Extreme Value Analysis of Heart Beat RR Intervals or Are Long-term Correlations a General Feature of Heart Beat Time Series ?

Cecilia Pennetta[1], Danuta Makowiec[2]

[1]Dip. Ingegneria dell'Innovazione, Univ. del Salento and CNISM, Lecce, Italy
[2]Institute of Theoretical Physics and Astrophysics, Gdańsk, Poland

Corresponding author: cecilia.pennetta@unile.it

INTRODUCTION

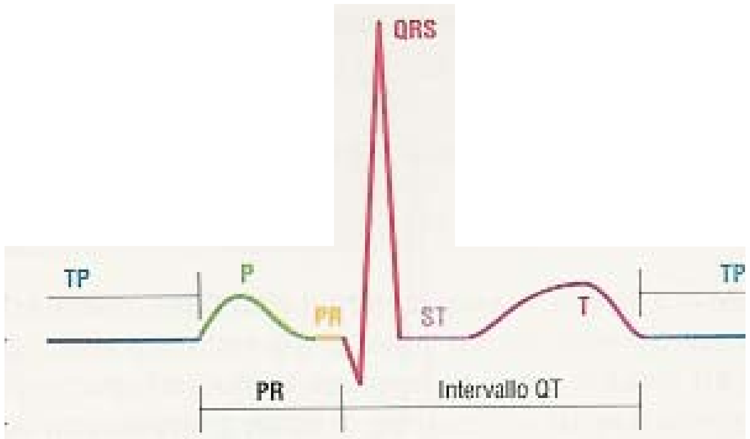
- In recent years it has become clear that many physiological signals display fairly complex dynamics, like for example long-term correlations, multifractality, non-Gaussianity etc., which reflect the complex interplay of different biological mechanisms acting and competing in highly-organized organisms [1,2,3] In particular, it has been realized that many biomedical signals contain much more information than can be catched directly "by eyes". Moreover, such hidden information cannot be extracted by using conventional statistical tools.

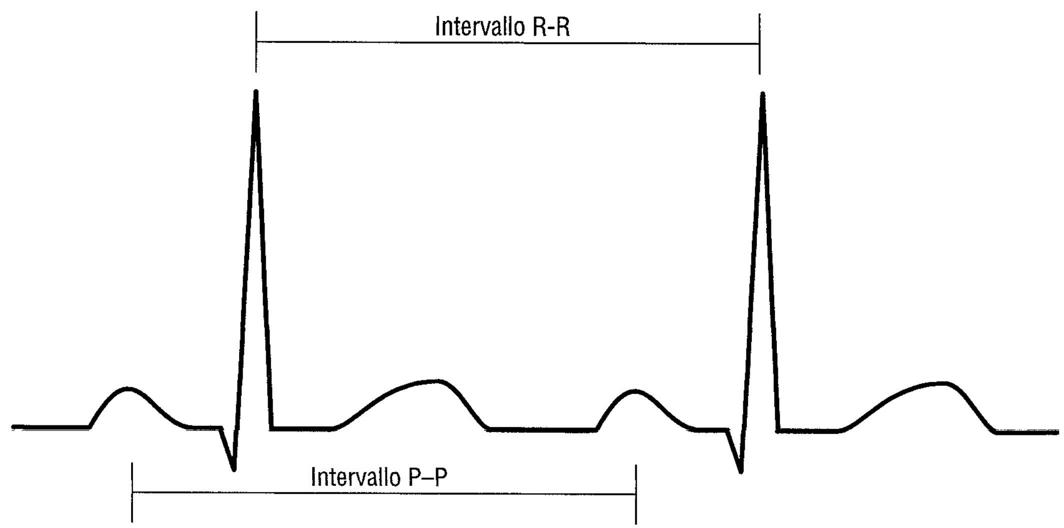
- For this reason, advanced statistical methods, conceived in the context of complex physical systems, like detrended fluctuation analysis (DFA) [1,2,3,4,5], multifractal detrended fluctuation analysis (MDFA) [1,2,3,4,5] or wavelet transform modulus maxima (WTMM) [5] have been applied to biomedical time series, like for example heart beats or neural records [6]. By MDFA and WTMM methods it is found that the control of the autonomic system is significantly weaken when one compares group averages of healthy and unhealthy patients [5]. However, neither MDFA nor WTMM method provide a tool to classify an individual signal.

- Recently, some authors [7,8,9,10] have highlighted the effectiveness of extreme value analysis (EVA) in the study of complex systems. The aim of this work is to explore the ability of EVA to extract significant information from physiological time series.

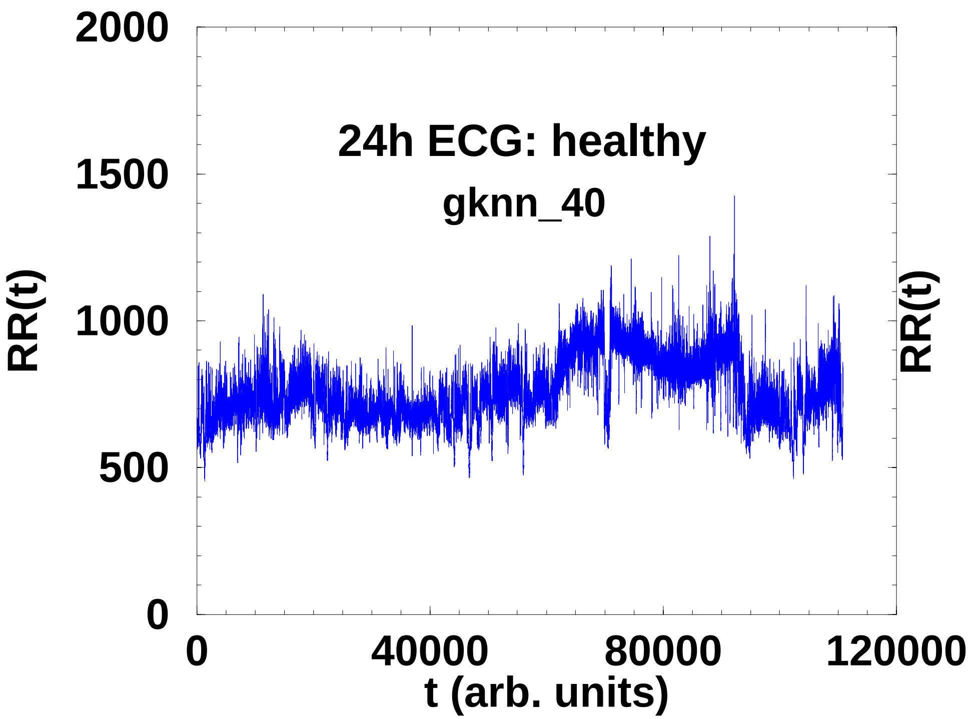
HEART RATE FLUCTUATIONS

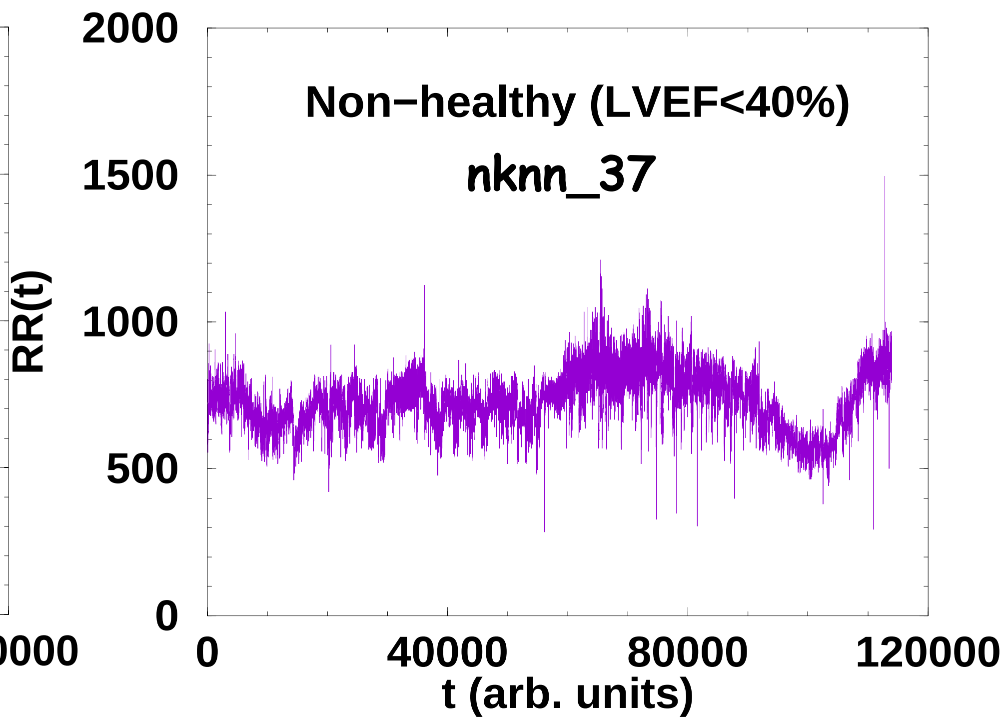
We consider RR heart beat time series, i.e. time series whose records are the time intervals between two subsequent picks of the so called R waves, as measured in 24-h ECG Holter signals [5,6]. These electric signals are known to fluctuate in a way that reflects autonomic neural control on the sinus node [11,12], the heart first pacemaker.



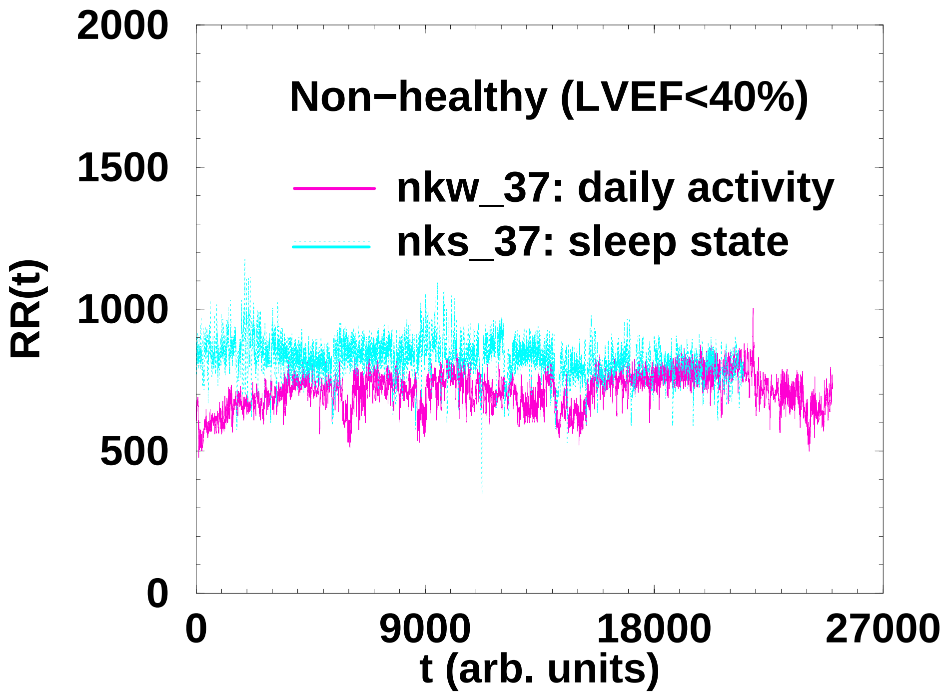


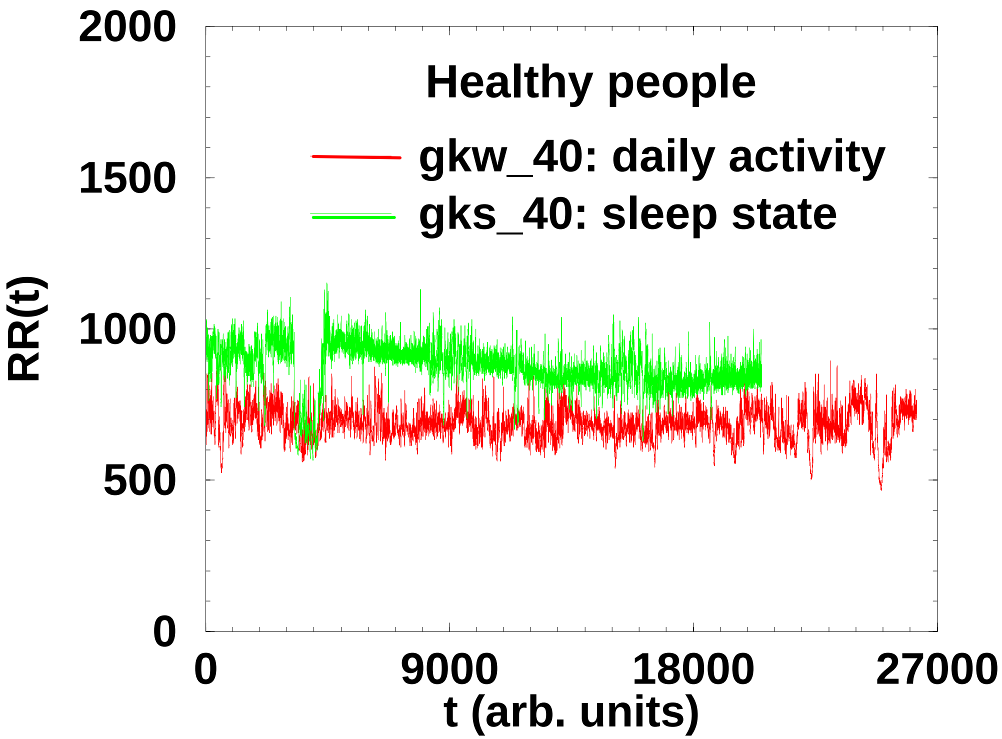
Two sets of signals are analysed: GK and NK, corresponding respectively to 40 healthy people and to 90 unhealthy patients with reduced left ventricular systolic function (rlvs), recognized by echocardiogram in terms of low values of left ventricular ejection fraction, LVEF ≤ 40% [5,6].





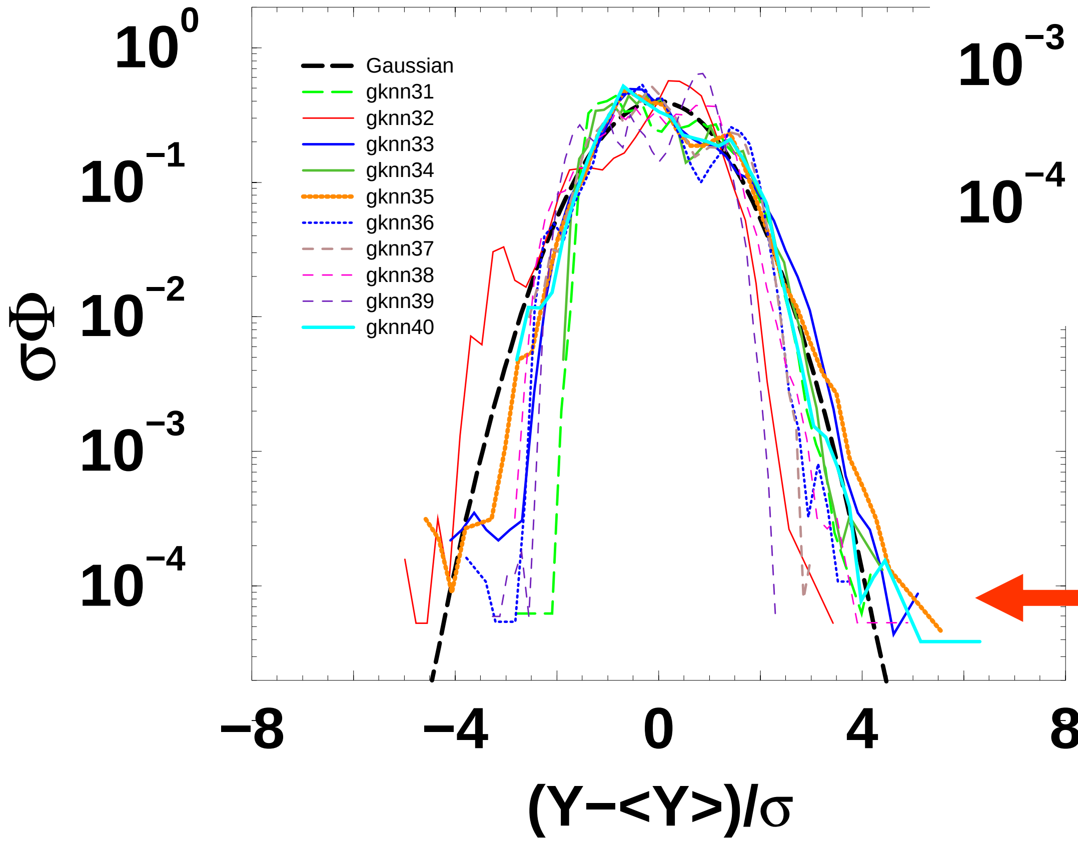
From each 24-h ECG signal two 5-h subsets were extracted manually corresponding to daily activity and to sleep state:



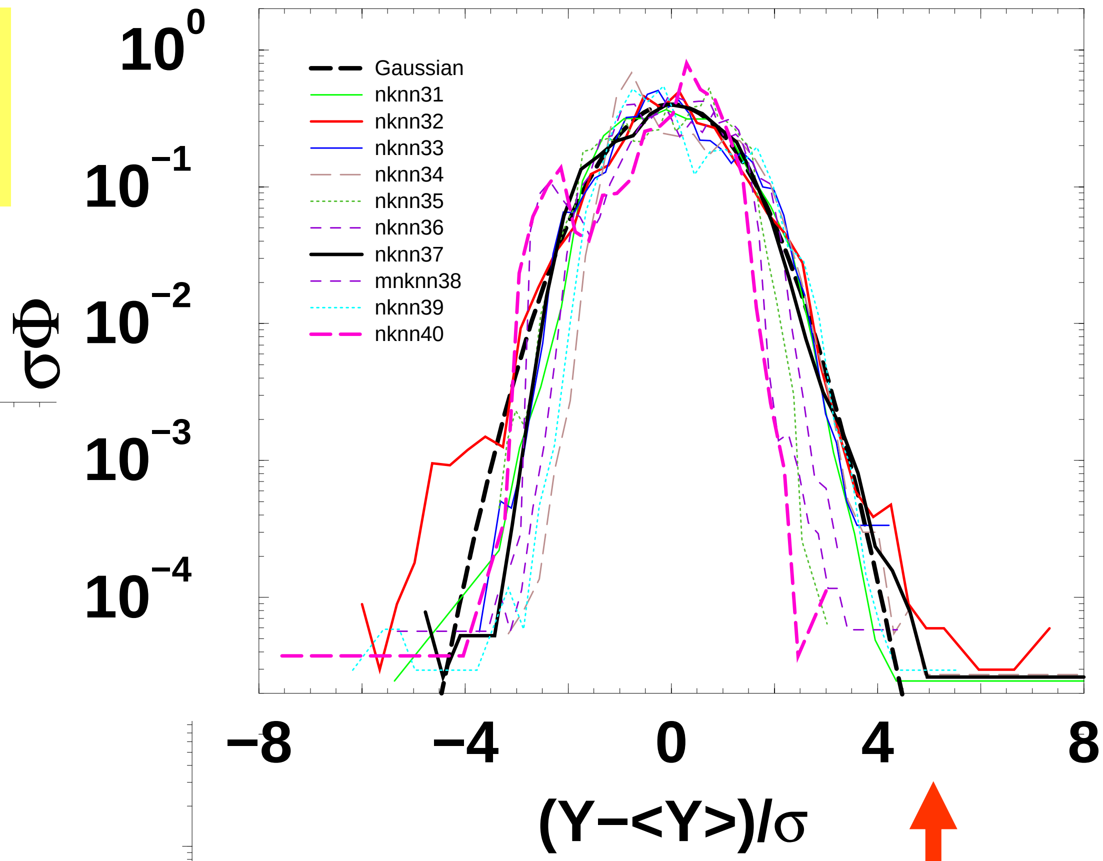


Heart rate fluctuations during daily activities and sleep exhibit subtle but significant differences in healthy and unhealthy people that cannot be seen by eyes

RR distribution: probability density



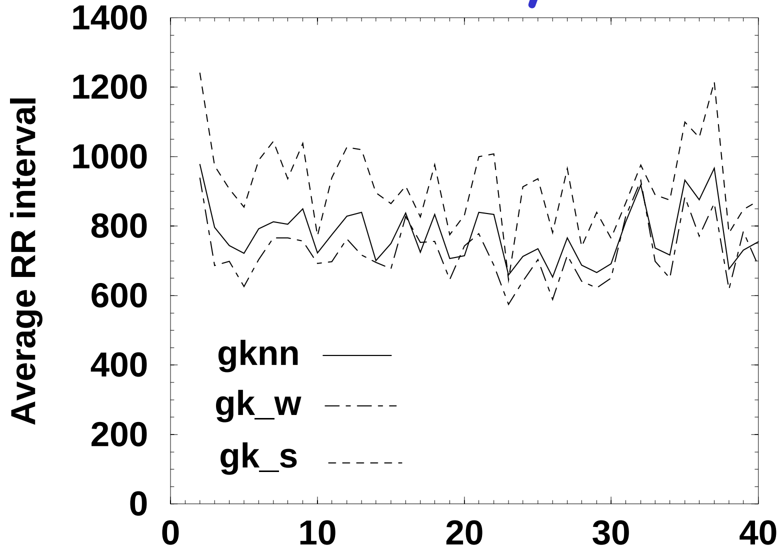
Healthy



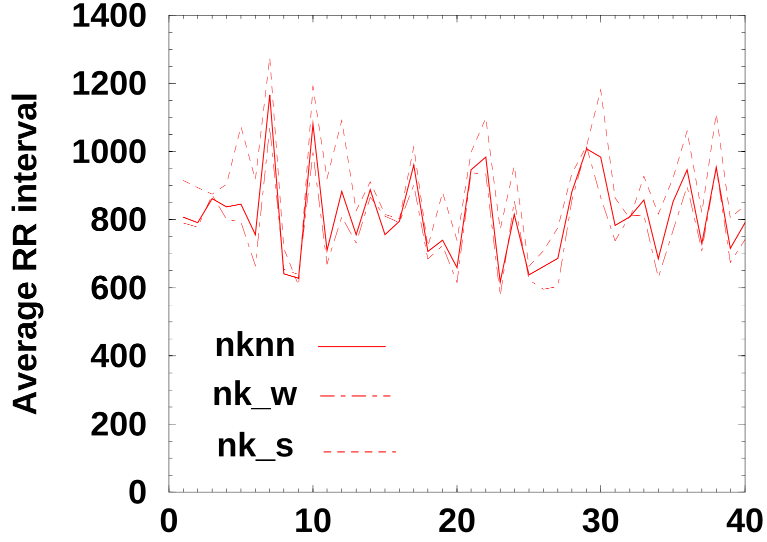
Unhealthy

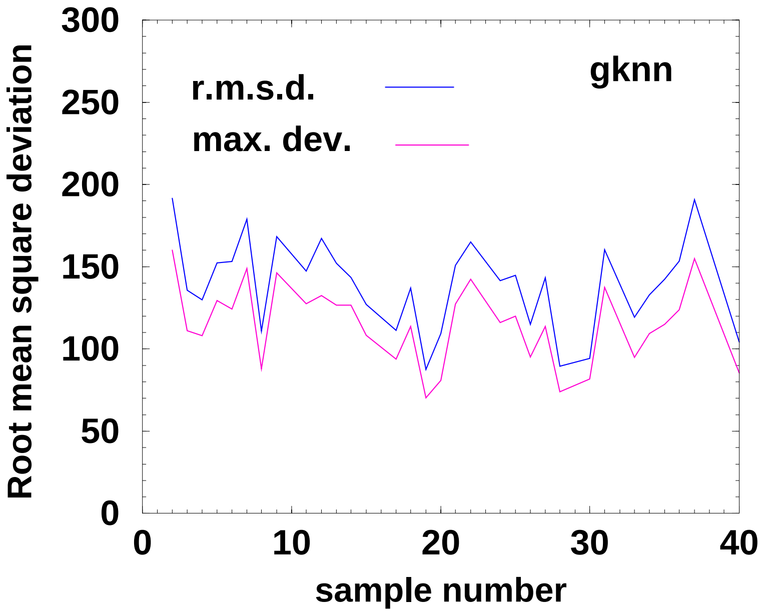
Lowest-order moments of the RR distribution

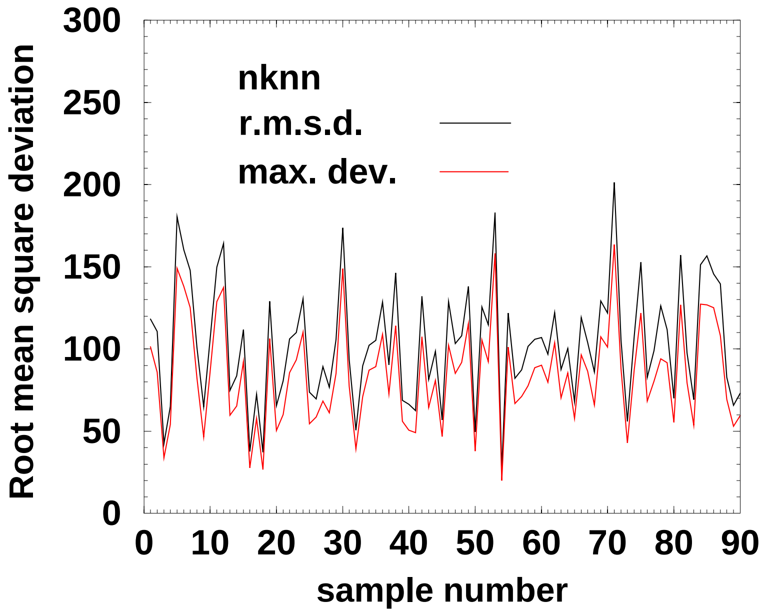
Healthy



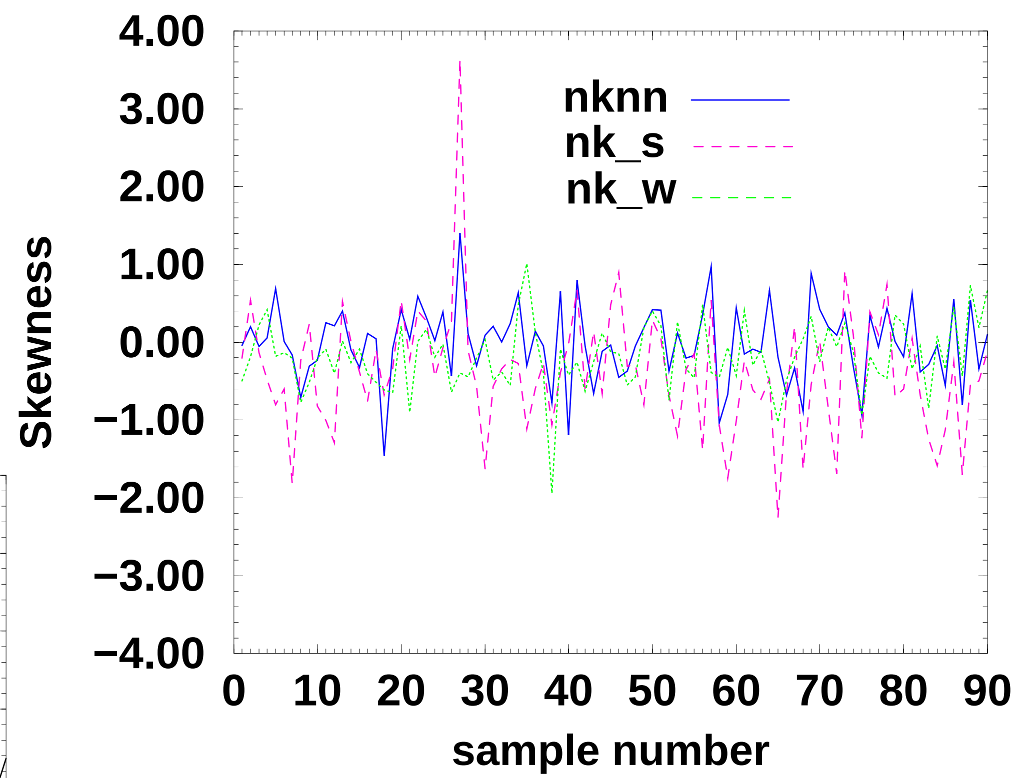
Unhealthy

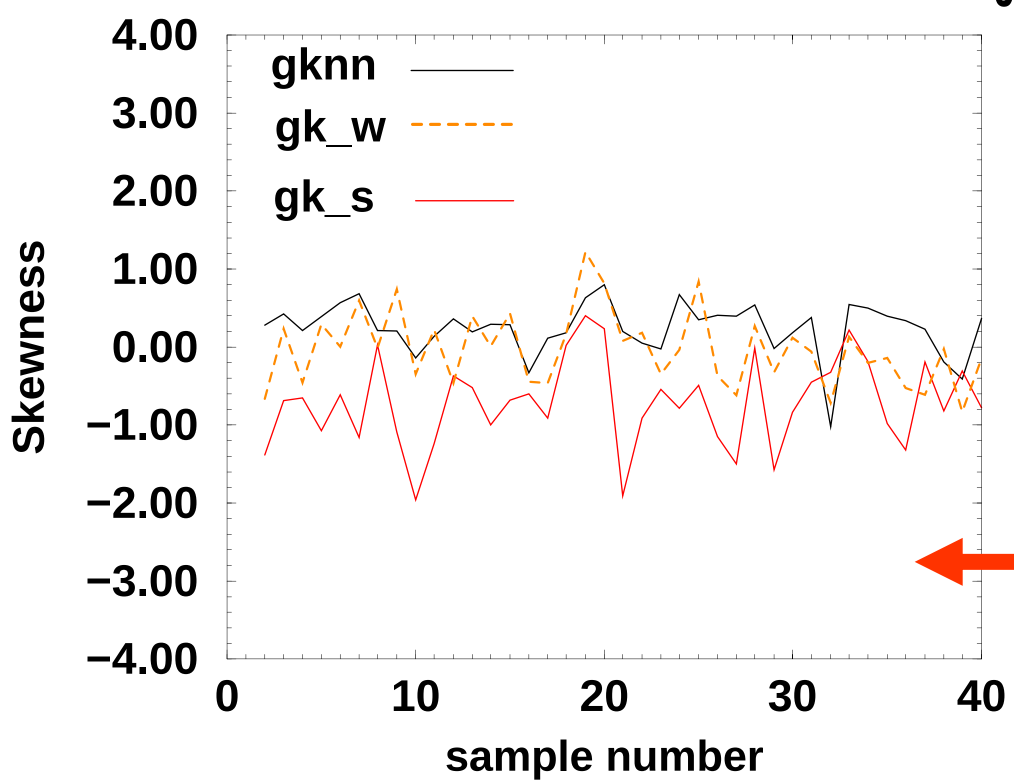






3° order moment of the RR distribution: skewness





Healthy

Unhealthy

Correlation properties

Many authors have enlighted the presence of long-term correlations in heart beat time series, characterized by a power-law decay of correlations [1,2,3,4,5].

$$C(t) = \langle \Delta x_i \Delta x_{i+t} \rangle \approx t^{-\gamma} \qquad 0 < \gamma < 1$$

These studies have shown that different correlation exponents γ characterize the heart rates of healthy and unhealthy subjects. Moreover, different values of γ have been found for the wake and sleep periods. Such difference in the γ values has been proposed as a diagnostic tool.

In many of these studies the value of the correlation exponent has been estimated **not by a direct calculation of the auto-correlation function C(t)** (which usually presents a high level of noise in relatively short time series) **but by calculating the fluctuation function F(t) which in case of long-term correlations behaves as** [2,4,14,15]:

$$F(t) \approx t^{\alpha}$$

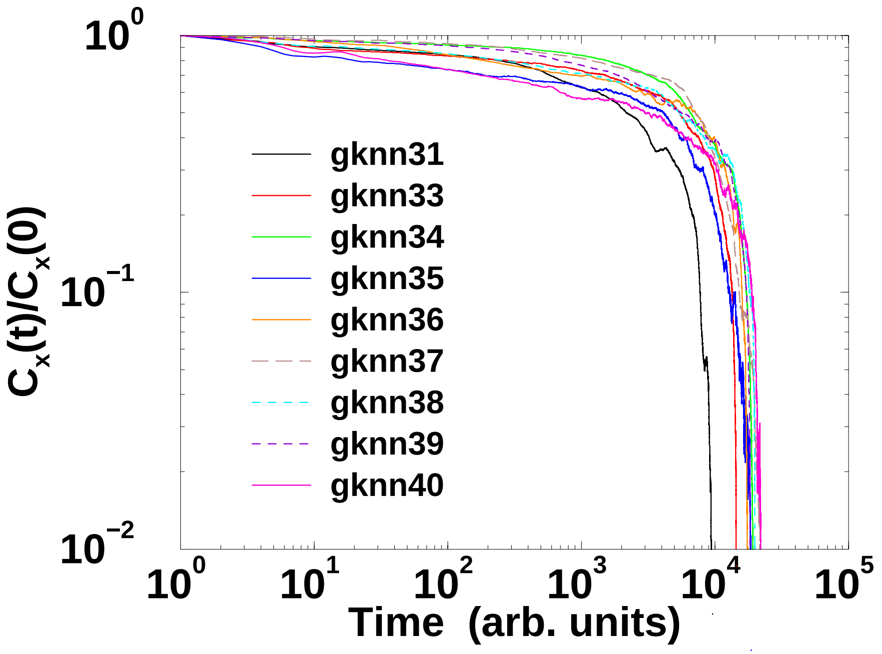
where: $\alpha = 1 - \gamma / 2$, $\alpha > 0.5$

To estimate the correlation properties of our time series (ECG 24-h , wake 5-h and sleep 5-h) and to check the procedure, **we have calculated both the fluctuation and the auto-correlation function**. In all cases the time series have been normalized:

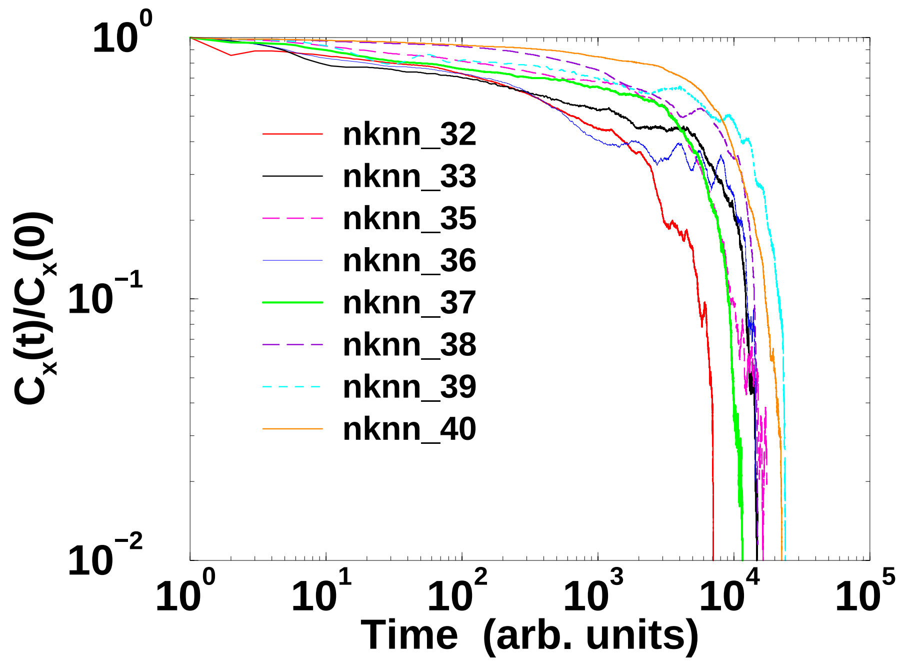
$$x(t) \equiv \frac{u(t) - <u>}{\sigma}$$

to provide a signal x(t) with zero average and unitary variance (here u indicates the interval RR and σ the root mean square deviation).

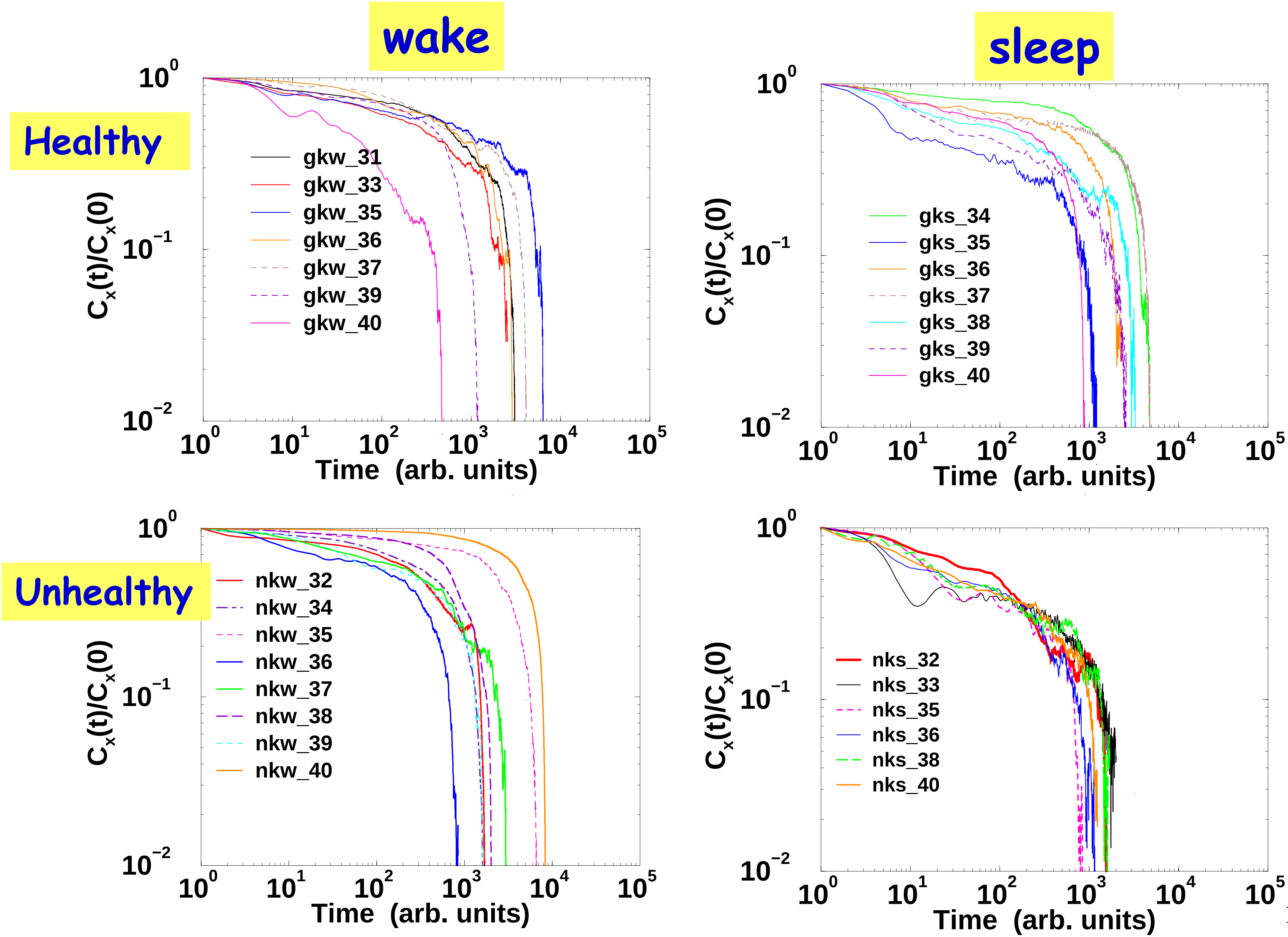
Typical behavior of the auto-correlation functions are shown in the following:



24-h ECG, healthy



24-h ECG, unhealthy


wake
sleep
Healthy
Unhealthy
$C_x(t)/C_x(0)$
Time (arb. units)
gkw_31
gkw_33
gkw_35
gkw_36
gkw_37
gkw_39
gkw_40
gks_34
gks_35
gks_36
gks_37
gks_38
gks_39
gks_40
nkw_32
nkw_34
nkw_35
nkw_36
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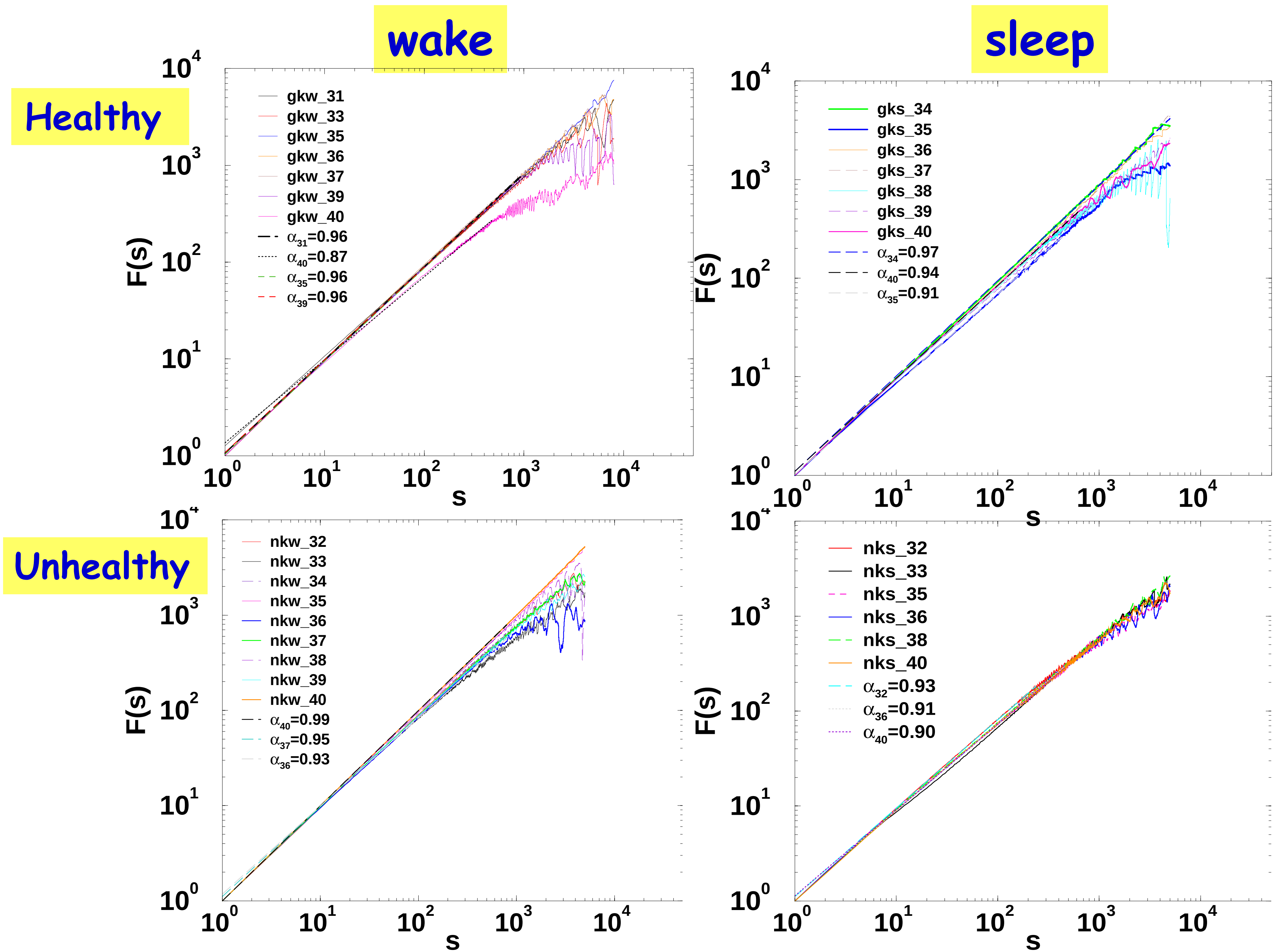
nks_36
nks_38
nks_40



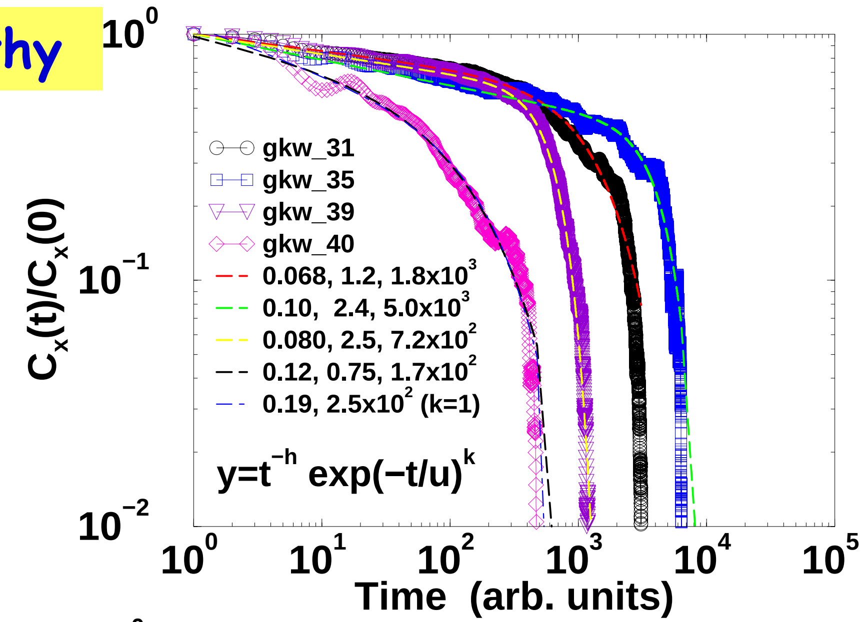
wake
sleep
Healthy
Unhealthy
F(s)
s
gkw_31
gkw_33
gkw_35
gkw_36
gkw_37
gkw_39
gkw_40
α_{31}=0.96
α_{40}=0.87
α_{35}=0.96
α_{39}=0.96
gks_34
gks_35
gks_36
gks_37
gks_38
gks_39
gks_40
α_{34}=0.97
α_{40}=0.94
α_{35}=0.91
nkw_32
nkw_33
nkw_34
nkw_35
nkw_36
nkw_37
nkw_38
nkw_39
nkw_40
α_{40}=0.99
α_{37}=0.95
α_{36}=0.93
nks_32
nks_33
nks_35
nks_36
nks_38
nks_40
α_{32}=0.93
α_{36}=0.91
α_{40}=0.90

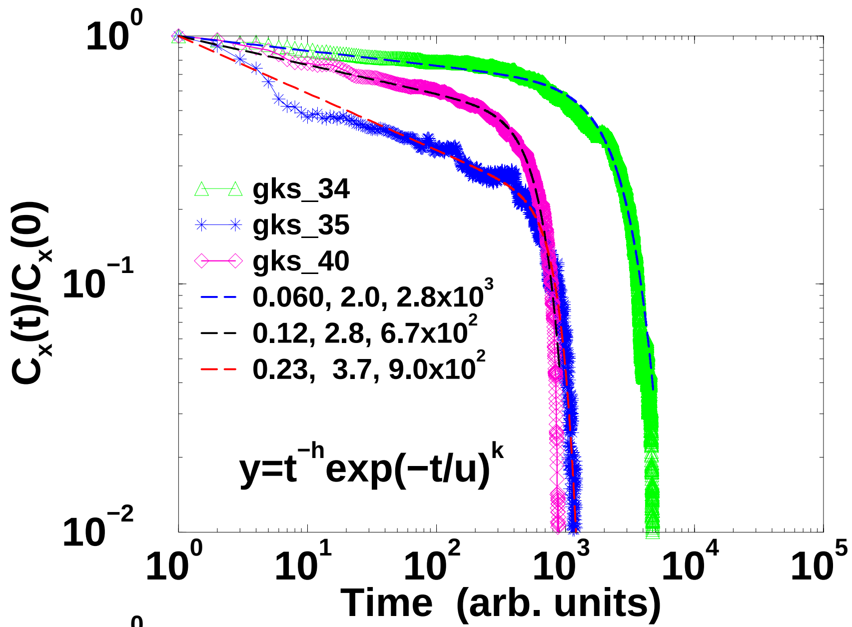
wake

Correlation time $\tau = \frac{u^{1-h}}{k}\Gamma\left(\frac{1-h}{k}\right)$

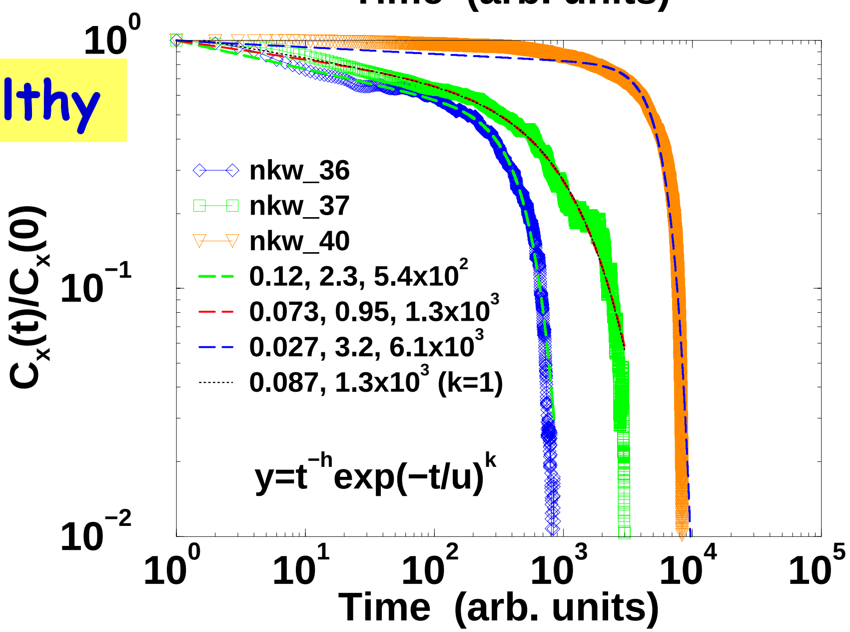
sleep

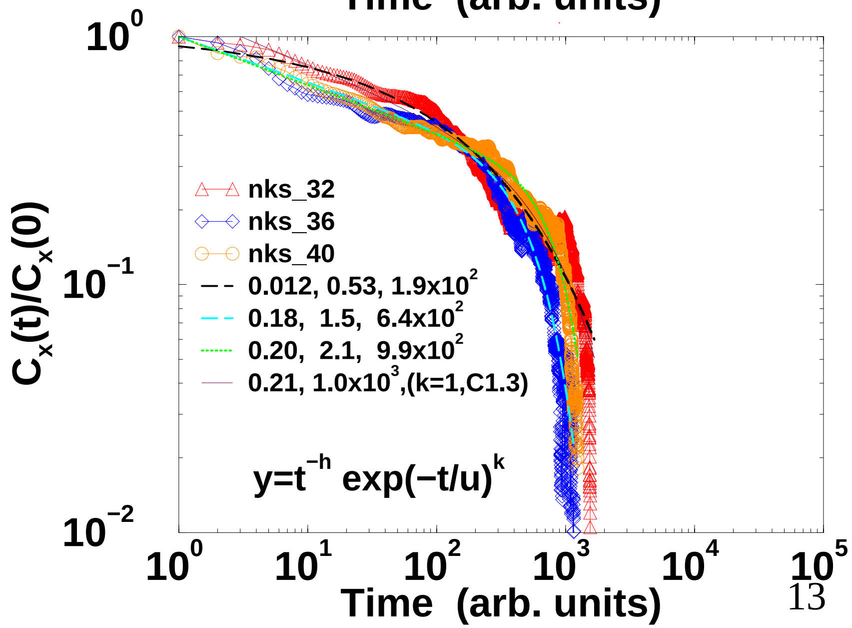
Healthy





Unhealthy

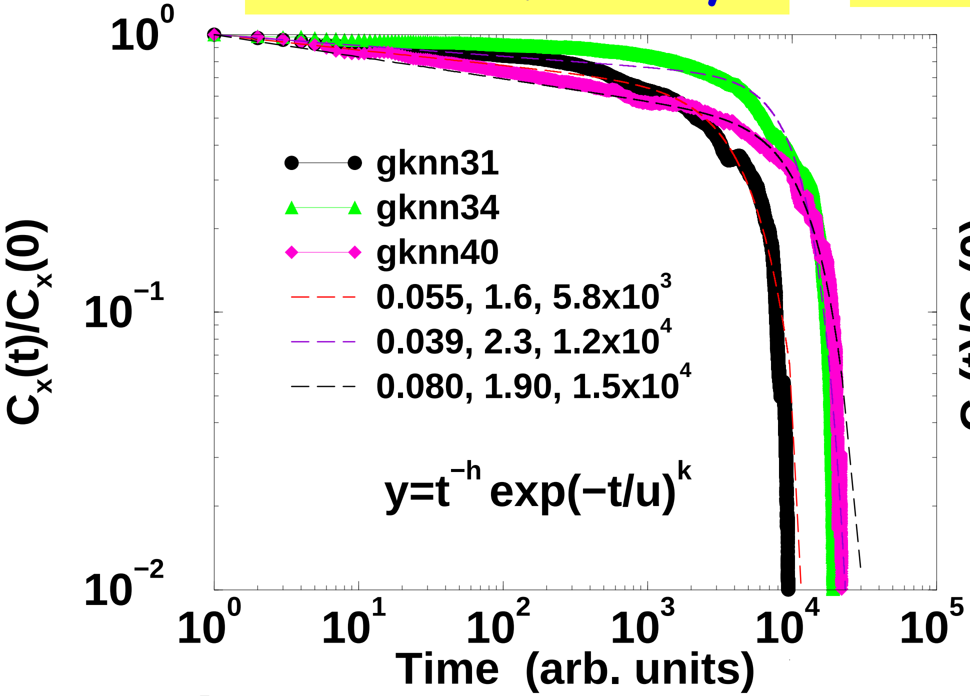


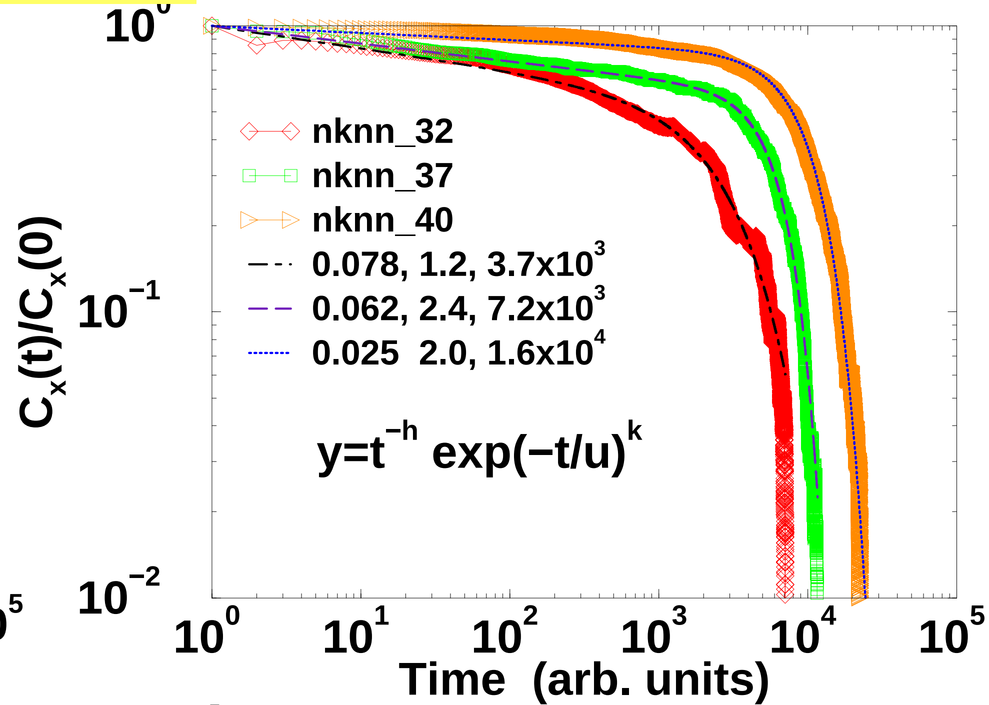


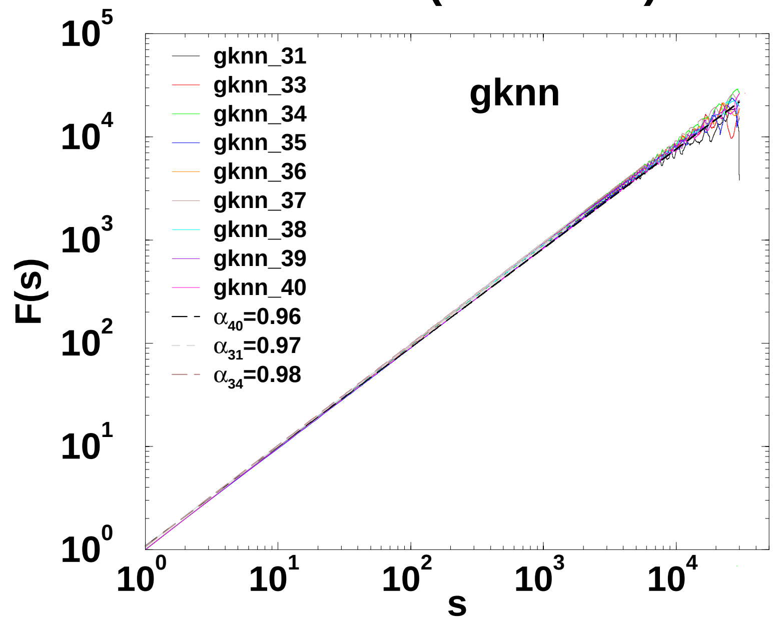
24-h ECG,healthy

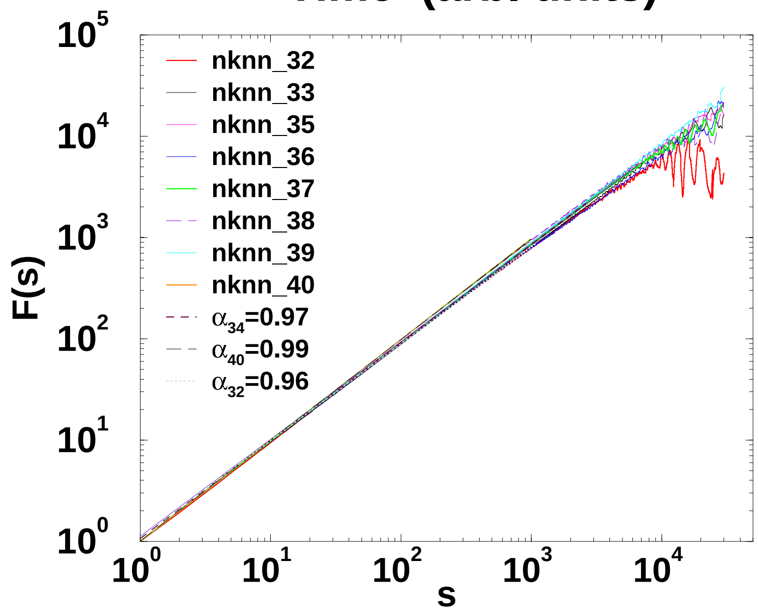
$$\tau = \frac{u^{1-h}}{k}\Gamma\left(\frac{1-h}{k}\right)$$

24-h ECG, unhealthy









Thus, the combined analysis of both, the auto-correlation and the fluctuation functions shows:

- In many cases, for both healthy and unhealthy people and in both states, wake and sleep, the correlations decay as a power law over a significant time scale, after which a stretched exponential cut-off emerges, thus we can really speak of long-term correlated signals.

- However, in other cases, for both healthy and unhealthy people and in both wake and sleep states, the time scale over which the correlations decay as a power-law is too short and we cannot actually speak of long-term correlations.

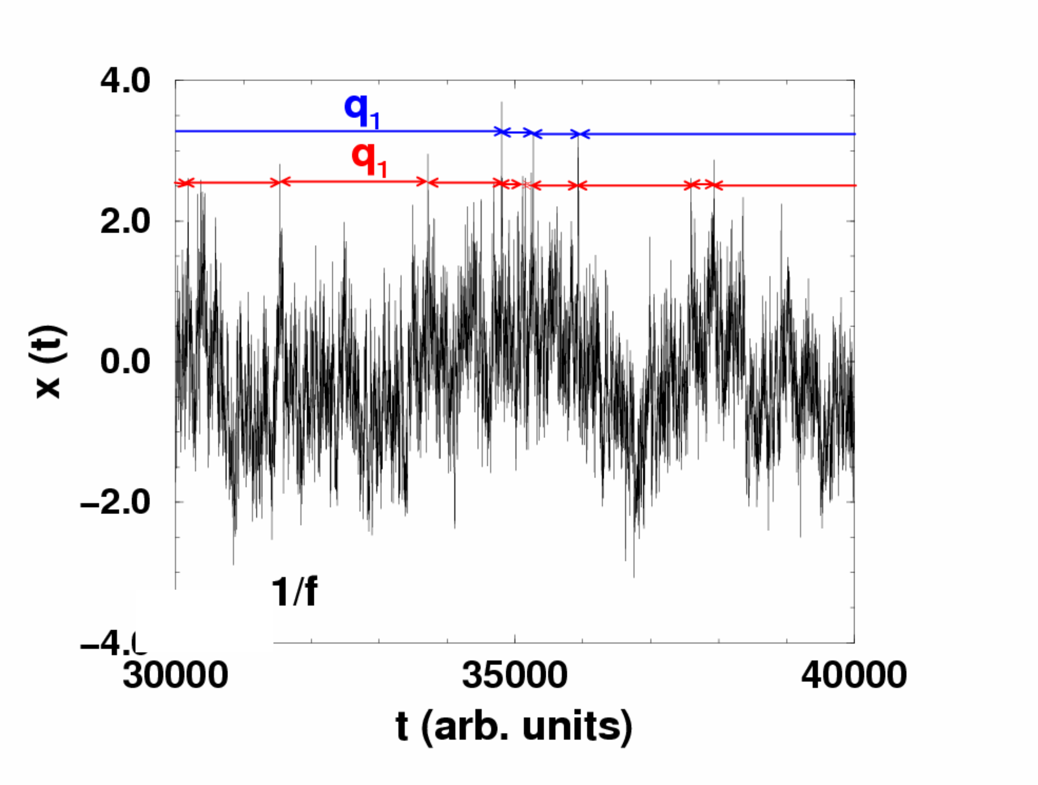
- In any case, the fluctuation function F(t) correctly estimates the correlation exponent, i.e. the exponent of the power-law describing the correlation decay on a wide or on a limited time scale.

- Nevertheless, the fluctuation function does not allow an accurate estimation of the cross-over time after which the stretched exponential cut-off dominates.

- Thus, the analysis of the fluctuation function cannot be used to prove the existence of long-term correlations and this analysis can be used only to obtain a clean estimation of the correlation exponent, when such kind of correlations are already known to exist in a given class of signals.

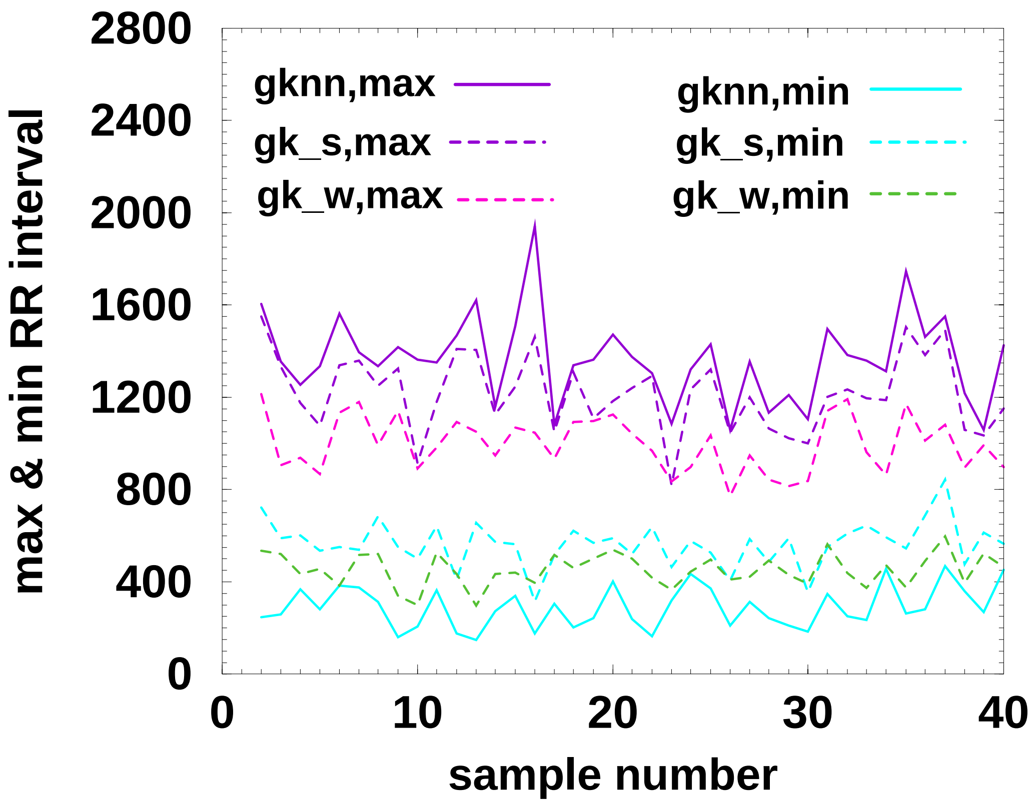
Retur Times of Extreme Values

The extreme value analysis has been performed mainly by considering the return time distribution, i.e. the distribution of the time intervals associated with two consecutive overcomings of a given threshold value by the signal [8,9,10]

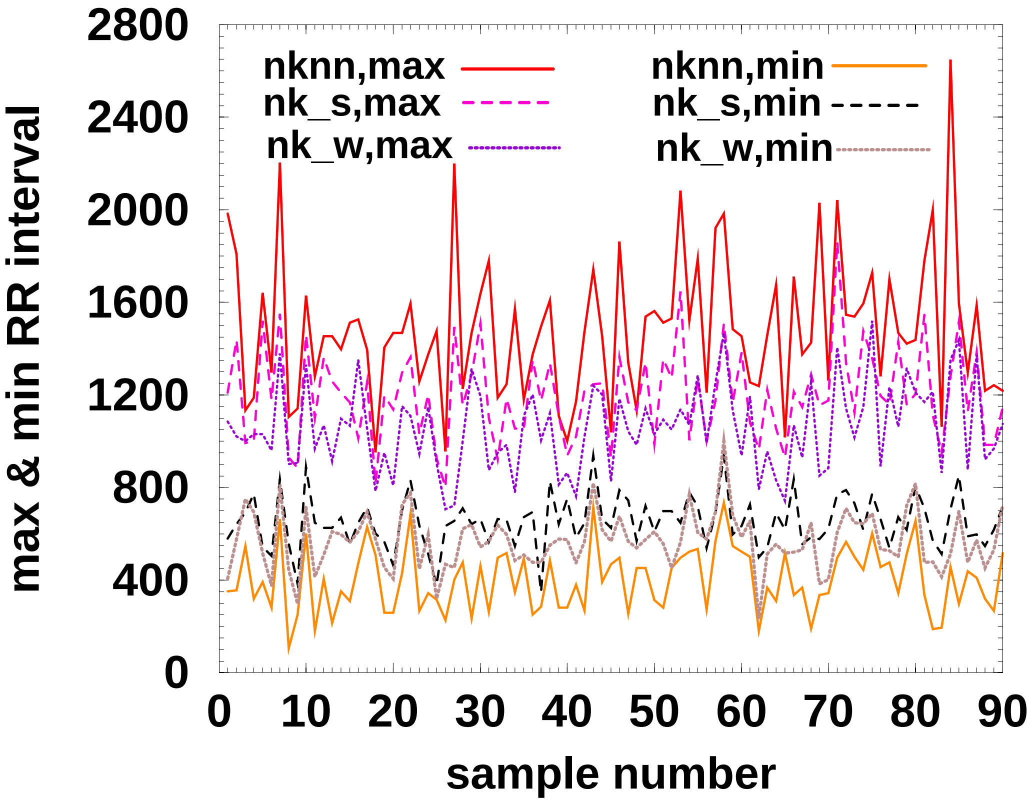


Maximum and Minimum Values of the RR Intervals

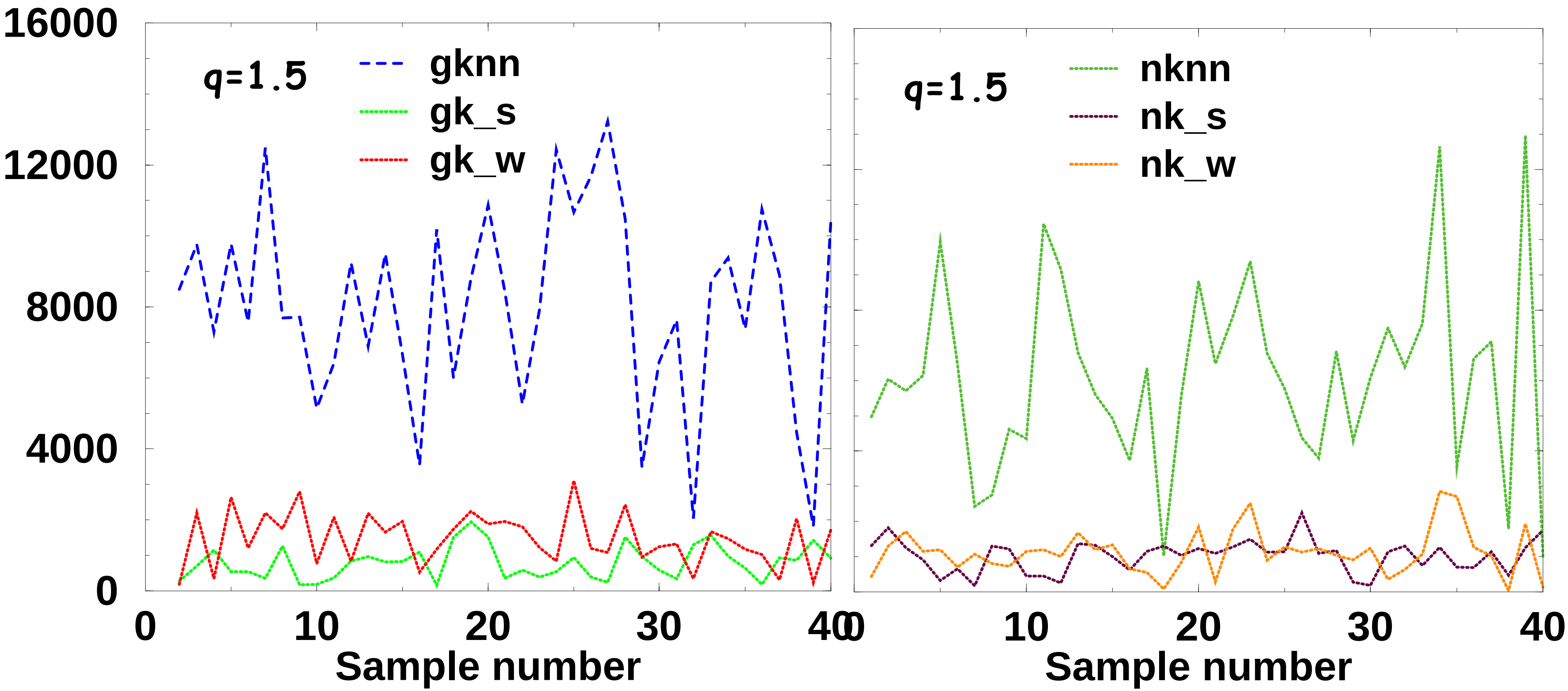
Healthy



Unhealthy



Number of Retur Intervals for the Threshold q=1.5



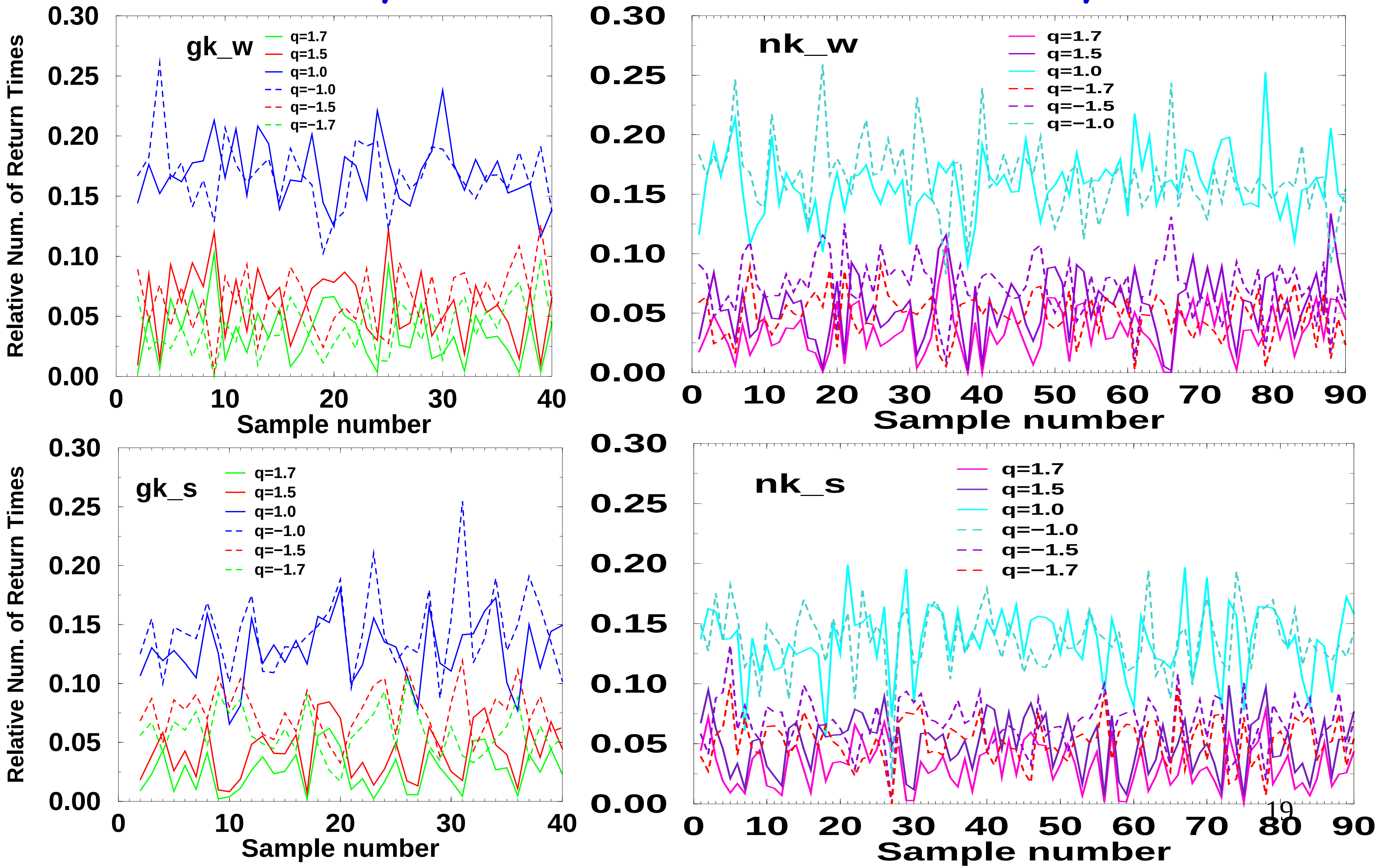
24-h ECG, healthy

24-h ECG, unhealthy

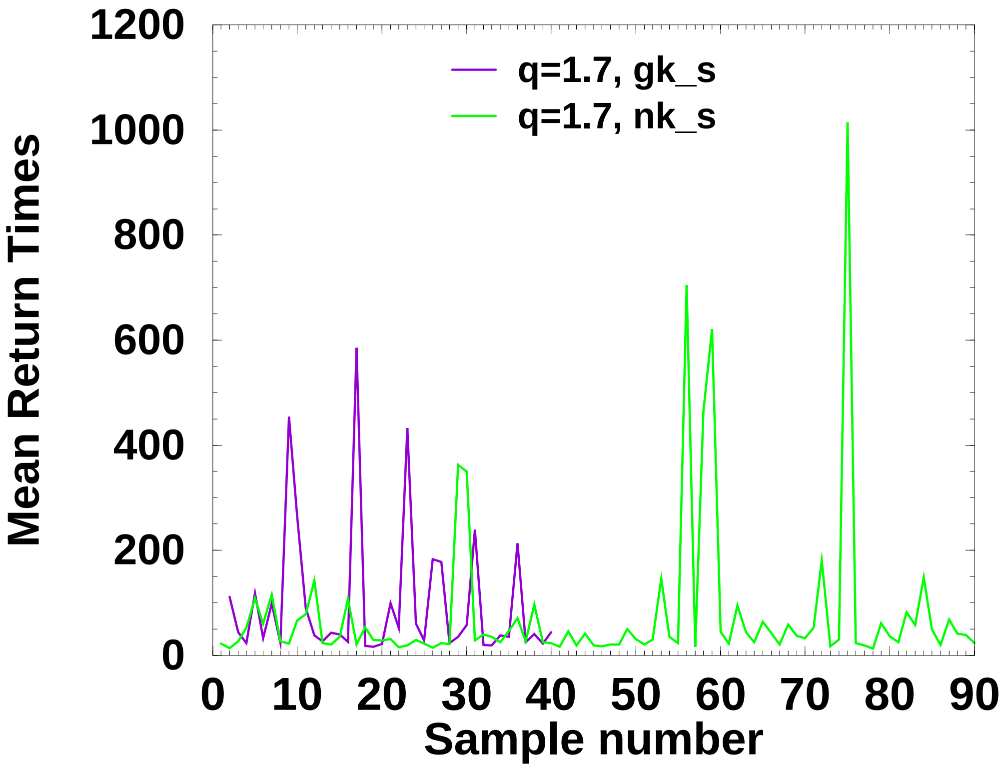
Relative Number of Retur Intervals: N_{ret}/N_{dat}

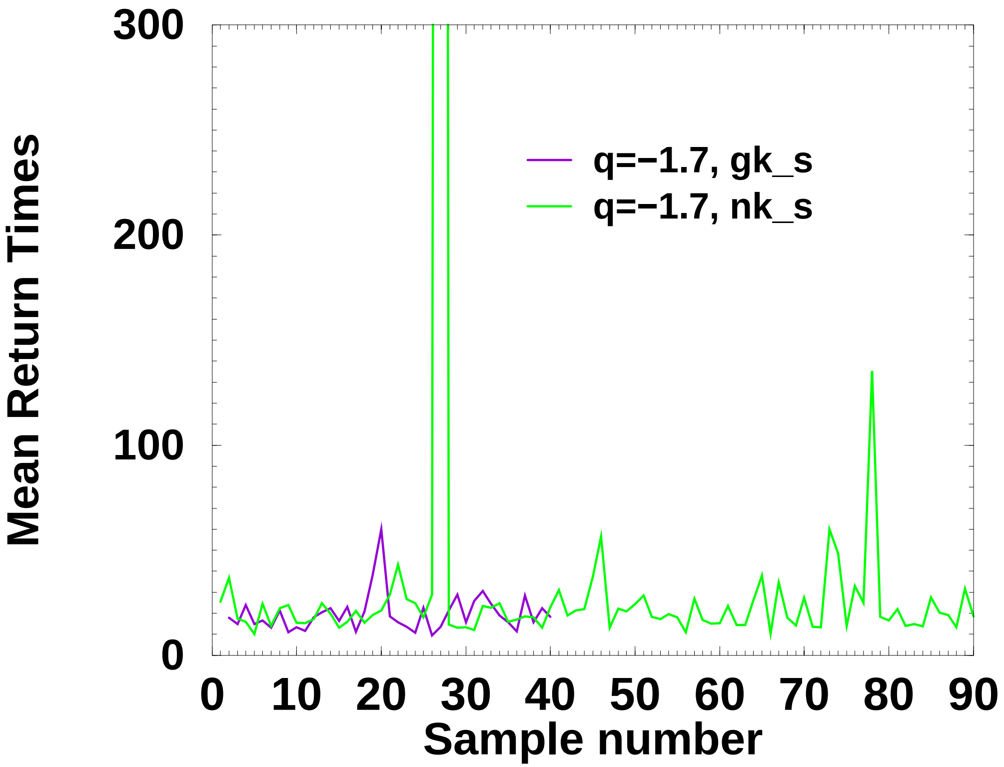
Healthy

Unhealthy



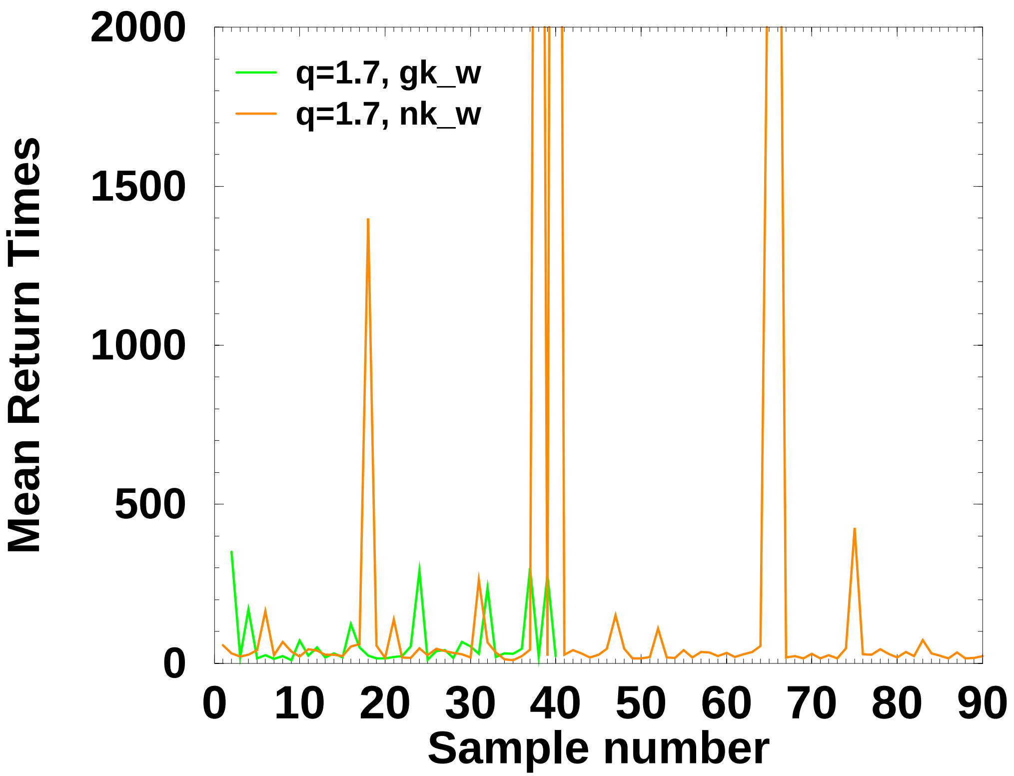
Mean Retur Interval of a Given Threshold

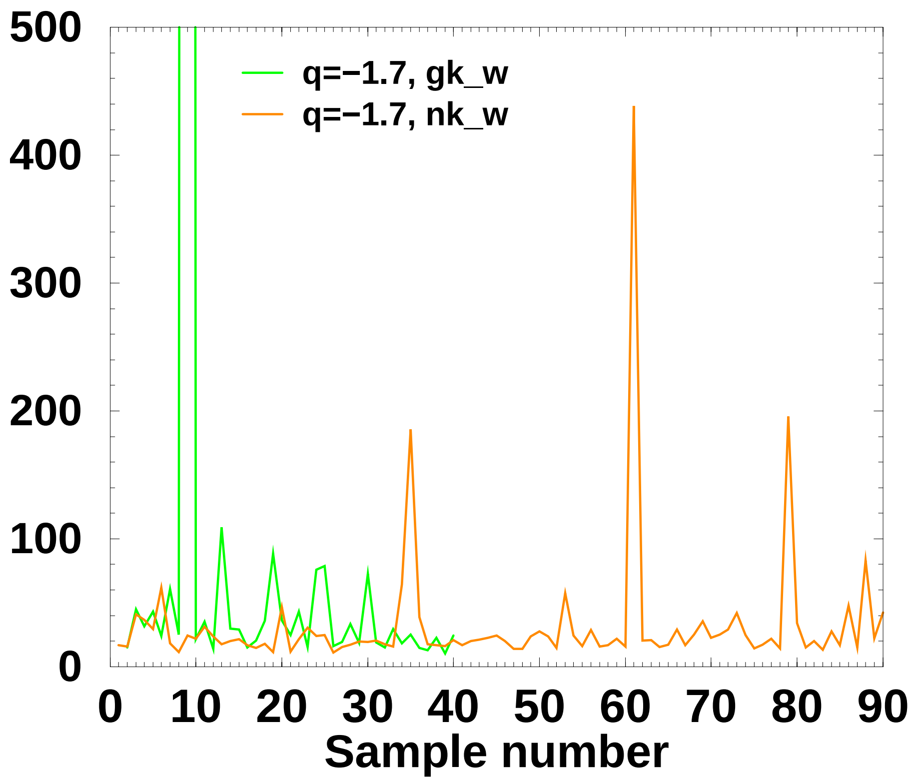




5-h sleep records : healthy and unhealthy

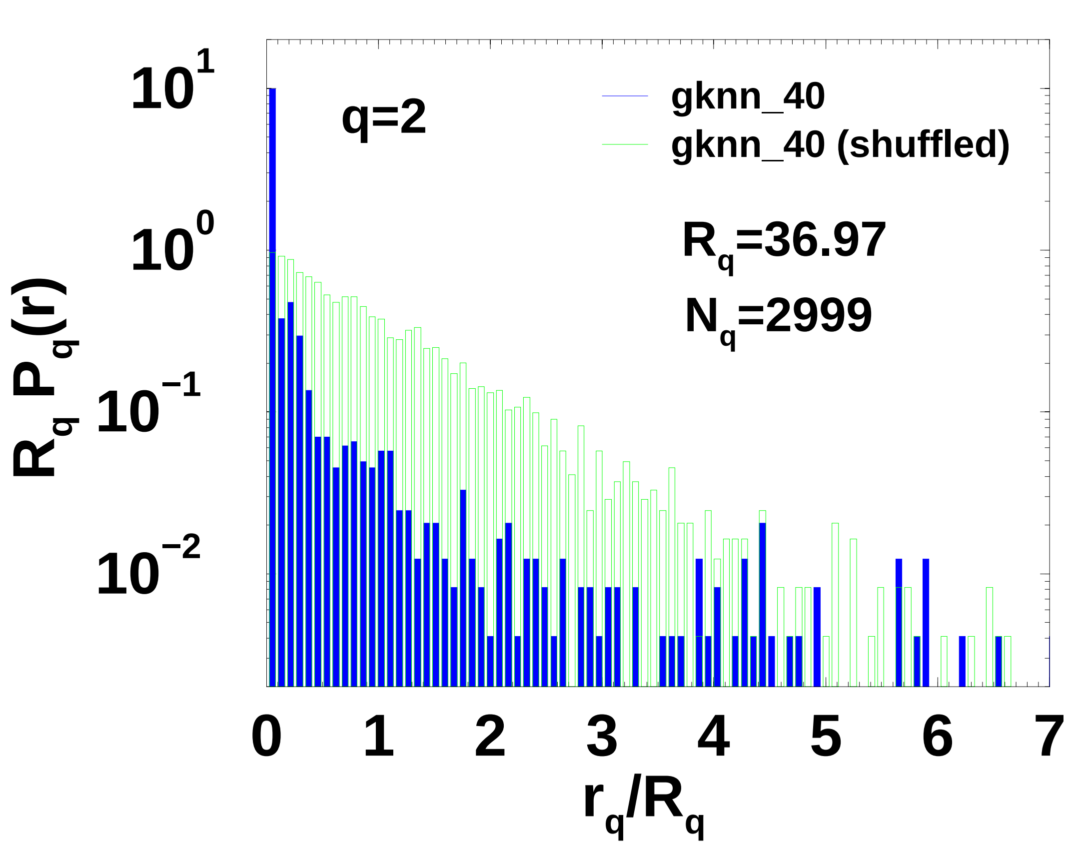
Mean Retur Interval of a Given Threshold



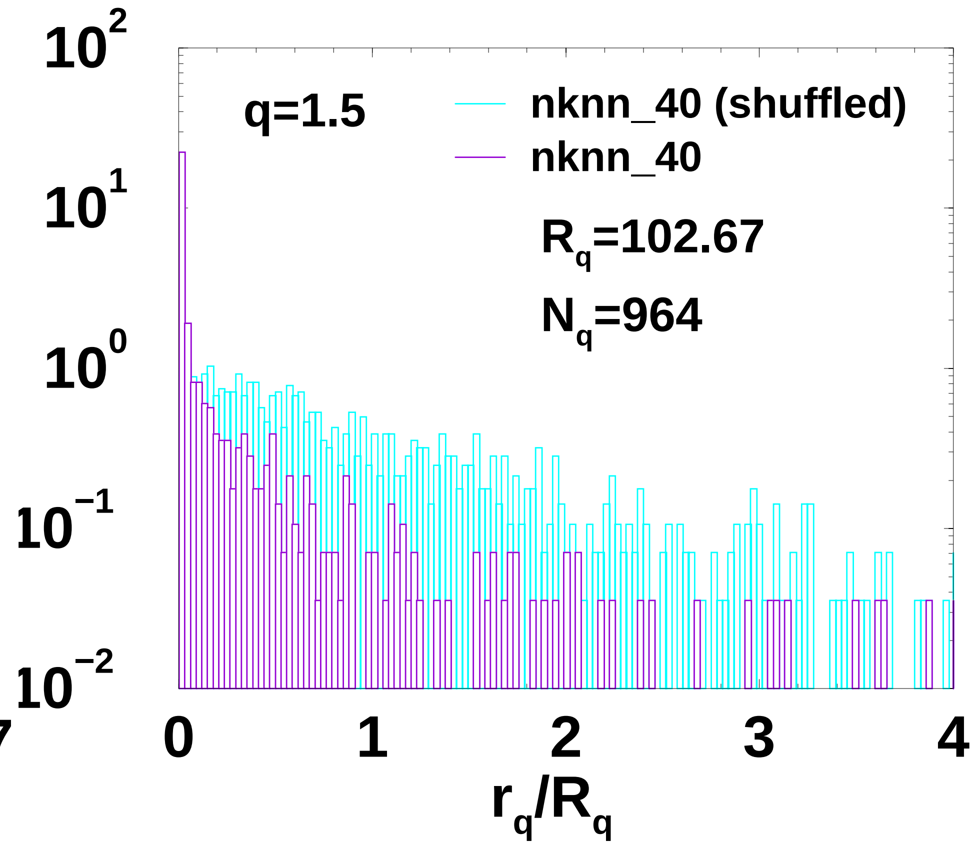


5-h wake records : healthy and unhealthy

Retur Times Distribution



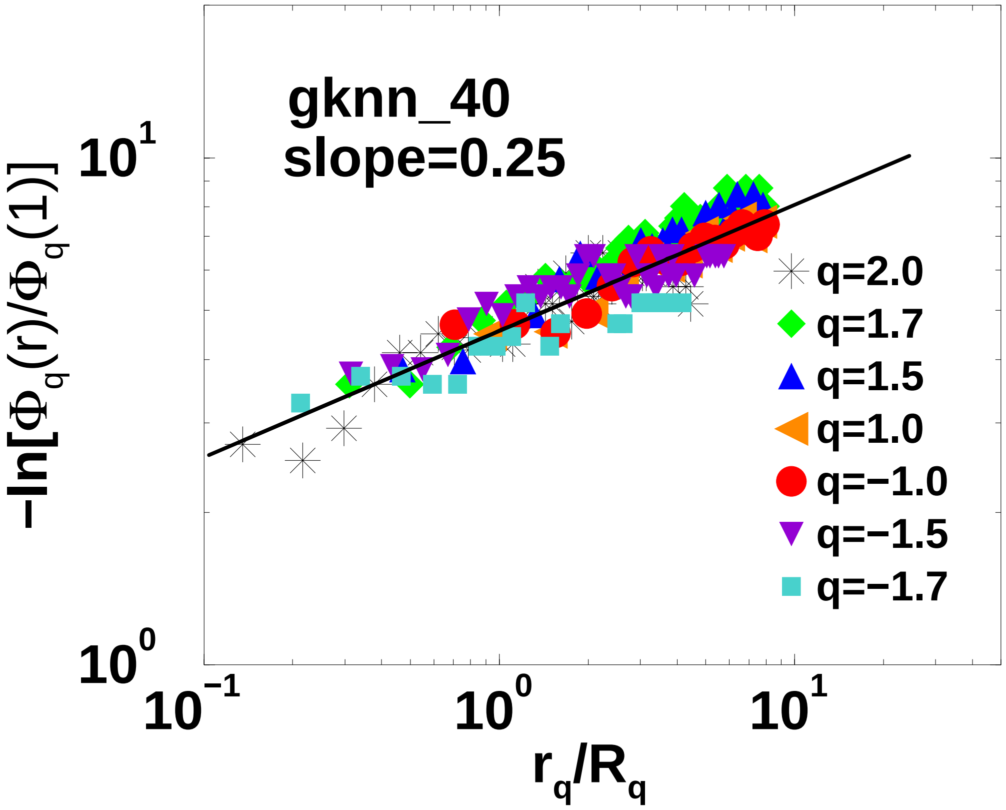
24-h ECG, healthy



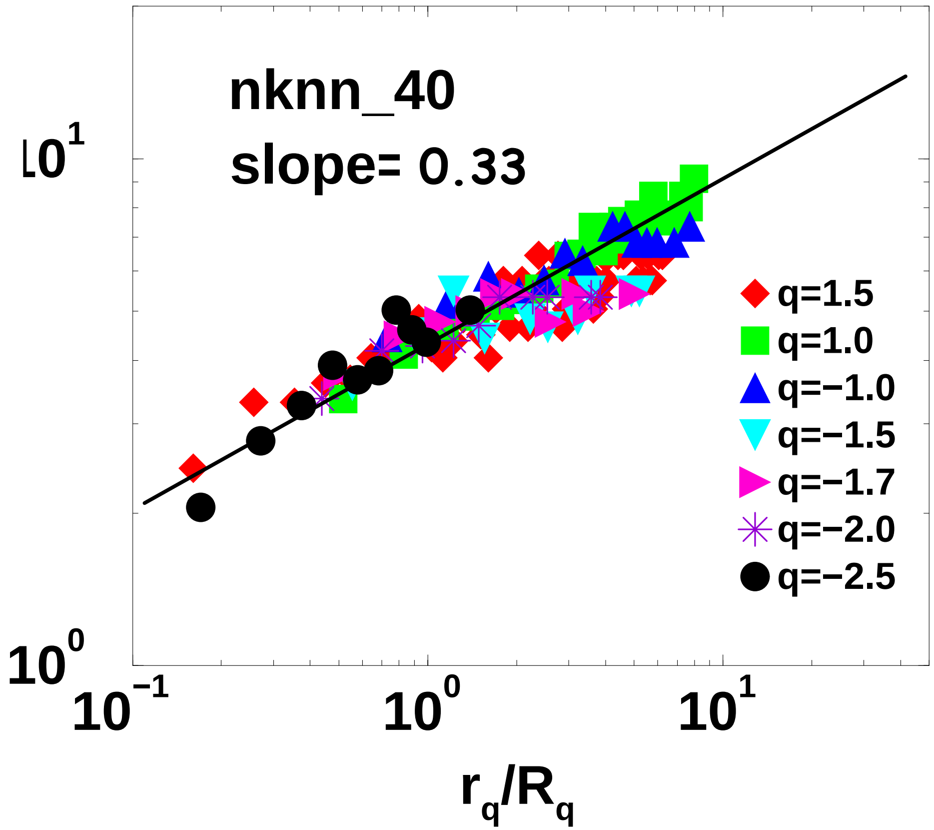
24-h ECG, unhealthy

Retur Times Distribution

Stretched exponential distribution? The differences between healthy and unhealthy people are statistically significant?



24-h ECG, healthy



24-h ECG, unhealthy

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