# Nonlinear analysis of cardiological signals towards clinical applications

A diploma thesis presented by
Pierre-Antoine Absil*
at the University of Liège, Belgium,
in partial fulfillment
for the degree of Ingénieur Physicien (Physics Engineering),
June 1998.
Advisor: Rodolphe Sepulchre*

Original title: "Analyse non linéaire de signaux cardiologiques en vue d'applications cliniques".

*Institut d'Electricité Montefiore, Université de Liège,
Bât. B28 Systèmes, Grande Traverse 10, 4000 Liège, Belgium.
E-mail: {absil,sepulchre}@montefiore.ulg.ac.be. Fax: +32-4-366 29 89

EXTENDED SUMMARY

**Abstract**

This work is dedicated to the study of cardiac rhythm. It results from a collaboration with the Cardiology and Neurology Departments at Liège University Hospital. The applications considered are essentially twofold: on the one hand, prognosis regarding the health of patients suffering from congestive heart failure, through studying long range correlations and scale invariance in their cardiac rhythm; one the other hand, diagnosis of sleep apnea by means of a dedicated processing of the patient's cardiac rhythm. Both studies are based on the so-called $RR$ signal, i.e. the sequence of time intervals between successive ventricular contractions.

## 1 Introduction

Heart rate variability (HRV), or the study of cardiac rhythm fluctuations, has attracted the interest of many physicists in the recent years for its potential predictive value in the evolution of heart disease.

For two main reasons, the ECG (electrocardiogram) is now the outstanding method of assessing cardiac rhythm. First, an ECG is easily recorded — one just has to fix a few electrodes on a patient's skin in order to capture the electrical activity of his heart. Second, the ECG chart of a full cardiac beat shows a characteristic peak, called $R$ peak, due to the ventricular contraction. This peak is high (thus easily detectable) and narrow (thus localized with high precision). The $RR$ time interval between two $R$ peaks (Figure 1) gives the heart beat period, and the $RR$ series (i.e. the succession of the $RR$ durations, see Figure 2) is the standard tool for measuring cardiac rhythm.

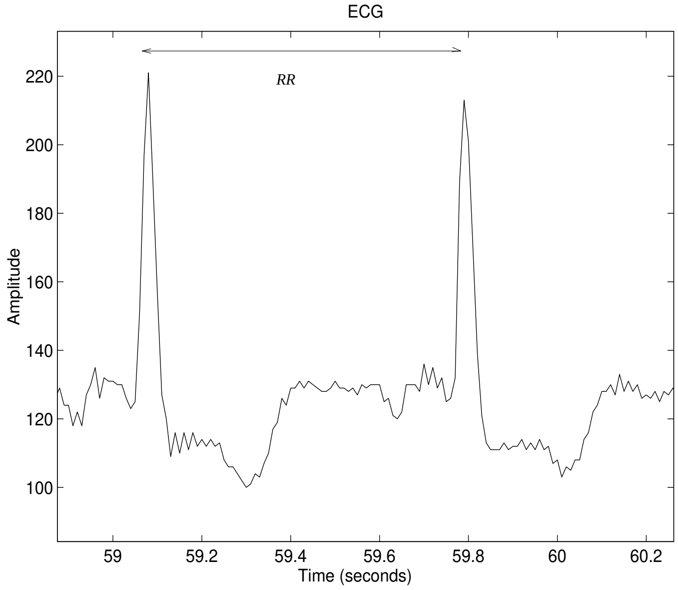


Figure 1: ECG of a full heart beat.

Although ECG recording has been a routine task for decades, cardiologists were hardly interested in heart rate variability until the year 1987 when Klieger et al. argued that an abnormally small standard deviation in the $RR$ series is a risk factor for cardiac disease [Klieger 1987]. Since then, a great number of methods have been elaborated in order to assess cardiac rhythm variability. The interest at stake is high, since cardiovascular casualty is the first mortality factor in the industrialized countries.

From an engineering or physics point of view, the $RR$ series is just a long discrete signal $RR[n]$ (about 100 000 values per 24 hours) to which signal processing methods can be applied. If heart beats were perfectly regular, the $RR$ series would give rise to a constant signal. Figure 2 shows that this is not the case and that the $RR$ series undergoes important fluctuations, similar to a stock market indicator for instance.

A question therefore arises whether efficient signal processing methods can be found to distinguish $RR$ series of healthy individuals from the diseased patients.

Cardiologists first used classical signal processing methods, either "temporal" (calculation of statistical parameters on the $RR$ series, e.g. the standard deviation used by Klieger), or "frequential" (spectral distribution of energy between high and low frequencies) [Task Force 1996, Bilge 1997].

More recently, the development of chaos theory has introduced many new tests meant to detect determinism in a signal and evaluate its complexity: standard methods include phase portrait reconstruction, Poincaré sections, Lyapunov exponents and Kolmogorov entropy [Babloyantz 1988].

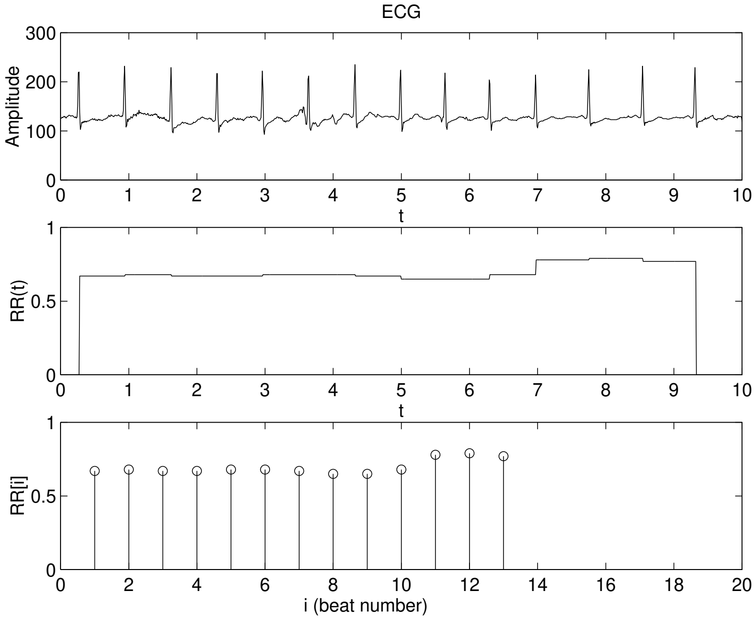


Figure 2: Upper: ECG signal (electrical potential as a function of time). Middle: signal $RR(t)$ giving at each time $t$ the duration of the current heart beat interval. Lower: the series $RR[i]$ giving the successive time intervals between heart beats. This signal $RR[i]$ is our raw data in this diploma thesis.

The diploma thesis [Absil 1998] summarized here is dedicated to the analysis of cardiac rhythm and several of its applications. The main results deal with congestive heart failure prognosis and sleep apnea diagnosis.

## 2 Is cardiac rhythm chaotic?

Since cardiologists make use of methods derived from chaos theory, it is natural to ask whether cardiac rhythm is chaotic indeed. The answer is not trivial because of a snag in the very definition of chaos in nondeterministic systems.

Among deterministic systems (and leaving aside a precise mathematical definition), are considered as *chaotic* those for which arbitrarily close trajectories diverge exponentially while staying in a bounded region of space.

Now, although it is clear that cardiac rhythm is somewhat deterministic (for example, in an extrasystole, an abnormally long interval will automatically be followed by an abnormally short interval), it is also clear that the evolution of cardiac rhythm depends on random exterior factors. When one observes a chaotic behaviour in such a system, one has to wonder if this behaviour comes from the intrinsic dynamics of the system or if it derives from exterior perturbations.

A method is proposed in [Chon 1997] to evaluate the chaotic character (measured by the presence of positive Lyapunov exponents) of a deterministic signal perturbed by noise. Applied to HRV, this method concluded that the deterministic component of cardiac rhythm is not chaotic. This questions is the object of the second chapter in the diploma thesis.

## 3 Prognosis for congestive heart failure

The third chapter of the diploma thesis studies the law governing the evolution of long term correlations in $RR$ series. Recent studies pointed out a power law behaviour in many biological signals [Peng 1996]. Such a behaviour is related to the absence of characteristic time, i.e. scale invariance. This is presumably an important advantage for a biological system to which it confers robustness to exterior trends.

Our study relies on the DFA (Detrended Fluctuation Analysis) function proposed in [Peng 1994] and applied to cardiac rhythm in [Peng 1996, Goldberger 1997]. In these articles DFA functions of different $RR$ series are approximated by power laws $n^\alpha$ and differences are observed between $\alpha$-indices of healthy and diseased patients.

Similar conclusions are obtained in the present study. In addition, we define a `residue` parameter, meant to measure the gap between a particular DFA function and its power law approximation. Extrapolating the physiological interpretation suggested above, a high residue could be related to a diminished ability of the heart to tackle exterior perturbations.

After defining the DFA function and the related indices, we apply it to various noises in order to infer the interpretation above. We then apply the DFA to 38 patients suffering from Congestive Heart Failure (CHF). These patients have been followed during 4 years after the ECG recording and are distributed in three prognostic groups: deceased or heart-transplanted — heart casualty — good health.

The statistical study shows up the discriminating power of DFA indices. In particular, one of the two parameters deduced from the DFA happens to be more efficient than classical methods in the task of sorting out the patients into their prognostic groups. Moreover, a high residue has been obtained for patients who later deceased or had heart-transplantation. This confirms the possible link between severity of illness and presence of characteristic times.

This study lead to the publication [Absil 1999].

## 4 Visualizing variability

The DFA gives a few very good results in statistical tests. Nevertheless, this method is computationally demanding and it only gives a few numbers which by themselves do not fully picture the complexity of cardiac rhythm. An interesting visual information about HRV is provided by the method of variability diagrams (VD) introduced by Babloyantz and her team [Babloyantz 1996, Babloyantz 1997]. This method is the object of the fourth chapter of the diploma thesis.

In the above-mentioned chapter, the usefulness of first order variability diagrams, compared to first return maps, in the detection of extrasystoles is confirmed, both theoretically and practically. A mixed VD is proposed for detecting *missed beats*. We also tried to apply the VDs to the diagnosis of congestive heart failure and of sleep apnea, but without success. Finally, in the case of the theoretical model of the "Bouncing Ball", we show that the first-order VD applied to only one of the two state variables of this discrete time system, reveals a structure that the first return map is unable to enlighten.

## 5 Sleep apnea

The last chapter of the diploma thesis described the program we developed for detecting sleep apnea by means of $RR$ series. This is part of a global project for developing an ambulatory device for sleep apnea detection. This device would dismiss two important drawbacks of the classical polysomnographic (PSG) analysis. First, PSG is demanding since it requires the patient to stay in hospital for one night (this can also jeopardize the validity of the test since the sleep of the patient is likely to be perturbed by the unusual environment). Second, PSG usually suffers from a low availability (long waiting lists).

## References


[Absil 1998] P.-A. Absil. *Analyse non linéaire de signaux cardiologiques en vue d'applications cliniques.* Travail de fin d'études, Université de Liège (1998).

[Absil 1999] P.-A. Absil, R. Sepulchre, A. Bilge and P. Gérard, *Nonlinear analysis of cardiac rhythm fluctuations using DFA method*, Physica A (272) 1-2 (1999) pp. 235-244.

[Babloyantz 1988] A. Babloyantz and A. Destexhe. *Is the normal heart a periodic oscillator?* Biol. Cybern. **58**, 203-211 (1988).

[Babloyantz 1996] A. Babloyantz, P. Maurer. *A graphical representation of local correlations in time series – Assessment of cardiac dynamics.* Physics Letters A **221**, 46-55 (1996).

[Babloyantz 1997] P. Maurer, Hai-Da Wang, and A. Babloyantz. *Time structure of chaotic attractors: A graphical view.* Physical Review E **56**, 1188-1196, July 1997.

[Bilge 1997] A. Bilge, P. Gérard, L. Piérard. *L'analyse de la variabilité de la fréquence cardiaque.* Cardioscopie, 45, 1997.

[Chon 1997] KH Chon, JK Kanters, RJ Cohen, N-H Holstein-Rathlou. *Detection of chaotic determinism in time series from randomly forced maps.* Physica D **99**, 471-486 (1997).

[Goldberger 1997] KKL Ho, GB Moody, C-K Peng, JE Mietus, MG Larson, D Levy, AL Goldberger *Predicting survival in heart failure case and control subjects by use of fully automated methods for deriving nonlinear and conventional indices of heart rate dynamics.* Circulation, Vol 96, No 3, 842-848, 5 August 1997.

[Klieger 1987] Klieger GM, Miller JP, Bigger JT, Moss AJ. *Decreased heart rate variability and its association with increased mortality after acute myocardial infarction.* Am. J. Cardiol. (1987), 59: 256-262.

[Peng 1993] Peng CK, Mietus J, Hausdorff JM, Havlin S, Stanley HE, Goldberger AL. *Long-range anticorrelations and non-gaussian behavior of the heartbeat.* Physical Review Letters, 70:1343-1346, 1 March 1993.

[Peng 1994] Peng CK, Buldyrev SV, Havlin S, Simons M, Stanley HE and Goldberger AL. *Mosaic organization of DNA nucleotides.* Physical Review E, 49,2:1685-1689, February 1994.

[Peng 1996] Peng CK, Havlin S, Hausdorff JM, Mietus J, Stanley HE, Goldberger AL. *Fractal mechanisms and heart rate dynamics: long-range correlations and their breakdown with disease.* J. Electrocardiology 1996; 28:59-65.

[Schuster 1995] Heinz Georg Schuster. *Deterministic chaos. Third augmented edition.* VCH, 1995.

[Task Force 1996] Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. *Heart Rate Variability – Standards of measurement, physiological interpretation, and clinical use.* Circulation, Vol 93, No 5, 1043-1065, 1 March 1996.