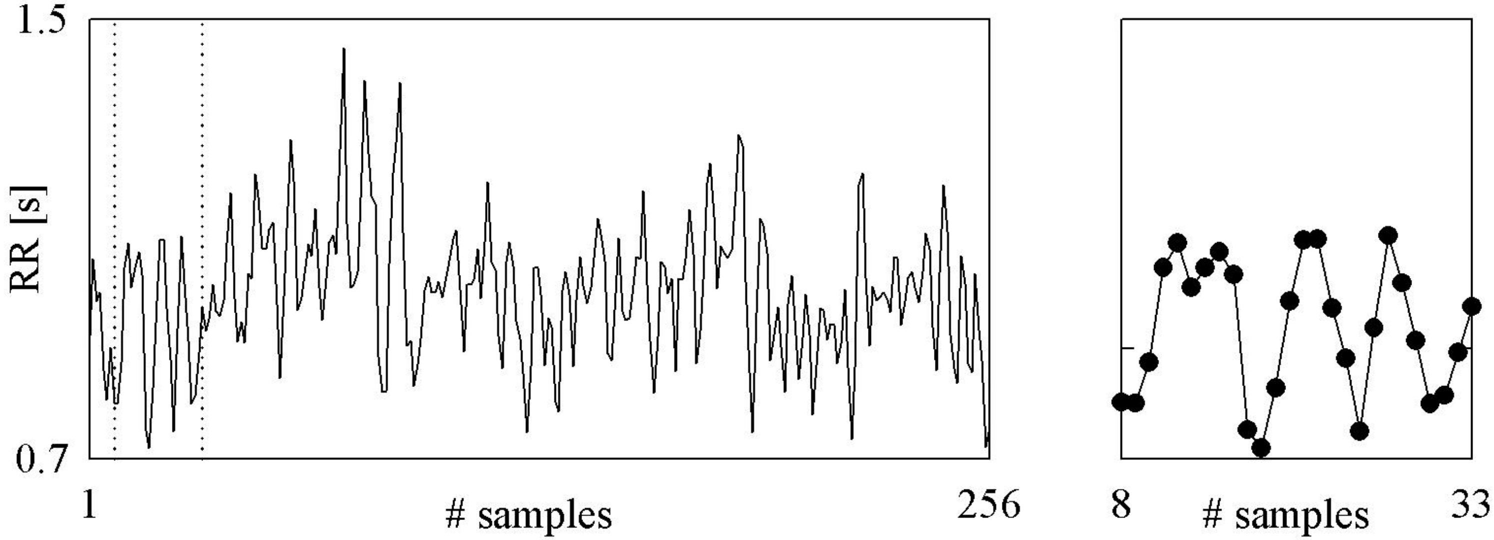
Irreversibility analysis provides indexes that may be helpful to identify non linear patterns

Since irreversibility is absent in linear dynamics, detecting irreversible dynamics indicates the presence of nonlinearities

Original RR series



IAAFT surrogate



A. Porta et al, Computers in Cardiology, 33:77-80, 2006

Aims

1) to exploit time irreversibility analysis to check for the presence of non linear dynamics in heart period variability

2) to typify patterns responsible for non linear behavior

3) to relate non linear patterns to specific physiological mechanisms

Formal definition of time reversibility

A time series $x=\{x(i), i=1,\dots,N\}$ is said to be reversible if its statistical properties are invariant with respect to time reversal

$$P(x(i), x(i+\tau)) = P(x(i+\tau), x(i))$$

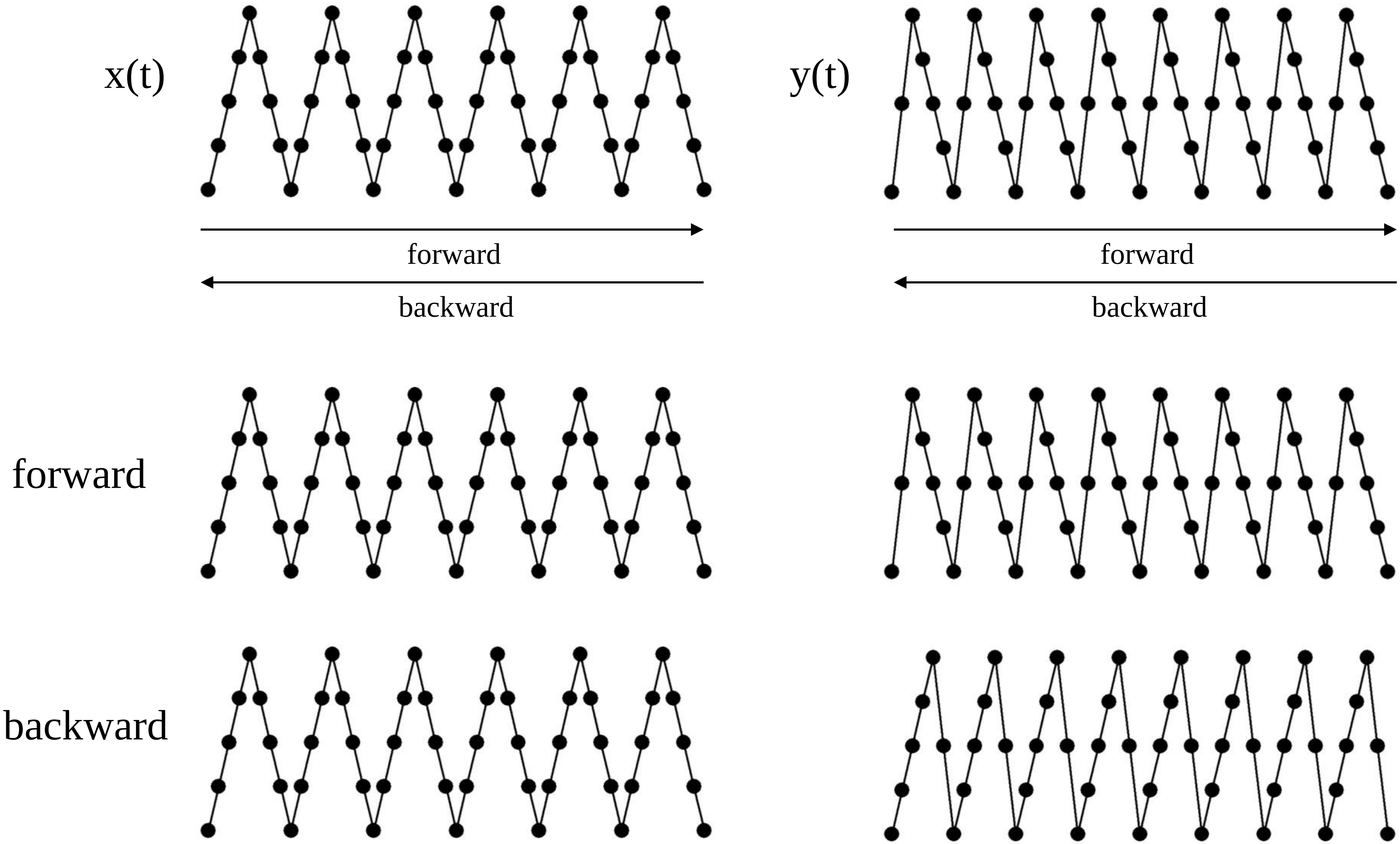
$$P(x(i), x(i+\tau), x(i+2\tau)) = P(x(i+2\tau), x(i+\tau), x(i))$$

......

$$P(x(i), x(i+\tau), \dots, x(i+(L-1)\cdot\tau)) = P(x(i+(L-1)\cdot\tau), \dots, x(i+\tau), x(i))$$

for any i, L and τ

Toward a simple index of time reversibility



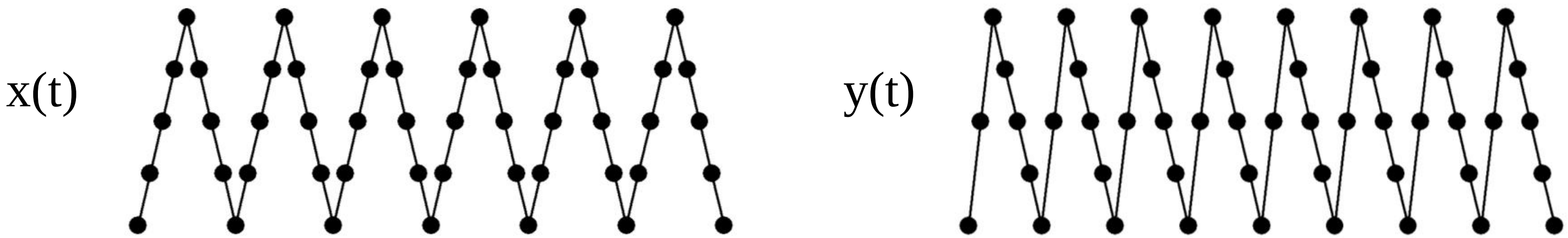
Simple index for the detection of irreversible series

Defined as $\Delta x = x(i+\tau) - x(i)$

$$NV\% = \frac{\text{number of } \Delta x<0}{\text{number of } \Delta x \neq 0} \cdot 100$$

A. Porta et al, Computers in Cardiology, 33, 77-80, 2006
A. Porta et al, Am J Physiol, 295, R550-R557, 2008

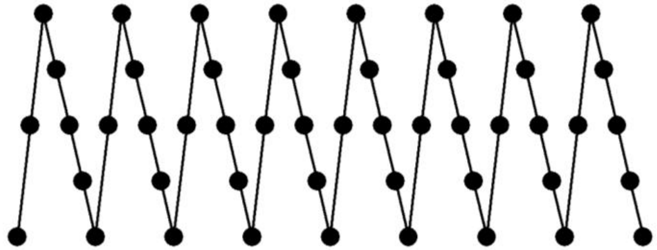
$NV\% \neq 50$ ⟹ the series is irreversible



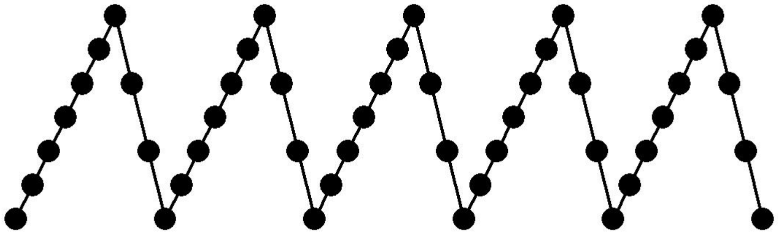
NV% = 50 NV% = 66

Detecting two different types of temporal asymmetries

x(t)



y(t)



x(t) is irreversible

y(t) is irreversible

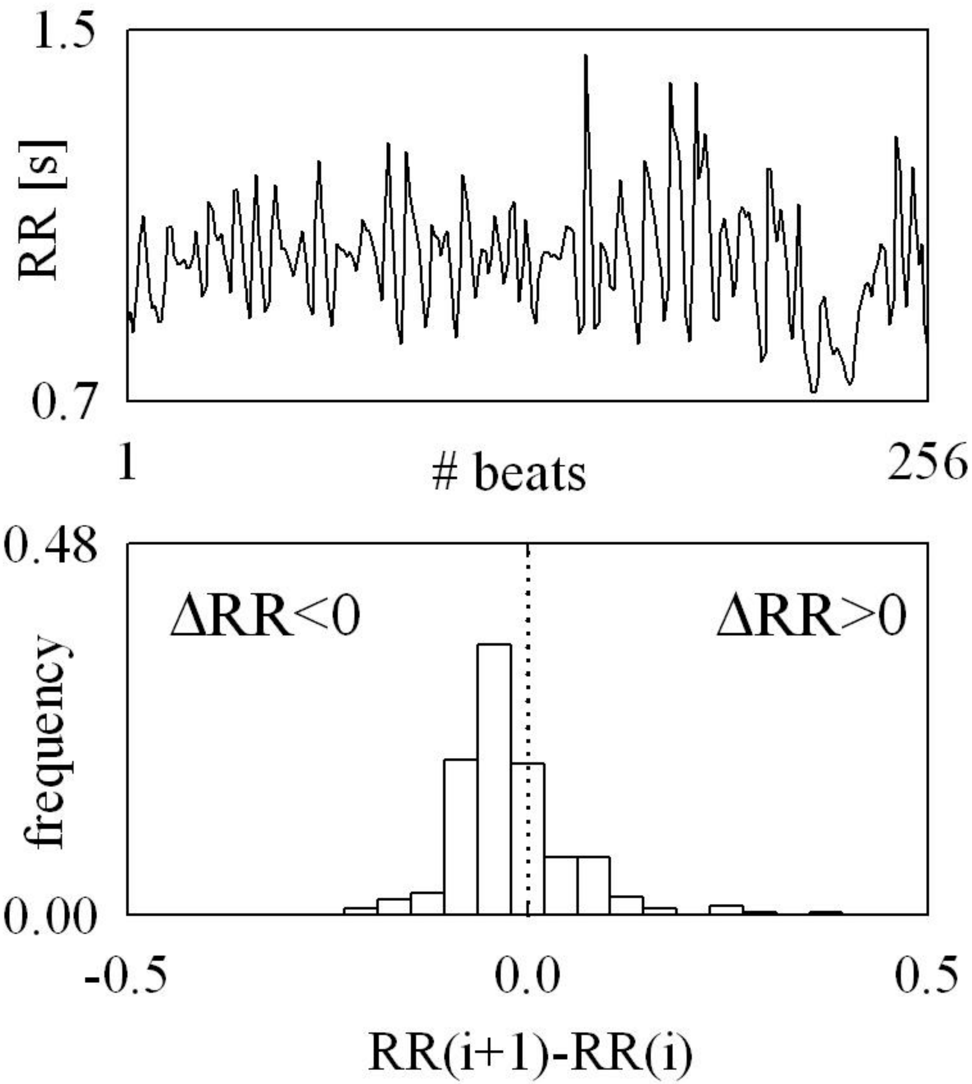
NV%>50

NV%<50

Type I^+
Ascending side shorter than the descending one

Type I^-
Ascending side longer than the descending one

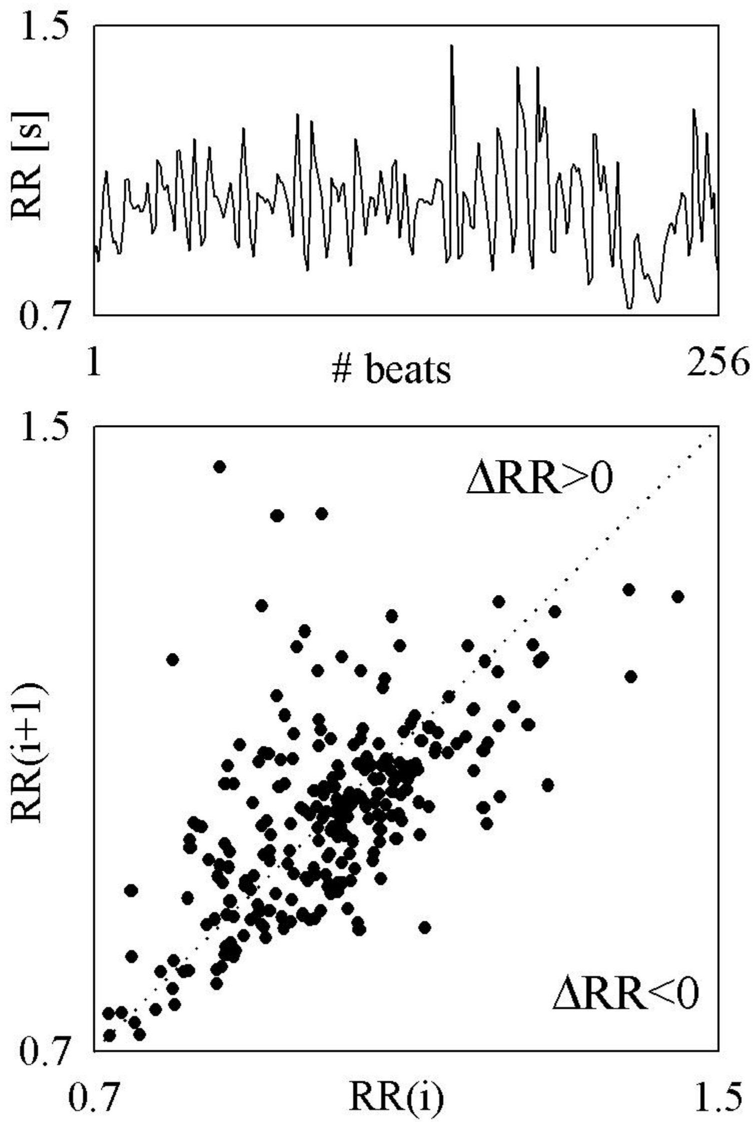
NV%



NV% = 60.39

NV% is a measure of the asymmetry of the distribution of the first variations

NV%



NV% = 60.39

NV% is a measure of the asymmetry of the distribution of points in the plane (RR(i),RR(i+1)) with respect to the diagonal line

Alternative indexes to detect time irreversibility

$$G\% = \frac{\text{sum of } \Delta x^2 \text{ with } \Delta x<0}{\text{sum of } \Delta x^2} \cdot 100$$

P. Guzik et al, Biomed Tech, 51, 272-275, 2006

$$E = \frac{\sum_{i=1}^{N-1} \Delta x^3(i)}{\left(\sum_{i=1}^{N-1} \Delta x^2(i)\right)^{3/2}}$$

C.L. Ehlers et al, J Neurosci, 18, 7474-7486, 1998

Surrogate data approach on discriminating parameter (DP)

We generated 500 iteratively-refined amplitude-adjusted Fourier-transform based (IAAFT) surrogates

T. Schreiber and A. Schmitz, Phys Rev Lett, 77, 635-638, 1996

Null hypothesis = the time series is reversible

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

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

If $DP_o < DP_{s,0.025}$ or $DP_o > DP_{s,0.975}$ ⟹ the series is irreversible

If $DP_o > DP_{s,0.975}$ ⟹ irreversibility of type-1
If $DP_o < DP_{s,0.025}$ ⟹ irreversibility of type-2

DP = NV%

Experimental protocol (fetuses)

We investigated 66 recordings of 22 healthy fetuses in singleton pregnancies recorded using fetal magnetocardiography (fMCG).

All the 22 fetuses had three recordings and one fell in each of the following periods of gestation (PoG):

i) PoG1: from 16^{th} to 24^{th} week of gestation;
ii) PoG2: from 25^{th} to 32^{nd} week of gestation;
iii) PoG3: from 33^{rd} to 40^{th} week of gestation.

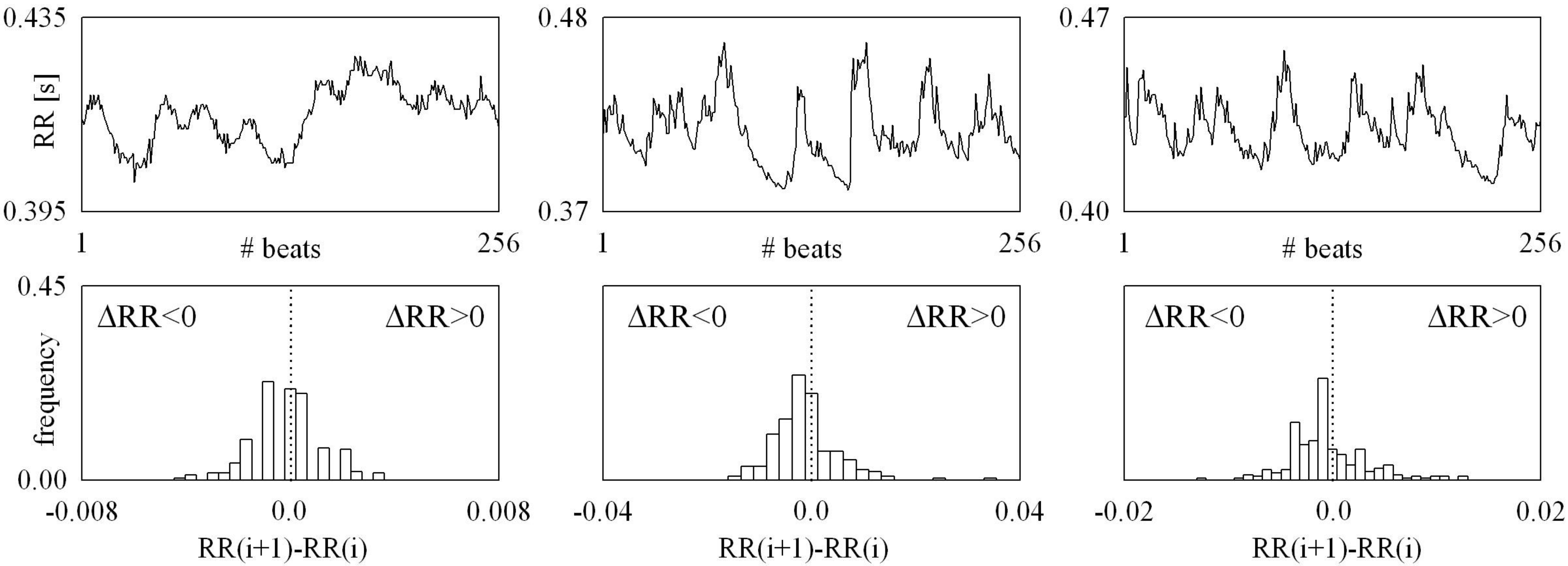
Stationary sequences of 256 RR intervals were randomly chosen from 5 min recordings.

Two strategies for the selection of the time shift τ

1) $\tau=1$
2) τ optimized according to the first zero of the autocorrelation function

Example of irreversibility analysis over fetal heart period variability

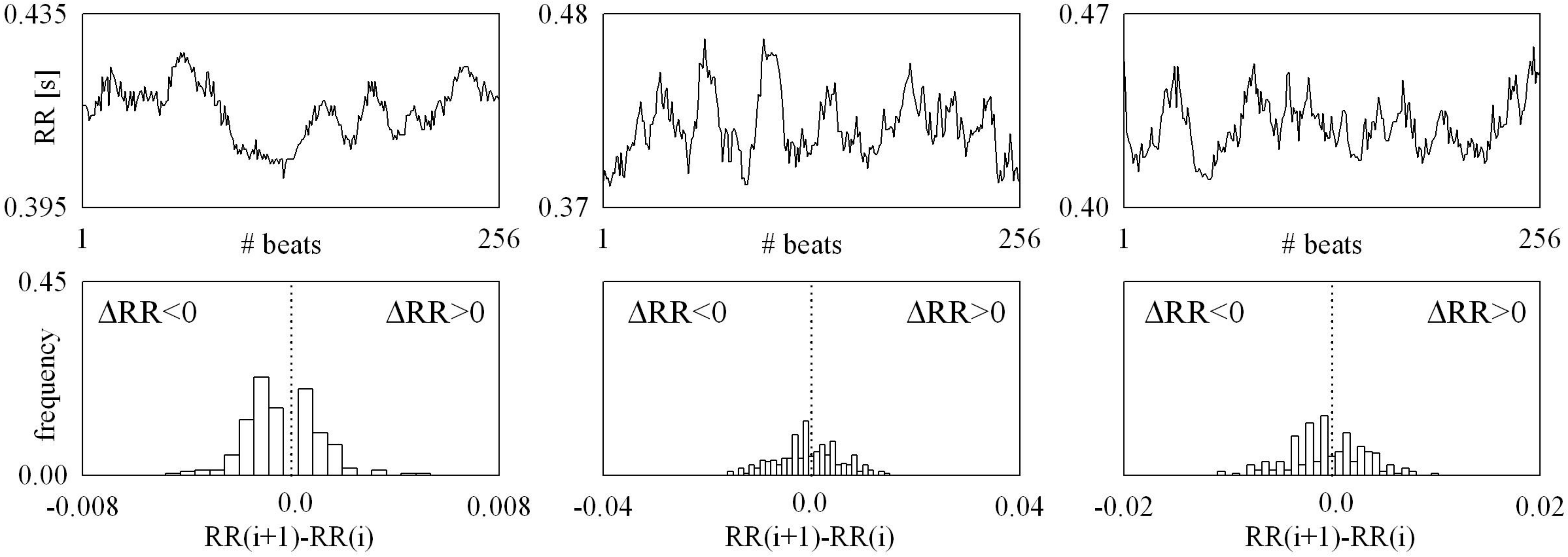
PoG1 **PoG2** **PoG3**



$NV\%_o=51.7$ $NV\%_o=59.8$ $NV\%_o=57.6$

Example of irreversibility analysis over IAAFT surrogates

PoG1 **PoG2** **PoG3**



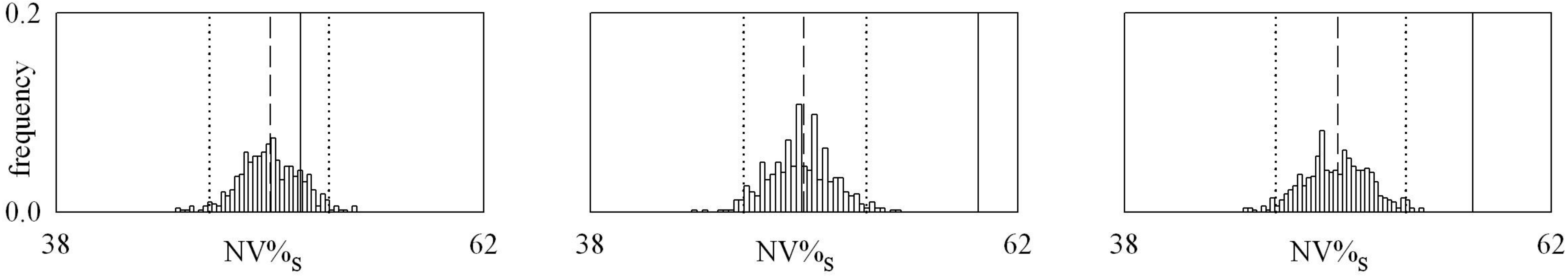
$NV\%_s$=52.1 $NV\%_s$=50.7 $NV\%_s$=48.7

Irreversibility analysis based on 500 realizations of IAAFT surrogates

PoG1

PoG2

PoG3



The Null hypothesis cannot be rejected

The Null hypothesis is rejected

The Null hypothesis is rejected

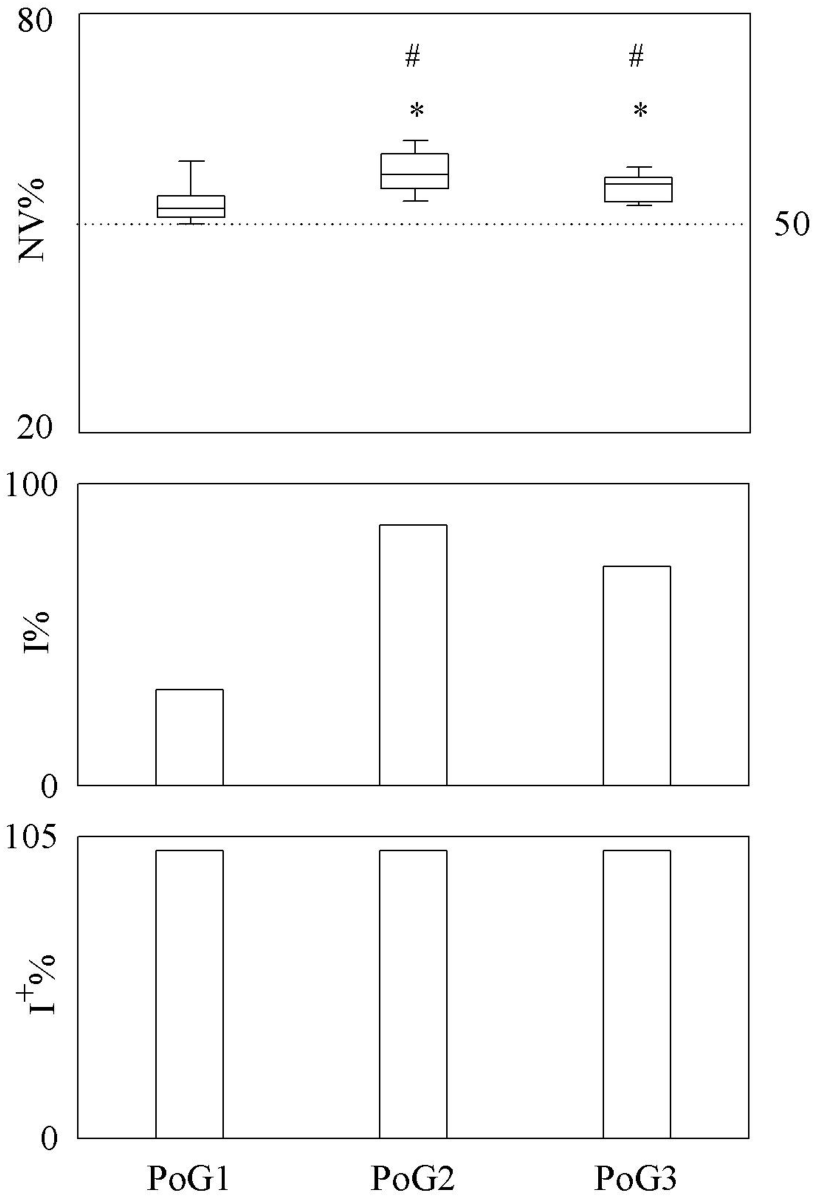
Type I+ irreversibility

Type I+ irreversibility

Irreversibility analysis of RR series in healthy fetuses

τ=1

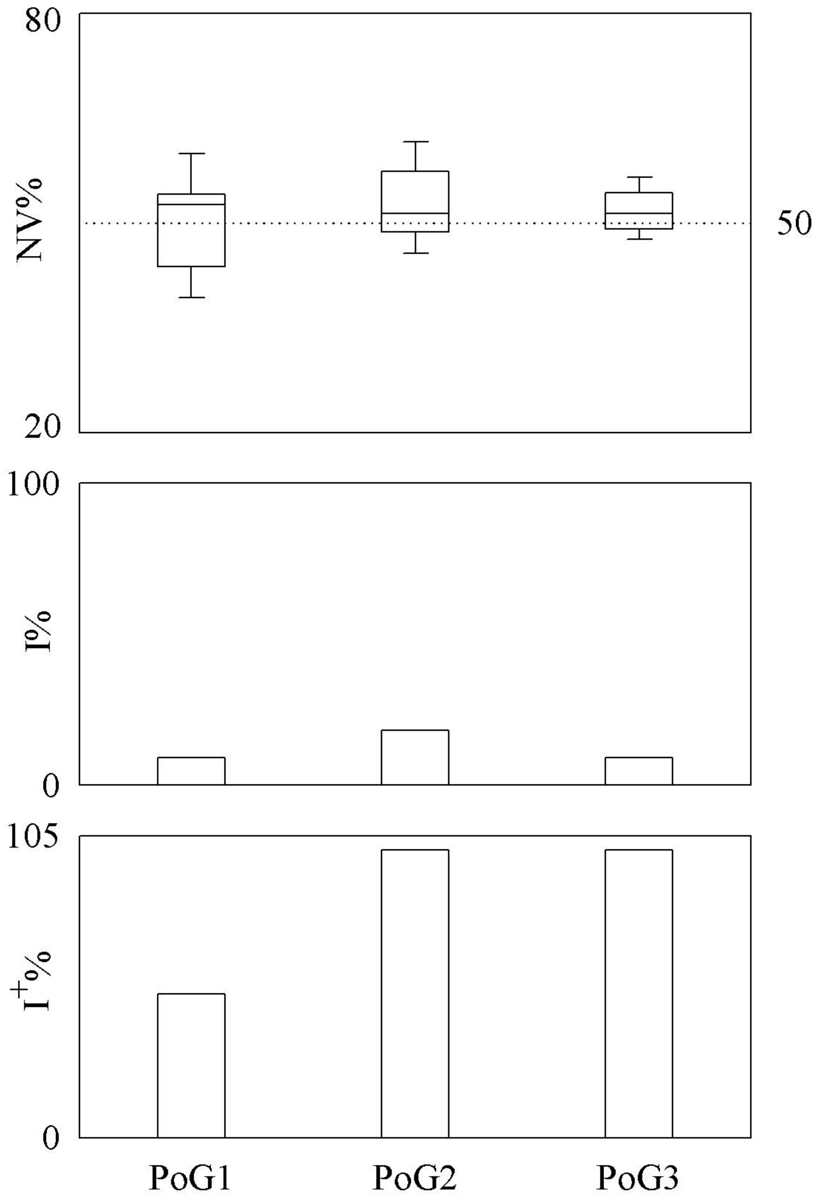
* NV%>50 with p<0.05
# PoG2 and PoG3 vs PoG1



A. Porta et al, Am J Physiol, 295.R550-R557, 2008

Irreversibility analysis of RR series in healthy fetuses

Optimized τ



A. Porta et al, Am J Physiol, 295.R550-R557, 2008

Conclusions (fetuses)

1) We found that the percentage of irreversible dynamics increases of a function of the week of gestation, thus linking the presence of non linear dynamics with a more developed autonomic nervous system

2) The non linear behavior was the result of bradycardic runs shorter than tachycardic ones

3) This pattern was more likely over short than over dominant, longer temporal scales

Experimental protocol (humans)

17 healthy young humans (age from 21 to 54, median=28)

We recorded ECG (lead II) and respiration (thoracic belt) at 1 kHz during head-up tilt (T)

Table angles were randomly chosen within the set {15,30,45,60,75,90}

Each T session (10 min) was always preceded by a session (7 min) at rest (R) and followed by a recovery period (3 min). Stationary sequences of 256 beats were randomly chosen inside each condition

Two strategies for the selection of the time shift τ

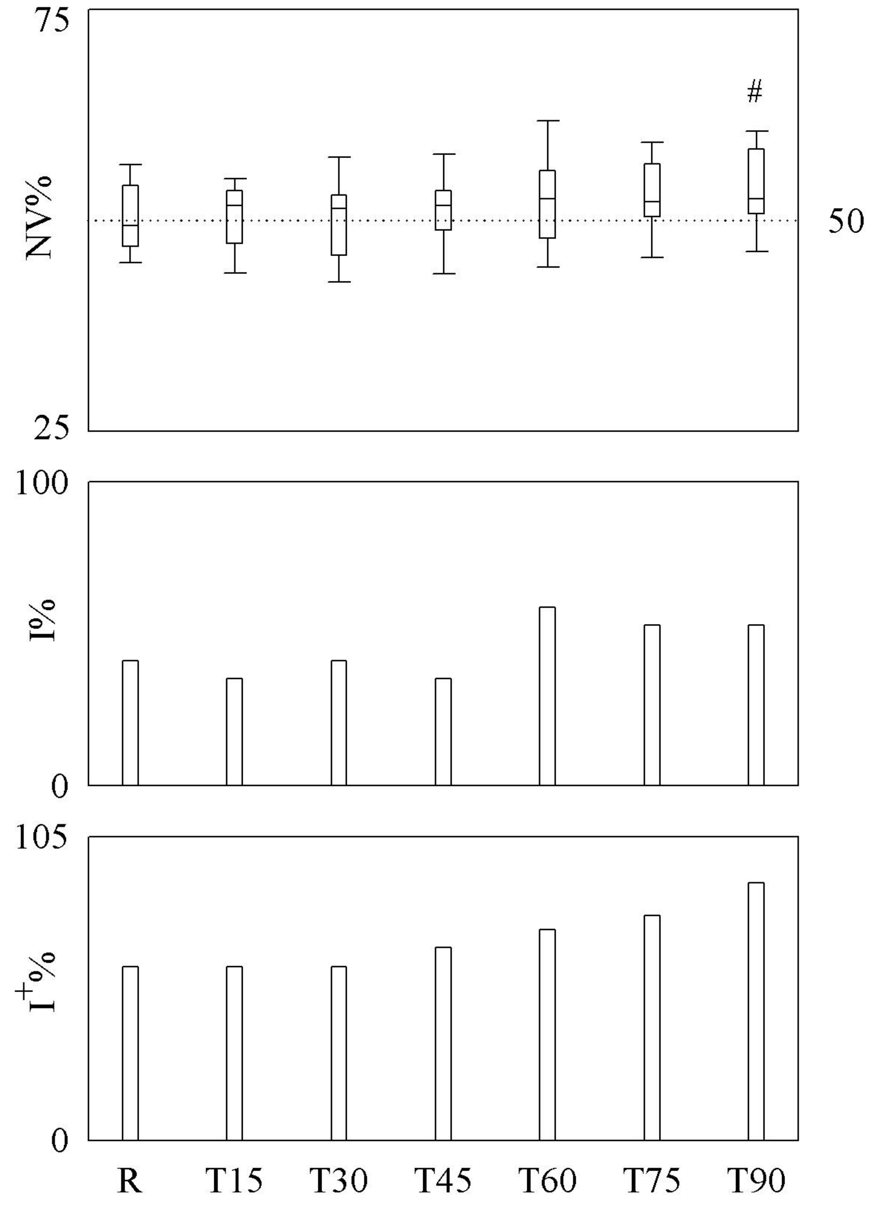
1) $\tau=1$

2) τ optimized according to the first zero of the autocorrelation function

Irreversibility analysis of RR series in healthy humans

τ=1

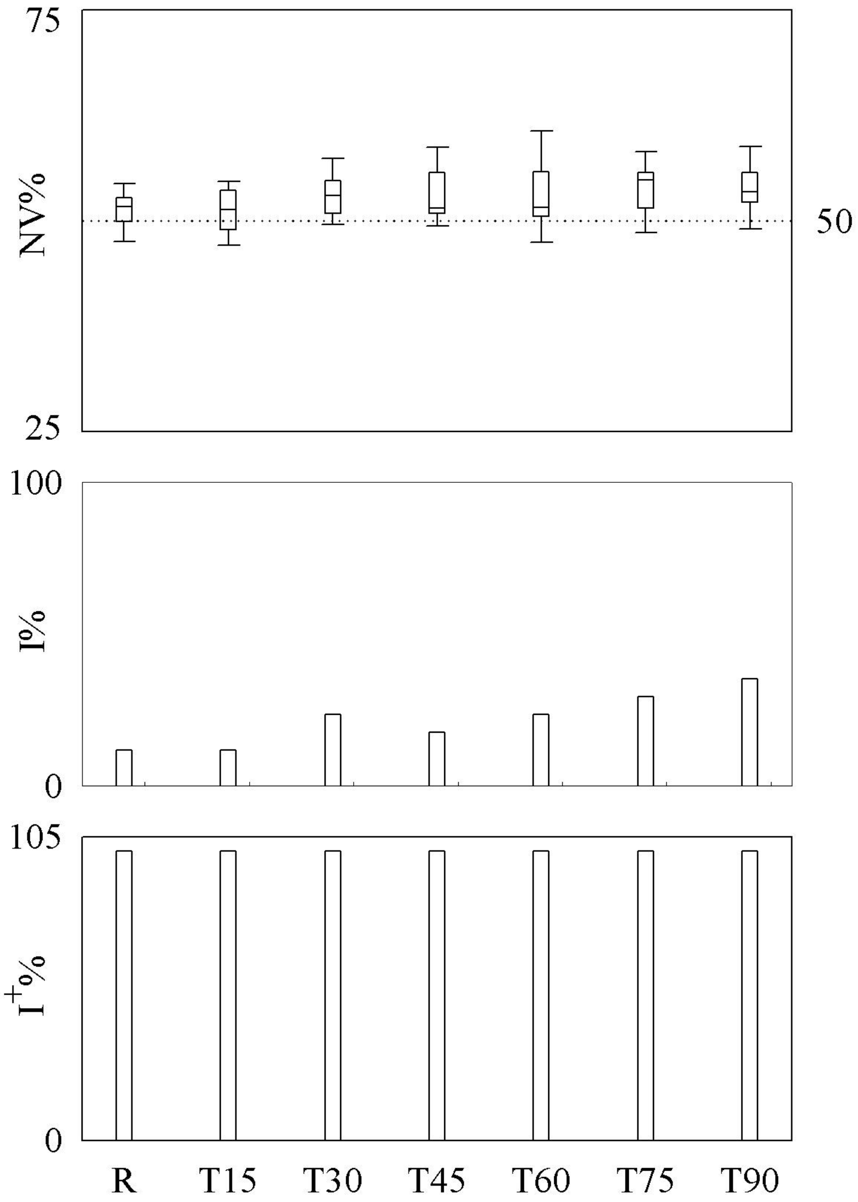
T90 vs R with $p<0.05$



A. Porta et al, Am J Physiol, 295.R550-R557, 2008

Irreversibility analysis of RR series in healthy humans

Optimized τ



A. Porta et al, Am J Physiol, 295.R550-R557, 2008

Conclusions (humans)

1) We found that the percentage of irreversible dynamics is significantly present at rest in healthy humans

2) The percentage of irreversible dynamics is weakly correlated with the importance of sympathetic activation (i.e. the tilt table inclination)

3) The non linear behavior was the result of bradycardic runs shorter than tachycardic ones

4) This pattern was more likely over short than over dominant, longer temporal scales

Experimental protocol (heart failure)

12 normal (NO) subjects (aged 34 to 55, median = 43)
13 chronic heart failure (CHF) patients (aged 33 to 56, median = 37)

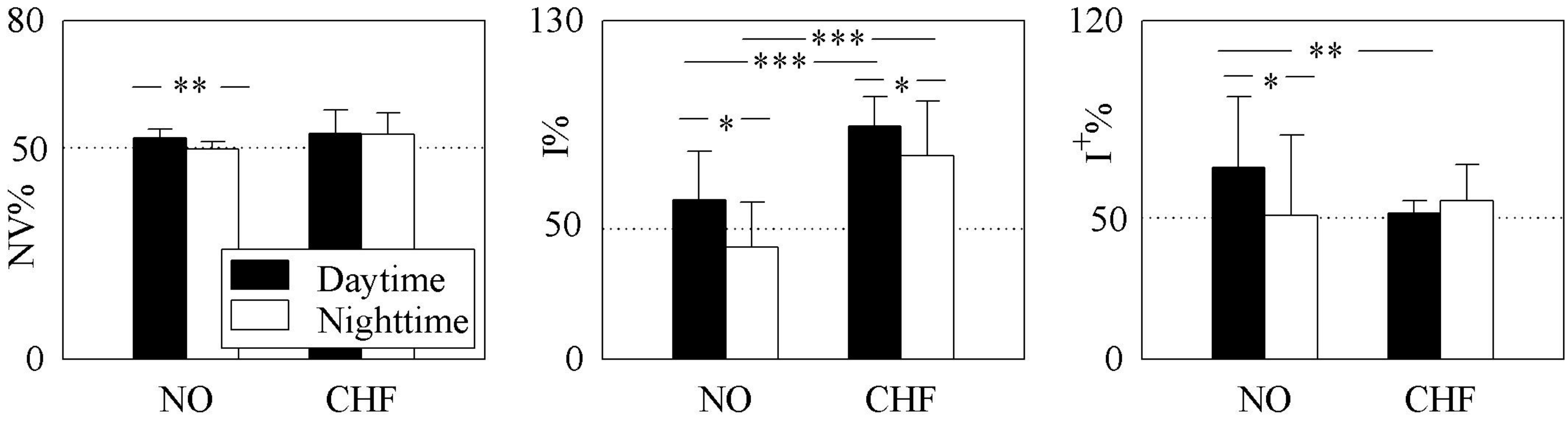
2 in NYHA class I, 2 in NYHA class II, 9 in NYHA class III
Ejection fraction ranges from 13% to 30%, median=25%

ECGs were recorded for 24h with a standard analogue Holter recorder
Sampling rate was 250 Hz

Irreversibility analysis was applied to sequences of 256 RR intervals with 40% overlap during daytime (from 09:00 to 19:00) and during nighttime (from 00:00 to 05:00).

The time shift τ was constant and equal to 1.

Irreversibility analysis of RR series in 24 RR Holter recordings in healthy subjects and heart failure patients



* with p<0.05
** with p<0.01
*** with p<0.001

A. Porta et al, Phil Trans R Soc A, 367, 1359-1375, 2009

Conclusions (healthy humans)

1) We found that the percentage of irreversible dynamics is significantly present during both daytime and nighttime

2) Irreversible dynamics is more present during daytime

3) The non linear behavior was the result of bradycardic runs shorter than tachycardic ones during daytime

4) During nighttime the two different non linear patterns are equally present

Conclusions (heart failure patients)

1) We found that the percentage of irreversible dynamics is significantly present during both daytime and nighttime

2) Irreversible dynamics are more present than in healthy subjects

3) The two different non linear patterns are equally present

High-dimensional irreversibility

Irreversibility was assessed in two-dimensional embedding space

However, assessing irreversibility in a low dimensional embedding space might be extremely limiting

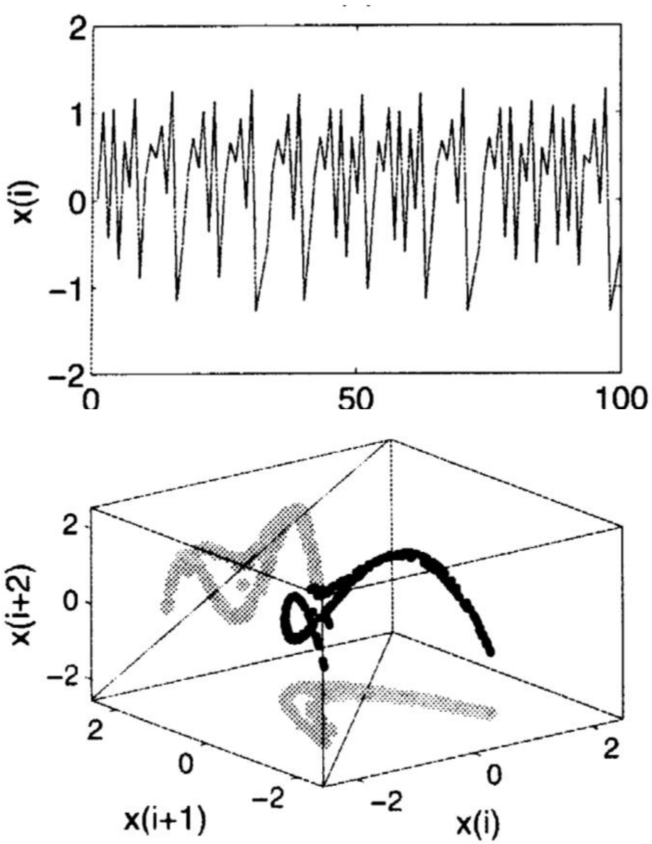
Indeed, if the mechanism responsible for the generation of the dynamics includes delays, a displacement of irreversibility toward higher dimensions can be observed.

High-dimensional irreversibility

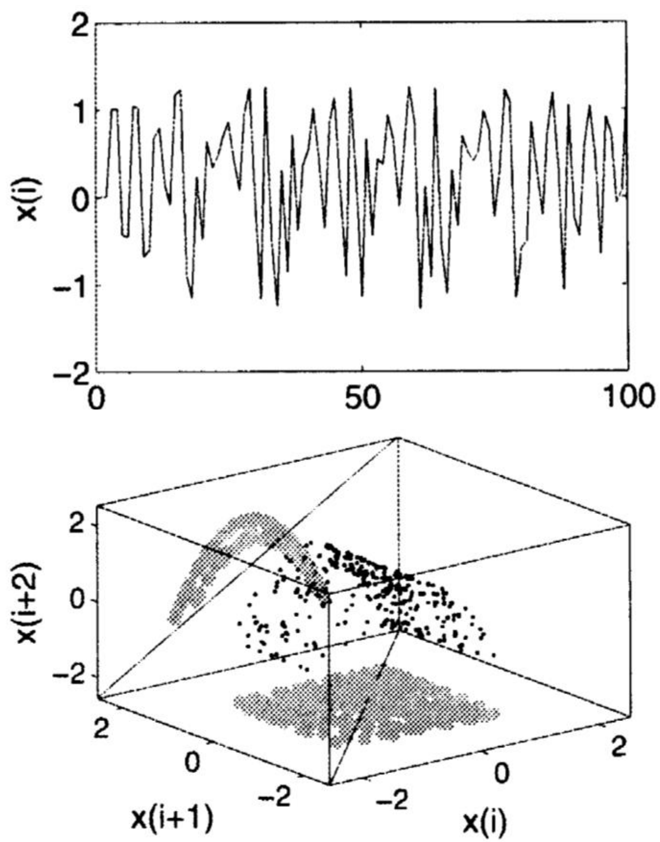
σ-order delayed Henon map

$$x(i+1) = 1 - a \cdot x^2(i-\sigma) + y(i-\sigma) \qquad \text{with } a=1.4,\ b=0.3$$
$$y(i+1) = b \cdot x(i-\sigma)$$

0-order delayed Henon map
(i.e. nondelayed Henon map)

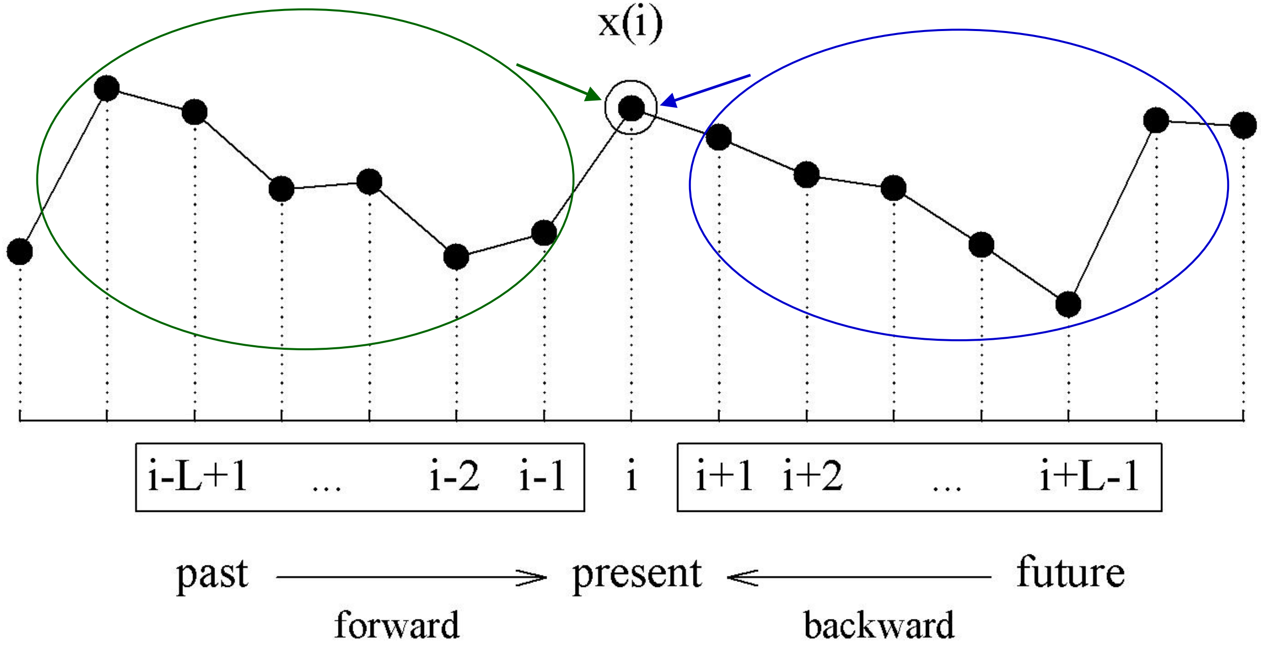


1-order delayed Henon map



K.R. Casali et al, Phys Rev E, 77, 066204, 2008

Detection of irreversible series through local nonlinear prediction



$x(i) = f_f(x(i-1), \ldots, x(i-L+1))$ ⟹ forward relationship

$x(i) = f_b(x(i+1), \ldots, x(i+L-1))$ ⟹ backward relationship

Local nonlinear prediction

Let us estimate $f_f(\cdot)$ and $f_b(\cdot)$

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

i) construct the forward and backward patterns of L samples

$x_{f,L}(i)=(x(i-1),\ldots,x(i-L+1))$ forward pattern

$x_{b,L}(i)=(x(i+1),\ldots,x(i+L-1))$ backward pattern

ii) evaluate the distance between patterns as a measure of their similarity

iii) predict x(i) based on the forward and backward patterns

Forward predictor: $\hat{x}_{f,L}(i)$ = median of $x(j)|\ x_{f,L}(j)$ is similar to $x_{f,L}(i)$

Backward predictor: $\hat{x}_{b,L}(i)$ = median of $x(j)|\ x_{b,L}(j)$ is similar to $x_{b,L}(i)$

Assessment of local non linear prediction

Defined the prediction errors as

$e_{f,L}(i) = x(i) - \hat{x}_{f,L}(i)$ forward prediction error

$e_{b,L}(i) = x(i) - \hat{x}_{b,L}(i)$ backward prediction error

the mean squared prediction error is

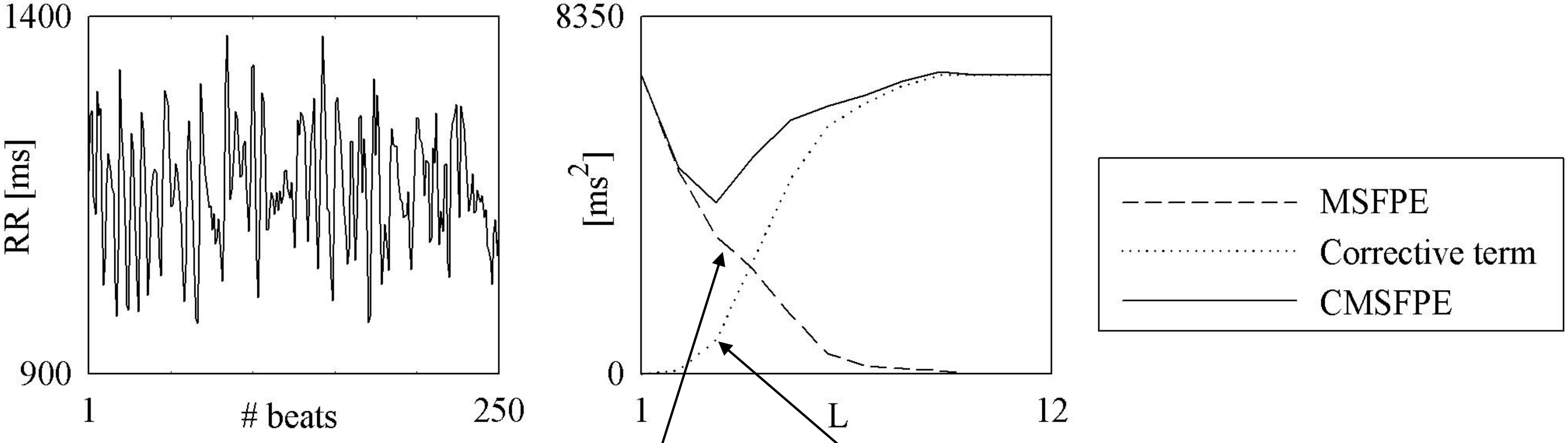
$$MSFPE = \frac{1}{N-L+1} \sum_{i=L}^{N} e^2_{f,L}(i)$$

$$MSBPE = \frac{1}{N-L+1} \sum_{i=1}^{N-L+1} e^2_{b,L}(i)$$

MSFPE (MSBPE) = 0 $\Longrightarrow$ perfect prediction

MSFPE (MSBPE) = mean squared deviation from the median (MSD) $\Longrightarrow$ null prediction

Corrected mean squared forward prediction error



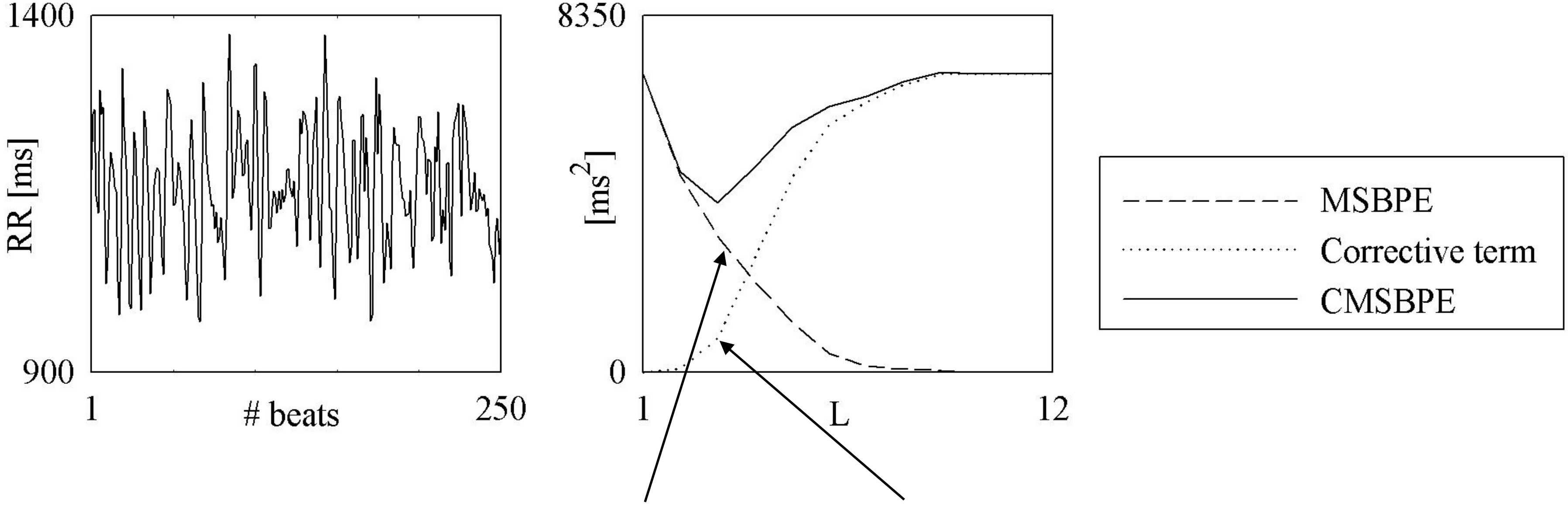
$$\mathrm{CMSFPE}(L) = \mathrm{MSFPE}(L) + \mathrm{MSD} \cdot \mathrm{perc}(L)$$

$$\mathrm{UPI}_f = \min_{L}(\mathrm{CMSFPE}(L))$$

$$\mathrm{NUPI}_f = \frac{\mathrm{UPI}_f}{\mathrm{MSD}}$$

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

Corrected mean squared backward prediction error



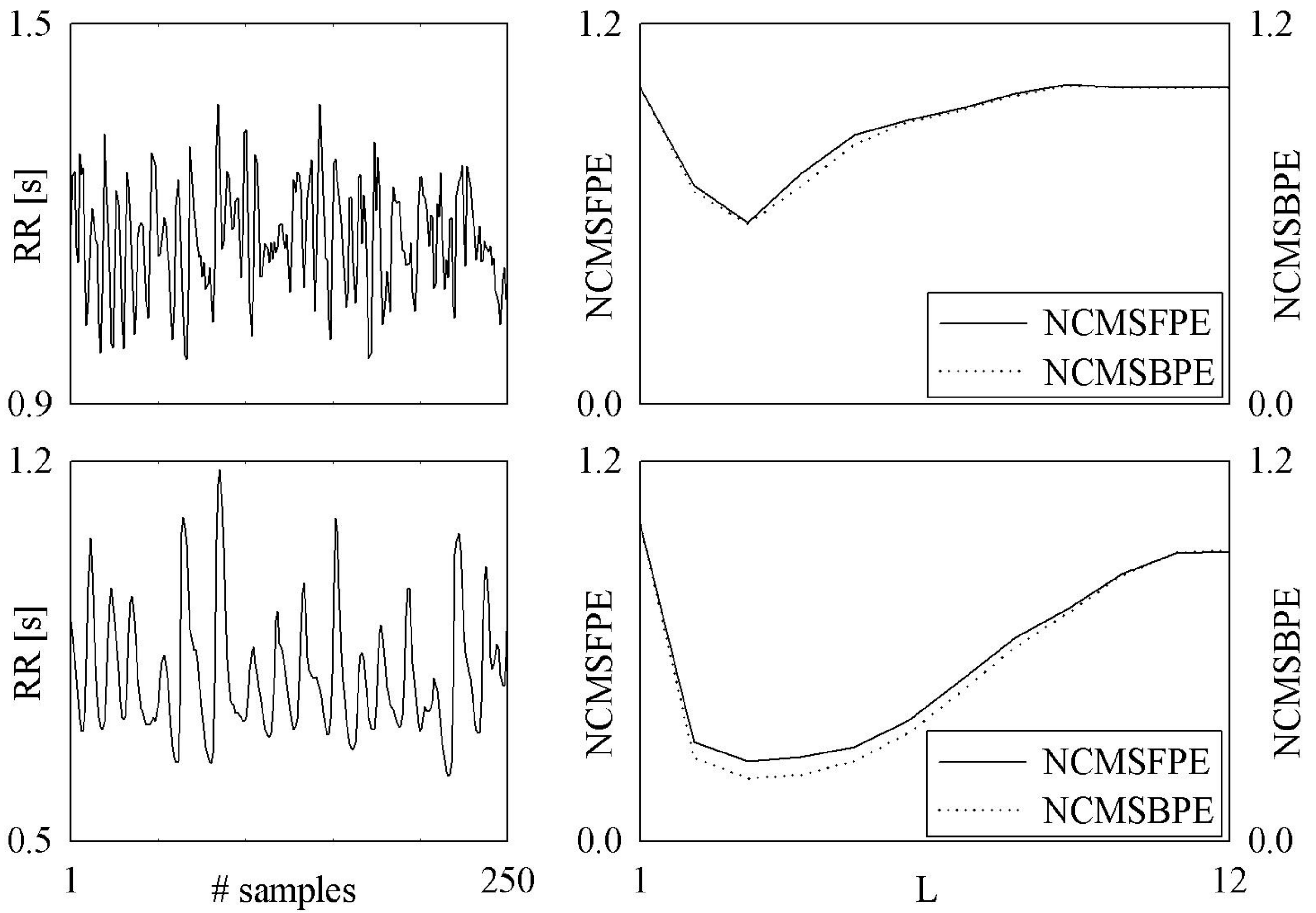
$$\mathrm{CMSBPE}(L) = \mathrm{MSBPE}(L) + \mathrm{MSD} \cdot \mathrm{perc}(L)$$

$$\mathrm{UPI_b} = \min_{L}(\mathrm{CMSBPE}(L))$$

$$\mathrm{NUPI_b} = \frac{\mathrm{UPI_b}}{\mathrm{MSD}}$$

A. Porta et al, Phil Trans R Soc A, 367, 1359-1375, 2009

Examples of calculation of MSFPE and MSBPE to short-term heart period variability



$NUPI_b \approx NUPI_f$

$NUPI_b < NUPI_f$

The normalized difference between backward and forward unpredictability indexes (BFUPI)

$$BFUPI = \frac{NUPI_b - NUPI_f}{NUPI_b + NUPI_f}$$

BFUPI > 0 ⟹ x is better predicted in the forward direction

BFUPI < 0 ⟹ x is better predicted in the backward direction

BFUPI ≠ 0 ⟹ x is irreversible

A. Porta et al, Phil Trans R Soc A, 367, 1359-1375, 2009

Surrogate data approach on discriminating parameter (DP)

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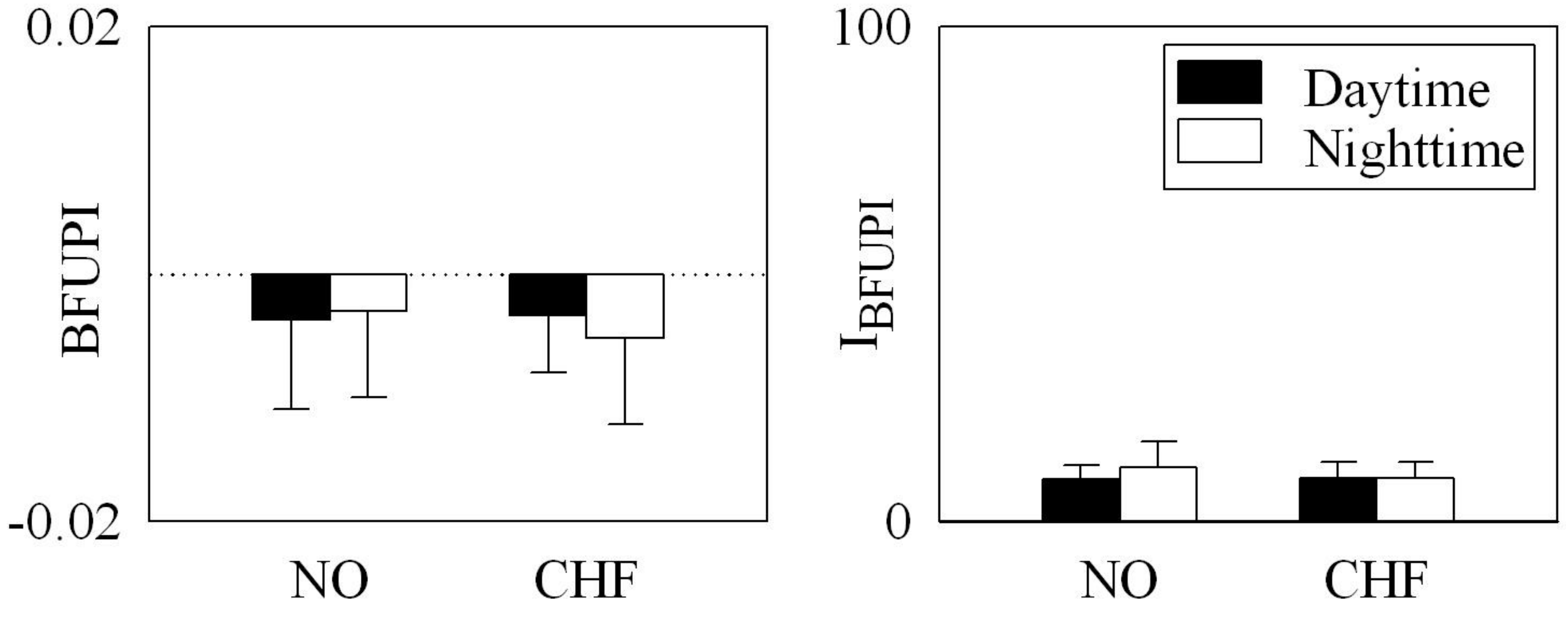
If $DP_o < DP_{s,0.025}$ ⇨ irreversibility of type-2

DP = BFUPI

Optimal embedding dimension of RR series extracted from 24 RR Holter recordings in healthy subjects and heart failure patients

Both in healthy subjects and chronic heart failure patients L at the minimum of CMSFPE and CMSBPE is significantly larger than 2

High dimensional irreversibility analysis of RR series in 24 RR Holter recordings in healthy subjects and heart failure patients



A. Porta et al, Phil Trans R Soc A, 367, 1359-1375, 2009

Conclusions

1) Time irreversibility of short-term heart period variability depends on the magnitude of the sympathetic modulation

2) Time irreversibility detects a significant amount of non linear dynamics especially in heart failure patients

3) The contribution of high dimensional (L>2) dynamical features to time irreversibility of short-term heart period variability is negligible