Chaos and Real World:
Nonlinear analysis of cardiovascular variability series

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<u>Nonlinear analysis</u>

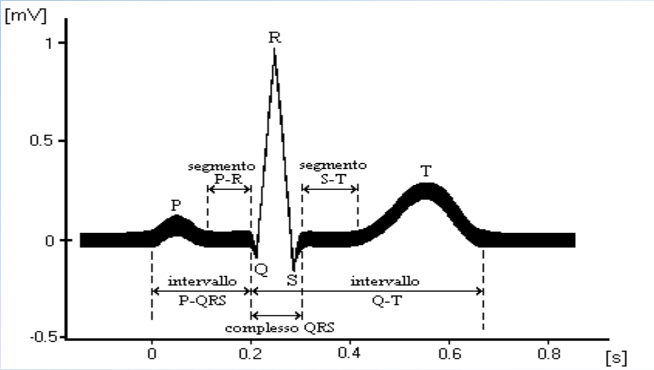
an introduction

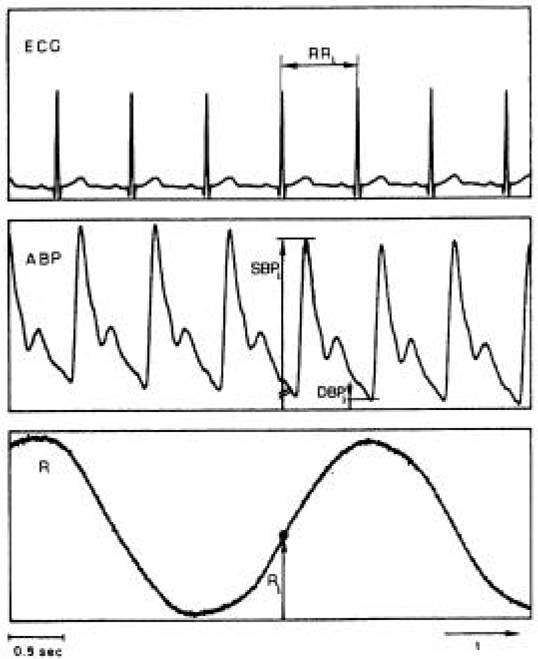
- Experimental findings support the hypothesis that the behavior of **many biological systems** could be **generated by a low-dimensional nonlinear system**.

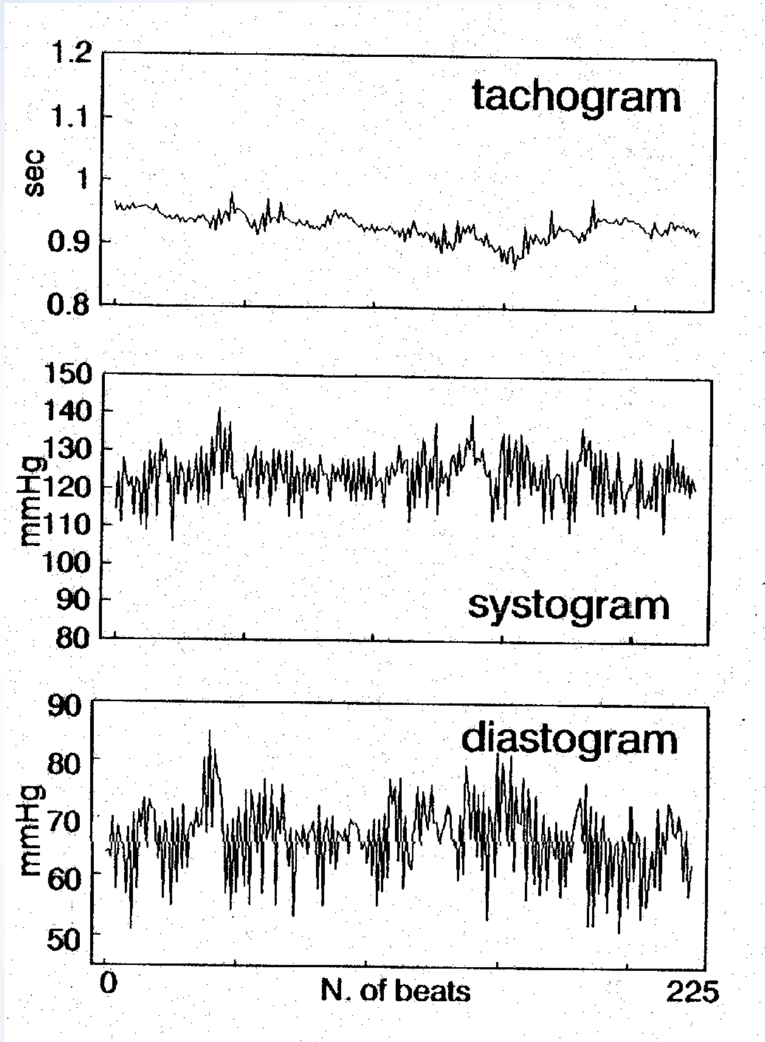
- Among these, the **cardiovascular system** shows the **fractal structure of the electrical conduction system**, the quasi-periodic but also **erratic behavior** of electrocardiographic, blood pressure and respiration signals.

- Moreover the **variability** is one of the **main properties** of the **healthy heart**.

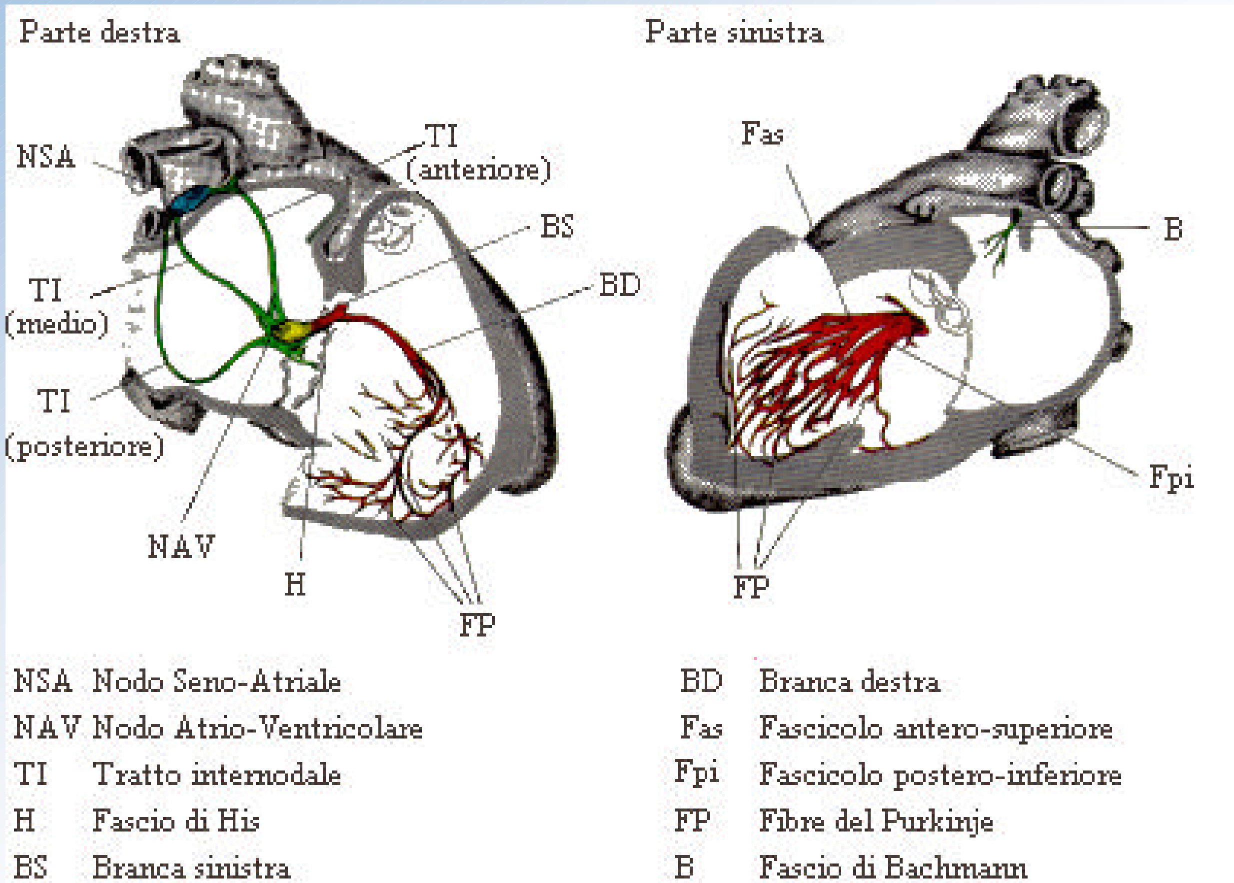
Cardiovascular Signals







Variability signals



Pathology of organs

vs.

Pathology of controlling systems

Dynamical Diseases

HRV in MI studies

➢ Parameters of interest

- VARIANCE
  - 1990 Kleiger RE, Miller JP, Krone RJ, Bigger JT The independence of cycle length variability and exercise testing on predicting mortality of patients surviving acute Myocardial Infarction. The Multicenter Postinfarction Research Group, ***Am J Cardiol***, 65 (7):408:11, 1990.
- POWER SPECTRAL PARAMETERS
  - 1987 Lombardi F., G, Sandrone, S., Pernpruner, et al. Heart rate variability as an index of sympatho-vagal interaction after acute myocardial infarction, ***Am. J. Cardiol.*** 60:1239-1245, 1987.
- 1/f α POWER LAW
  - 1996 Bigger, T.J.Jr., R.C., Steinman, L.M., Rolnitzky, J.L. et al, Power law behavior of RR interval variability in healty middle-aged persons, patients with recent acute myocardial infarction, and patients with heart transplant, ***Circulation,*** vol 93, 12, 2142-2151, 1996
  - 1996 Lombardi F, Sandrone G, Mortara A et al. Linear and nonlinear dynamics of heart rate variability after acute myocardial infarction with normal and reduced left ventricular ejection fraction ***Am.J.Cardiol*** 1996 77:1283-88.

Experimental Protocol

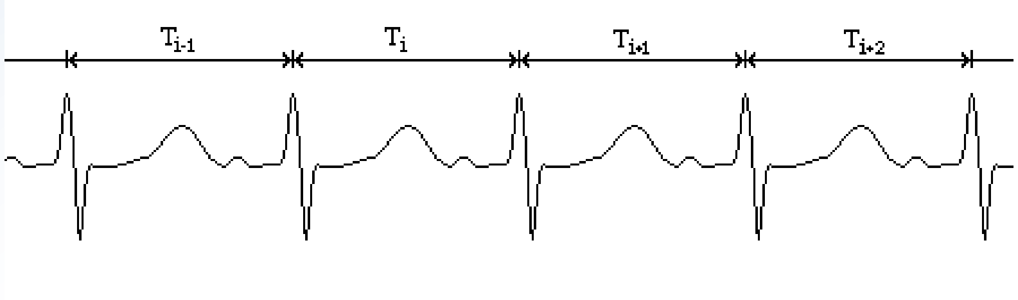
- **24-hour Heart Rate Variability** signals (HRV) from Holter recordings (80,000-120,000 R-R values):

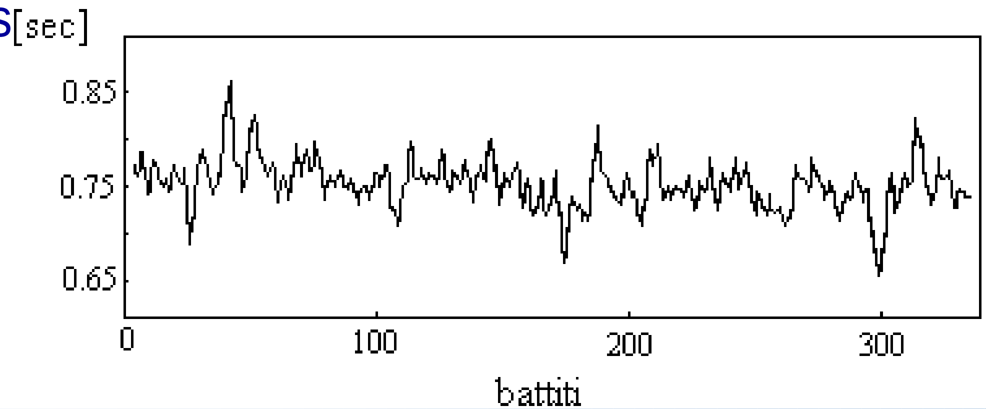
- **10 Normal** subjects
- **10 Heart Failure** (HF) patients
- **7 Transplanted** subjects
- **8 survived** + **9 dead** in **ICU**

- **For simulation** purpose:
- **Fractional Brownian motions** (Mandelbrot-Van Ness algorithm).
  - Hurst exponent values: H=0.1-0.9

HRV analysis

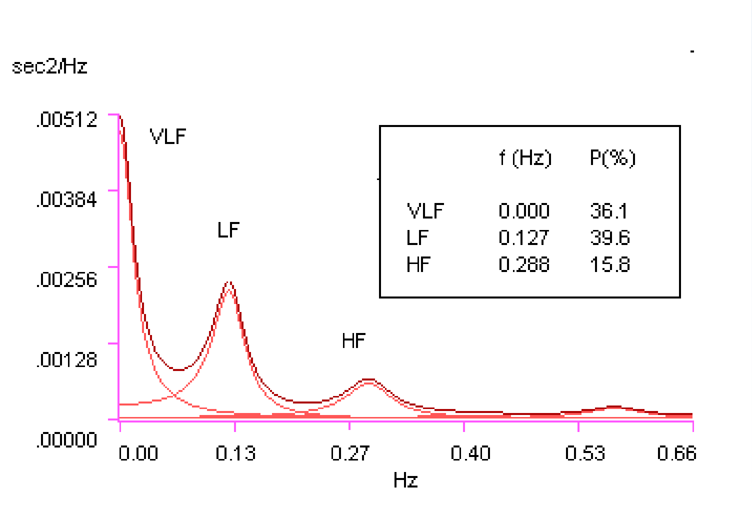
- Recent results show the heart rate variability signal (**HRV**) does **not only contain linear harmonic contributions** (traditionally identified through spectral analysis techniques) but it **possesses a fractal like geometry**
- **HRV** is characterized by **many rhythmic components** interacting **over different scales.**
- **HRV** time series **can show fractal characteristics** in their patterns, as well as in the temporal scales.
- **HRV** with different degrees of magnification of time step, **shows patterns possessing self-similar characteristics** (at a more or less extent).

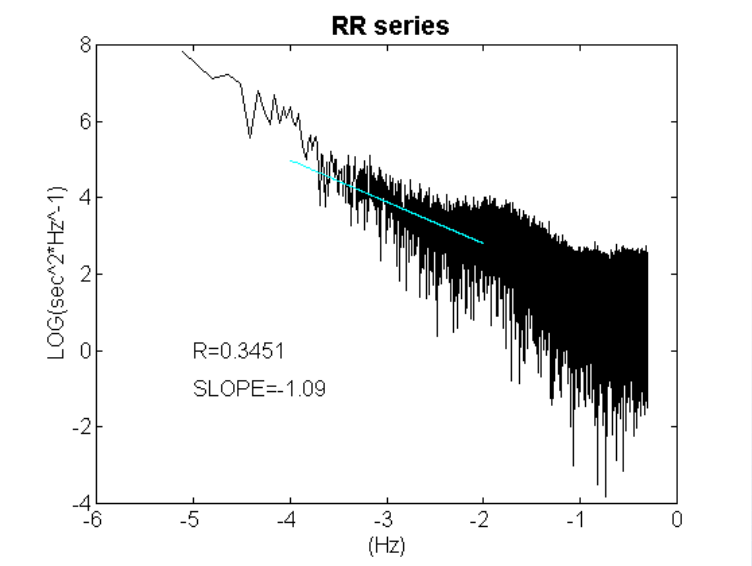




This observed pattern can be modified if pathological heart conditions take place.

HRV (short and long period analysis)





Task Force of the Europ. Soc. of Cardiol. & North Am. Soc. of Pacing and Electrophys.

Heart Rate Variability, standard of measurement, physiological interpretation and clinical use,

Circulation 1996, 93:1043-65.

Cardiovascular control systems

Short time

- 300 beats ~ 5 min
- Sympathetic and Parasympathetic control

(*sympatho-vagal balance*)

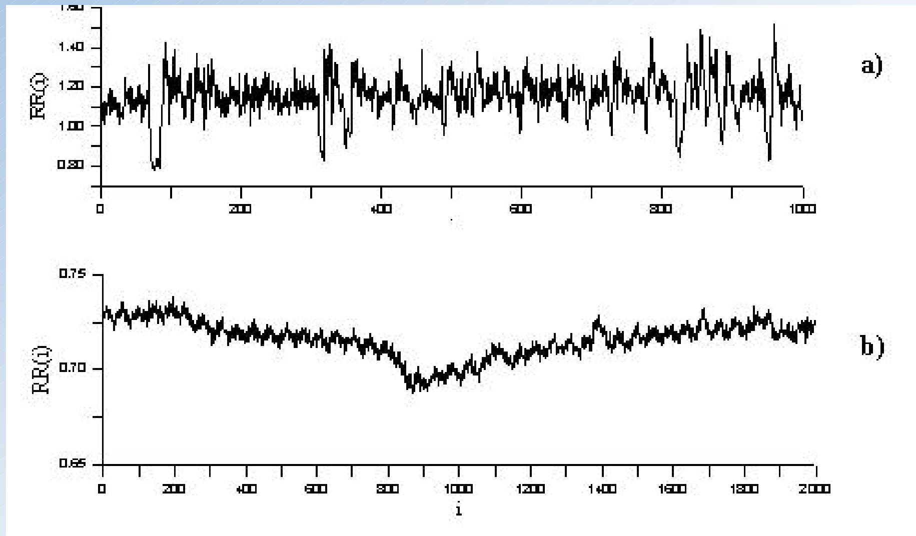
- **Analysis by LINEAR approaches**
- (PSD estimation by AR modelling)

Long time

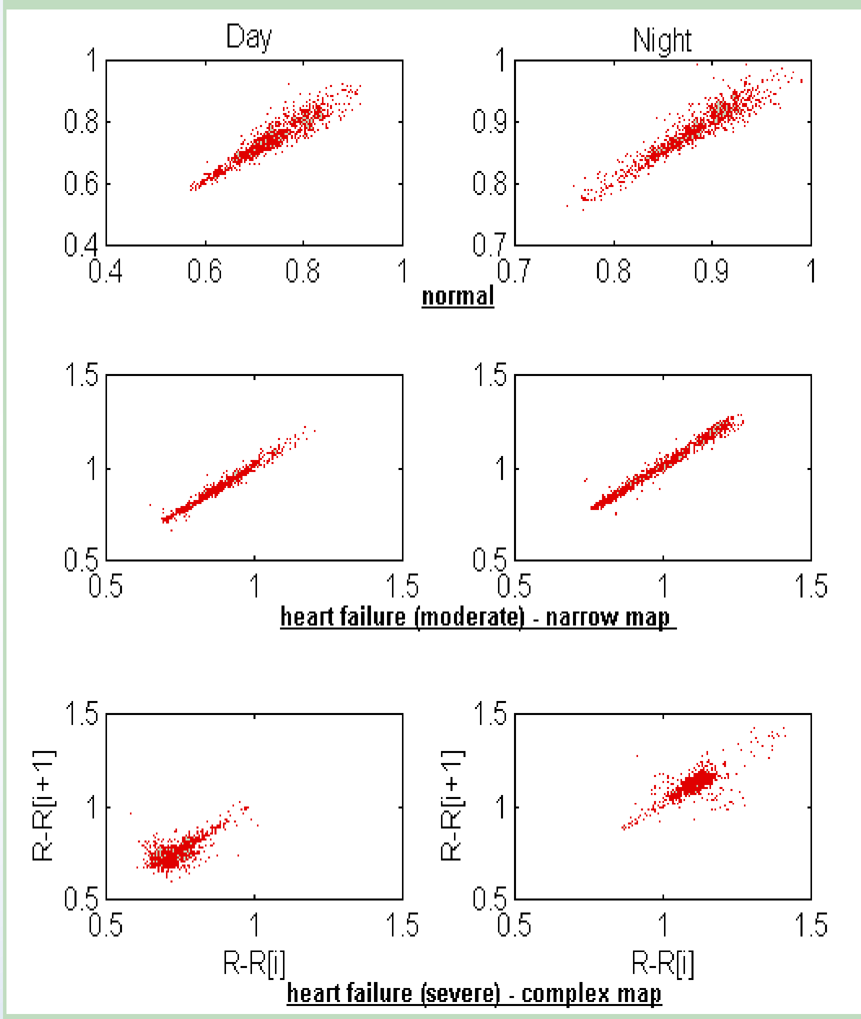
- 20.000-100.000 beats ~6-24 hours
- Long period "global" control
- **Analysis by**

  NONLINEAR methods

HRV: examples

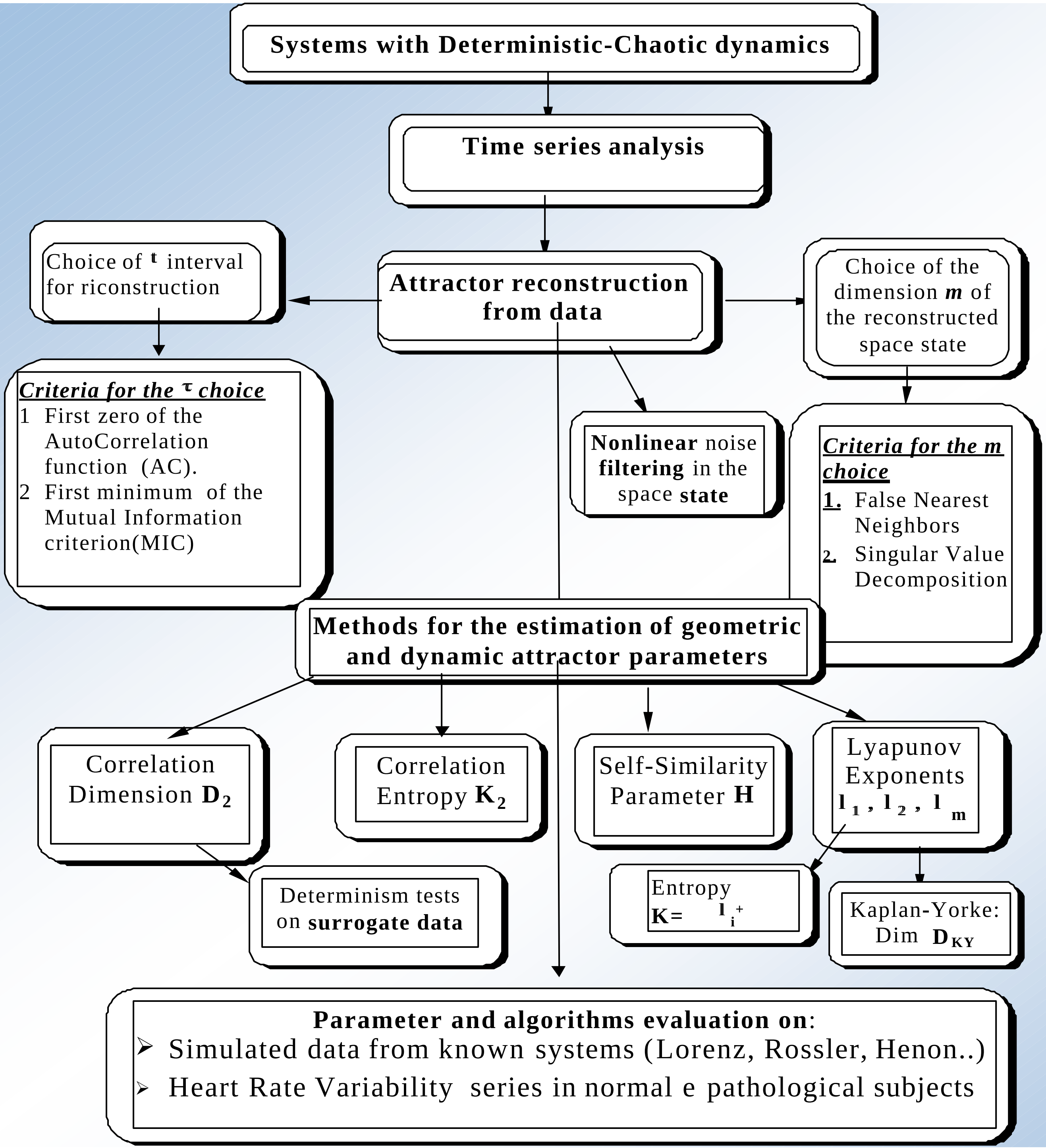


HRV of Normal (A) and Transplanted (B)

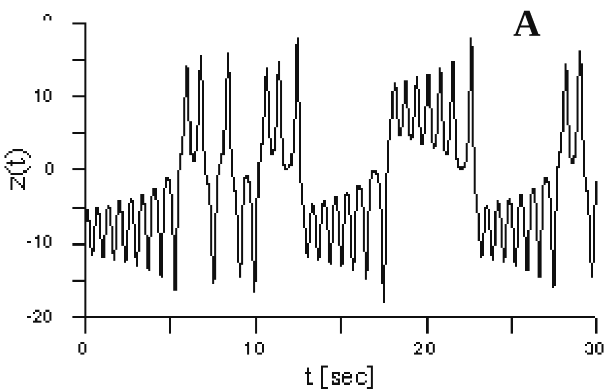


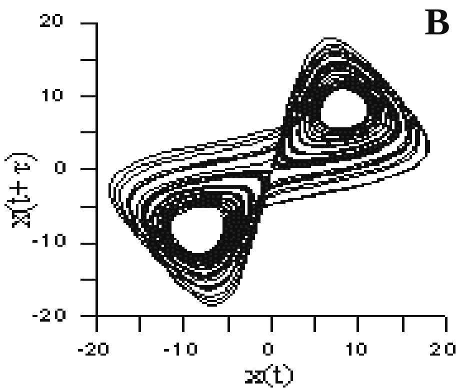
Delay Maps of Heart failure subjects

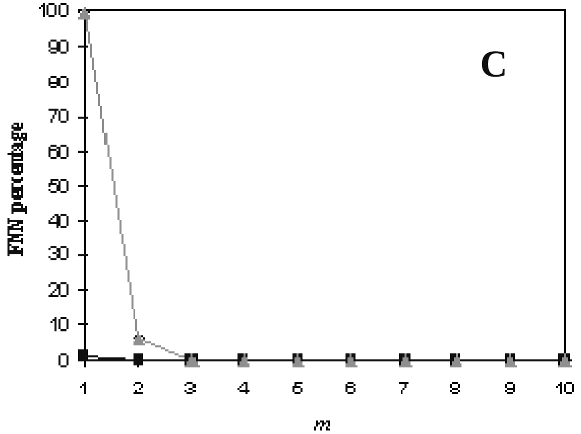
Methods:
an overview

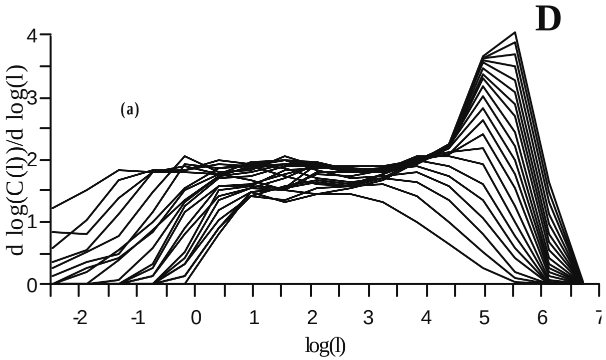


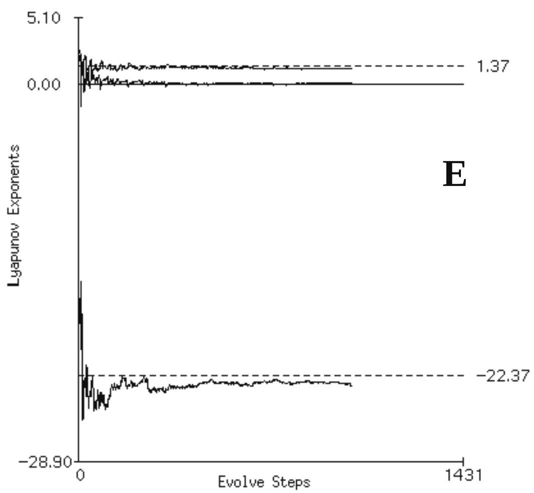
the Lorenz system example











F

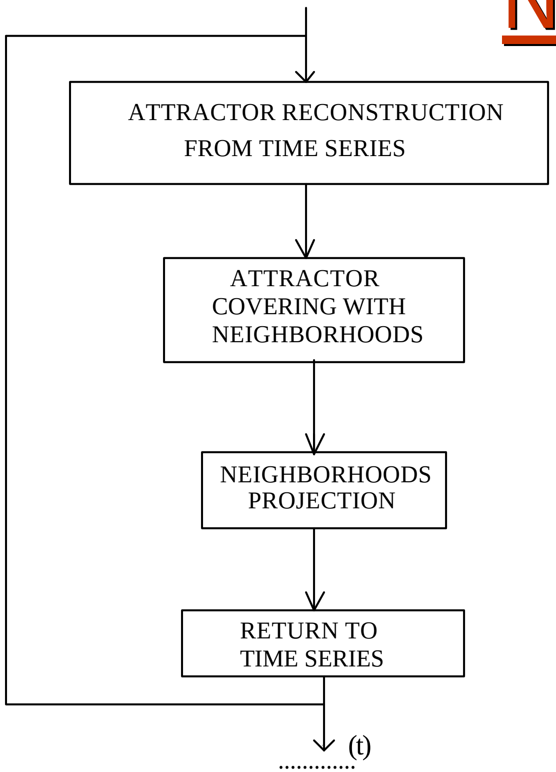
LORENZ Model (variable z)

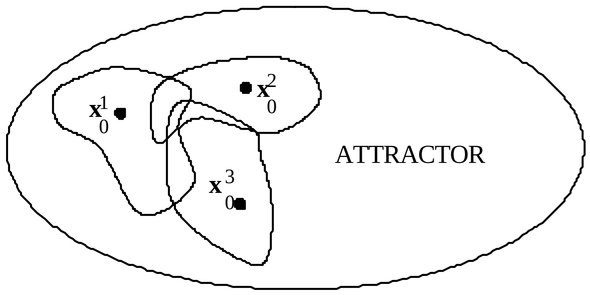
m	λ_1	λ_2	λ_3	λ_4	λ_5	λ_6
3	1,37	-0,03	-16,77			
4	1,36	-0,01	-5,98	-15,26		
5	1,42	-0,09	-2,33	-5,37	-14,25	
6	1,41	0,06	-0,62	-2,38	-5,39	-13,89

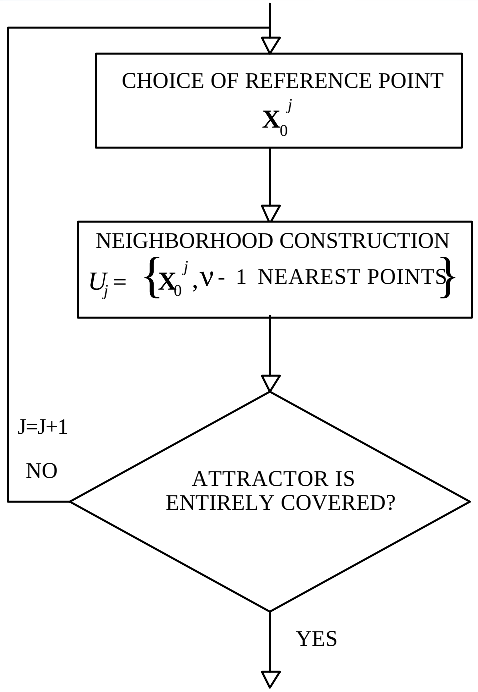
Correlation Dimension D_2=2,05

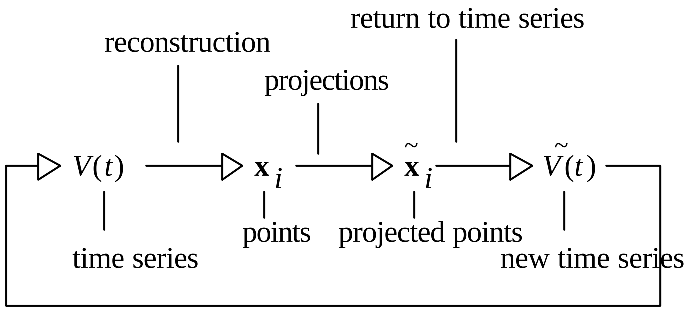
- **A** - Sampled time series
- **B** - Reconstructed Lorenz attractor (it looks similar to the original). **t** is the time delay.
- **C** - Evaluation of state space dimension (***FNN***)
- **D** - Correlation Dimension. Flat region provide ***D_2*** near 2
- **E** - Lyapunov Exponent (***LE***) spectrum
- **F** - LE values for growing ***m***

Nonlinear noise filtering - algorithm









b)

- **d** dimension for the attractor reconstruction;
- **t**: delay time of reconstruction;
- **k**: dimension of local subspaces;
- **n**: number of points of each neighborhood.

Lorenz attractor

Reconstructed Lorenz attractor and relevant time series:

a) Original without noise

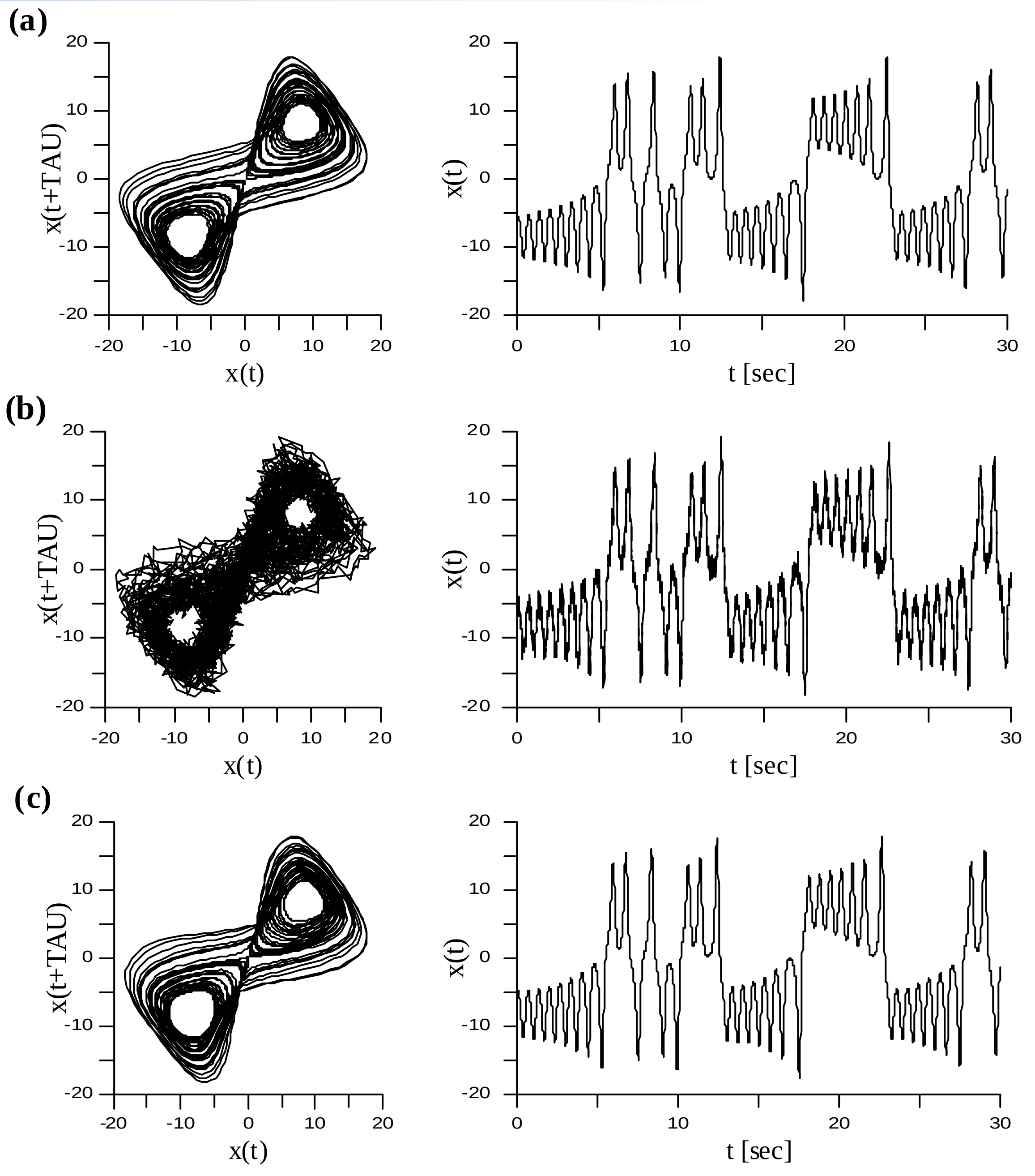
b) 10% white noise added

c) After nonlinear noise reduction

(GAIN=13.5 dB after 26 iterations;

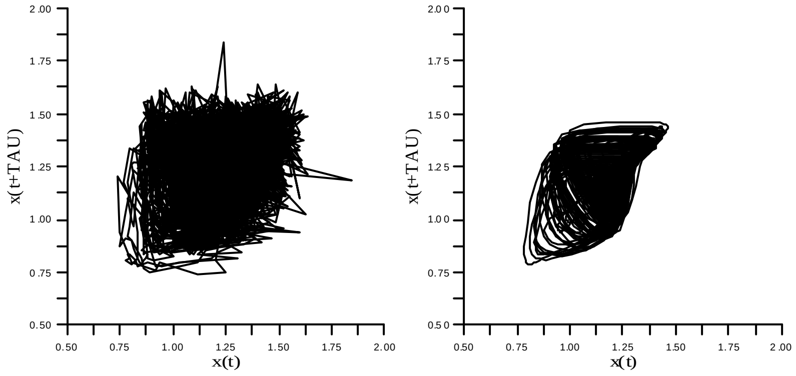
Algorithm parameters

d=20, τ=1, k=2,ν=40).

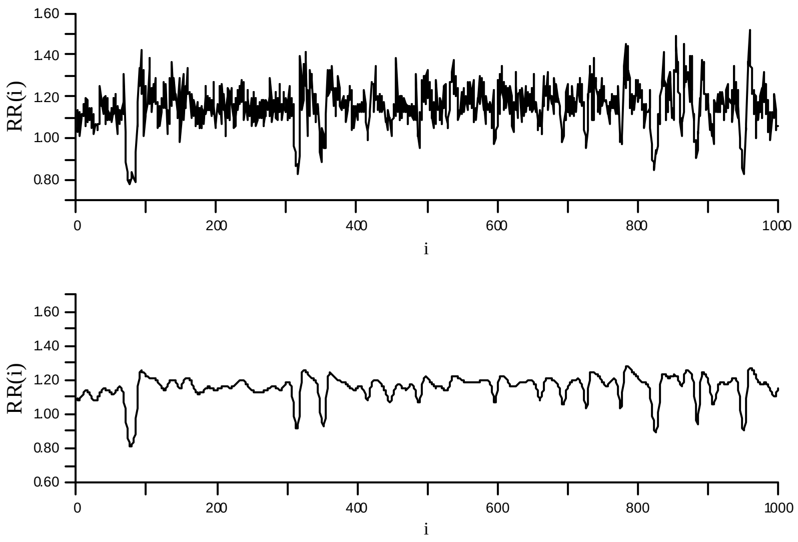


examples - HRV normal vs. transplanted

Nonlinear noise filtering -
results on HRV signal of a Normal subject during Night

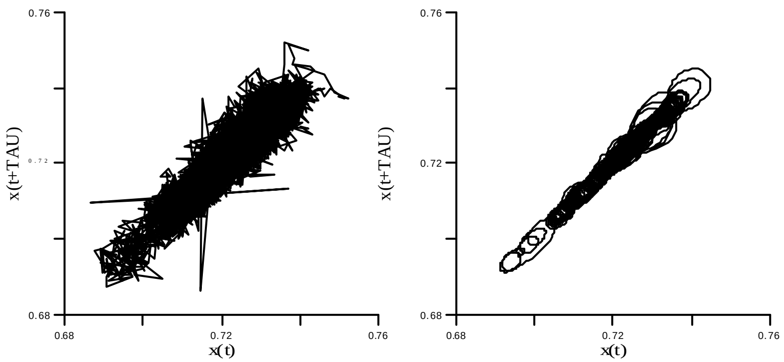


a) reconstructed attractor before and after noise reduction

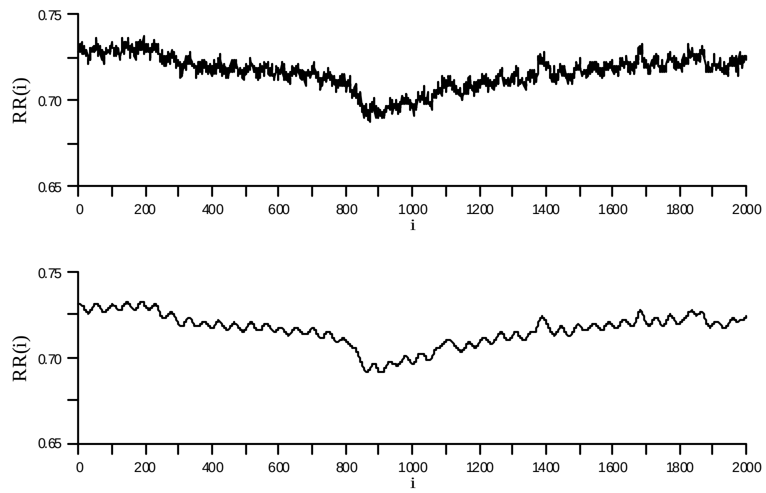


b) Tachogram (2000 points) before and after de-noise procedure.

Nonlinear noise filtering -
results on HRV signal of a Heart Transplanted subject during Night

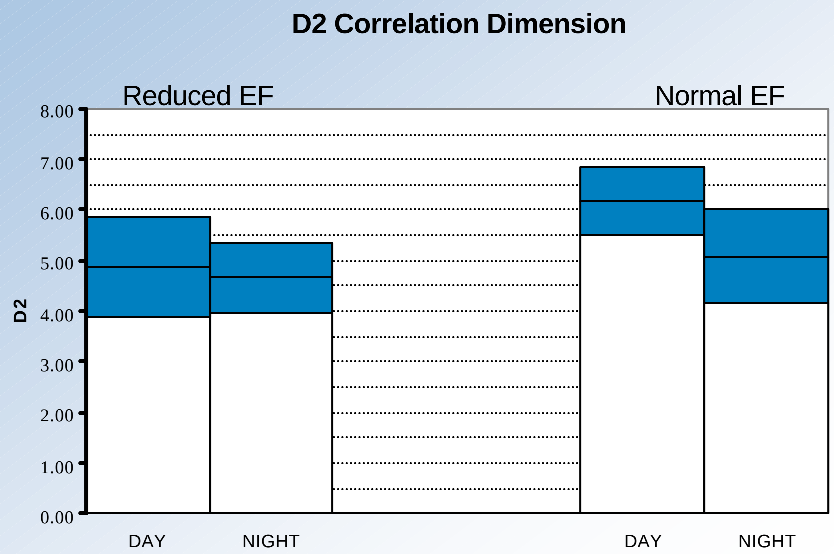


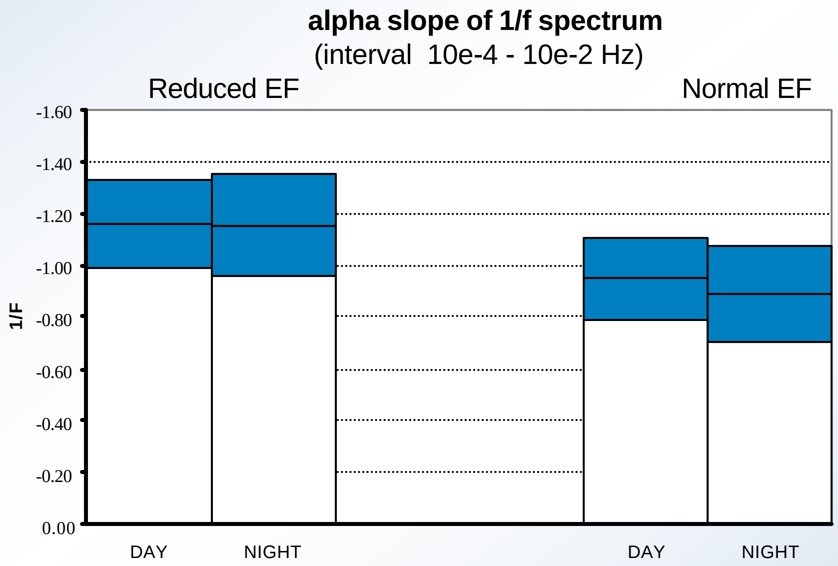
a) reconstructed attractor before and after noise reduction



b) Tachogram (2000 points) before and after de-noise procedure.

Results in AMI subjects



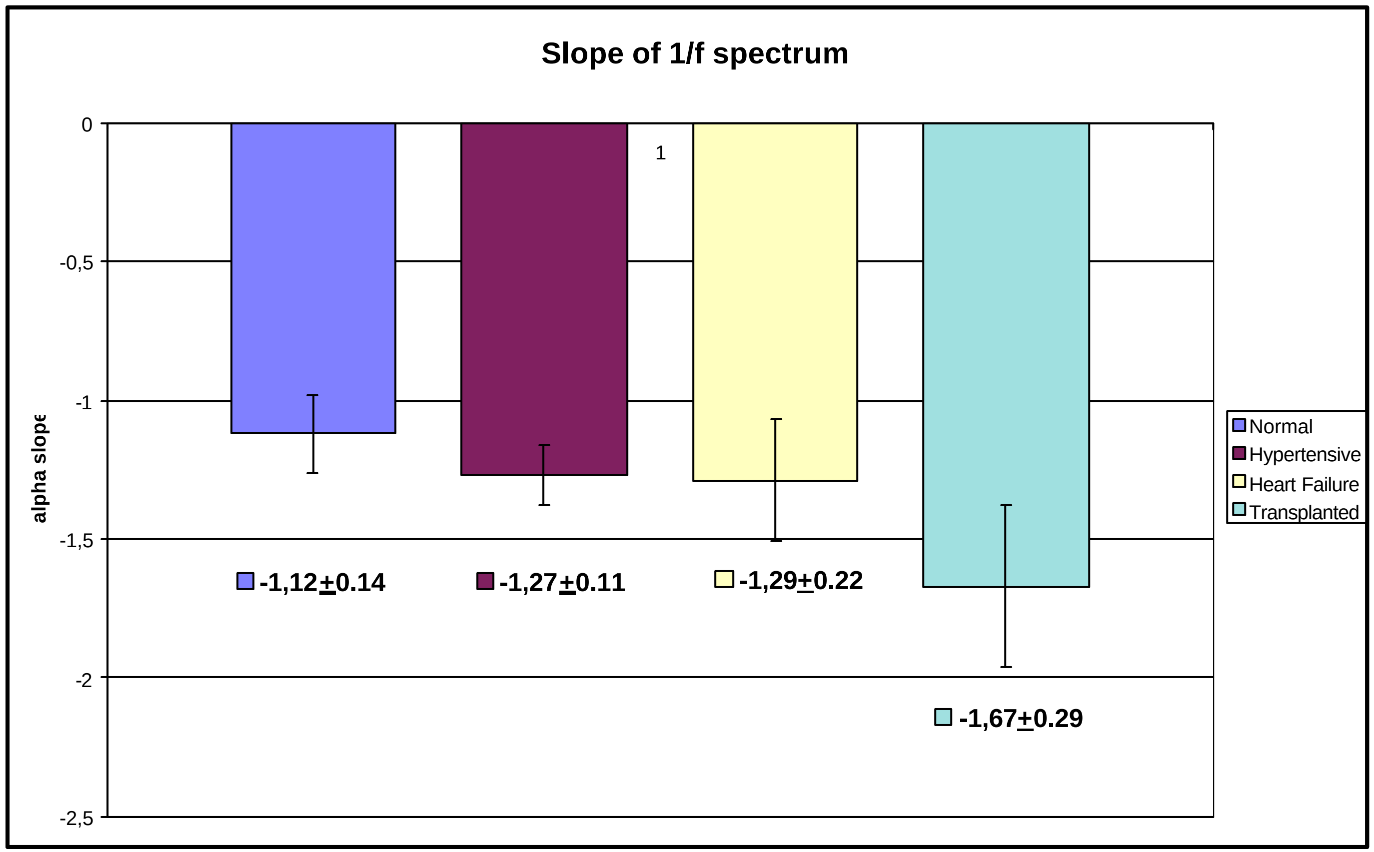


- **D2** and a perform a **significant classification ($p<0.05$) of AMI** subjects.
- They **separate** the **group** of subjects who after MI keep a **good performance of the cardiac pump** (NEF) **vs**. the group which after MI shows an **alteration of this function** (REF).
  - α values: 1.19±0.25 (LEF) vs. 0.98±0.16 (NEF) over 100.000 R-R values (24 hours)
  - D2 values: in day epoch are 5.2±1.0 (LEF) vs. 6.2±0.7 (NEF). R-R values =30.000 (6-7 hours)
- Variance of HRV series was not able to significantly separate NEF and LEF group.

a slope of 1/f spectrum of HRV signal

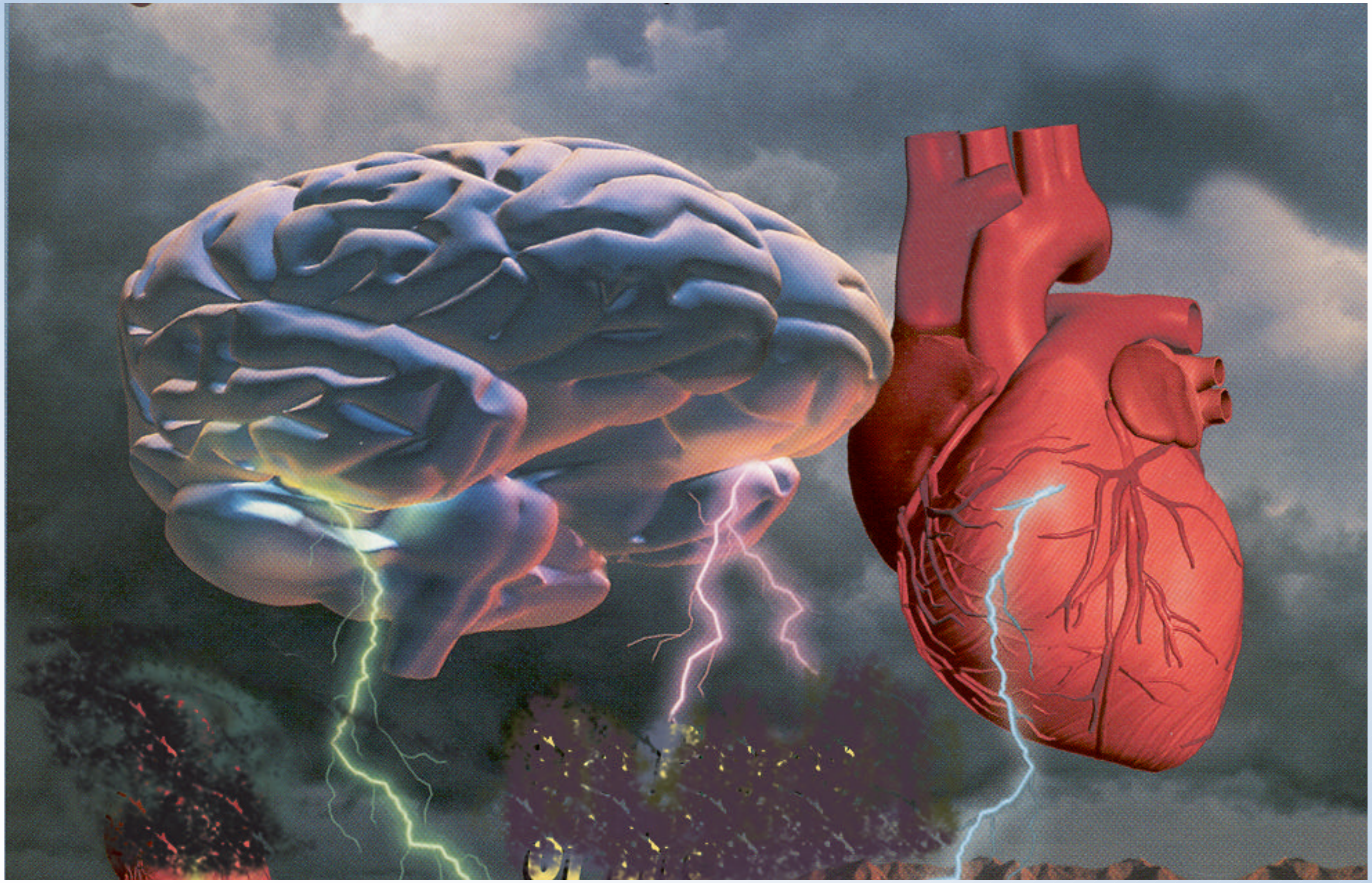
- 9 normal, 6 hypertensive, 11 heart failure, 7 heart transplant
- HRV signals collected in the 24 hours

- **Increase** of a **slope** with **pathology**



Conclusion

- Nonlinear parameters are able to **significantly separate** patients with **different pathological conditions**
- These parameters **coupled together with others more classical indicators** of the cardiac neural control function, **could improve understanding of heart dynamics**
- **Nonlinear characteristics** of the HRV control can assume a **clinical and predictive relevance.**
- As some authors hypothesized, healthy sistems have good lines of communication. On the opposite, **systems in deseased state** can show reduced speed in crucial biological messages transfert and reception, until they become **unable to connect with other system components**.
- **Complexity in biological control system** seems related to a **nonlinear model driving the system dynamics**. The knowledge of these system properties introduces a **new insight into the heart pathophysiology** study together with **more sensitive predictive parameters.**



Anaxagoras, fragment no. 12 (500 B.C.)

nous de paV omoioV esti kai o meixwn kai o elattwv.

The Mind is self-similar, no matter whether it refers to the large or to the small