# Complexity analysis of human physiological signals based on case studies

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**Abstract.** This work focuses on methods for investigation of physiological time series based on complexity analysis. It is a part of a wider programme to determine non-invasive markers for healthy ageing. We consider two case studies investigated with actigraphy: (a) sleep and alternations with insomnia, and (b) ageing effects on mobility patterns. We illustrate, using these case studies, the application of fractal analysis to the investigation of regulation patterns and control, and change of physiological function. In the first case study, fractal analysis techniques were implemented to study the correlations present in sleep actigraphy for individuals suffering from acute insomnia in comparison with healthy controls. The aim was to investigate if complexity analysis can detect the onset of adverse health-related events. The subjects with acute insomnia displayed significantly higher levels of complexity, possibly a result of too much activity in the underlying regulatory systems. The second case study considered mobility patterns during night time and their variations with age. It showed that complexity metrics can identify change in physiological function with ageing. Both studies demonstrated that complexity analysis can be used to investigate markers of health, disease and healthy ageing.

## 1. Introduction

In the past few decades there has been growing interest for modelling physiological systems using complex systems approaches. Here, a complex system is defined as a system featuring: (a) a large number of interactive components; (b) aggregate activity that is non-linear; and (c) exhibits self-organisation. There is a growing interest in the development of new techniques to analyse and describe the dynamics of physiological systems, especially for distinguishing between the dynamics of healthy and impaired systems, or more importantly predicting the onset of adverse health related events. Many of these techniques revolve around complexity analysis and are based upon fractals. The object of investigation is considered to be complex if it has a high fractal dimension. The term fractal, first used by Mandelbrot [1], describes an object that displays self-similarity across multiple scales, known as multi-scale invariance.

This invariance is also known as power-law scaling and is easily observed in natural objects, living organisms and groups of organisms. Lipsitz *et al* [2] showed a loss in the fractal structures of the dendritic arbor between a young and old male indicating a possible loss in fractality associated with the ageing process. The theory of fractals and self-similarity is not restricted to geometric objects or images, it can also be applied to time-series where the dynamics of the time series exhibits self-similarity in the time-domain.

The dynamical systems approach to physiological time series allows to study the dynamics of the regulating mechanisms underlying the physiological process. A large number of metrics have been introduced (see for examples [3] and the references therein), based on signal and spectral analysis, from which conclusions can be made about the dynamics of the underlying mechanisms. In this paper, we will illustrate, using two case studies, the application of fractal analysis to the investigation of regulation and control and change of physiological function.

The aim of this paper is to illustrate the concepts of complexity analysis via applications to two sets of health data. The first case study is based on sleep and alternation with insomnia [4], and the second one is focused on the mobility patterns and how the complexity metrics reflect the change of physiological function with age [5]. Both studies are based on actigraphy data. Lichstein *et al* [6] demonstrated actigraphy to be a satisfactory objective measure of sleep for 4 out of 5 sleep parameters, which motivated the data collecting method in the second case study.

This paper is organised as follows: Section 2 introduces the data for two case studies: sleep data and mobility data obtained via actigraphy, Section 3 introduces the complexity methods and techniques arising from fractal analysis, Section 4 shows the findings and Section 5 presents the results and final conclusions.

## 2. Data

For both case studies the data was collected with actiwatch. The device measures the amount of motor movement made during the day and night. It was worn at all times throughout the day and night. The actiwatch unit was fully waterproof and as such, did not need to be taken off. For these case studies, each dataset consists of activity counts, summated at one minute epochs for a period of two weeks.

For the first case study [4], measurements for 21 healthy subjects aged 23 to 65 (mean-40, standard deviation-16) and 26 patients with acute insomnia aged 18 to 64 (mean-32, standard deviation-12) were recorded. For the purpose of this study, only night-time periods, between the hours of 11pm and 6am (420 minutes), were analysed and daytime measurements were excluded.

For the second case study [5], the night-time periods of the actigraphy were considered. All recordings were grouped and analysed according to the age groups 20-30, 30-40, 60-70 and 80-90.

## 3. Methods

The dynamics of many physiological systems have been shown to contain fractal structures and these structures have also been known to deteriorate with both age and health problems [2, 7, 8]. In a frequency domain, the power-law relation of a time-series can be written as

$$S(f) \propto f^{-\beta}, \tag{1}$$

where $f$ is the frequency, $S(f)$ is the spectral power and $\beta$ is the scaling parameter (generally $0 \leq \beta \leq 2$) [9]. Long-range correlations exist in a time series if $\beta$ is around 1, such correlations are a sign of self-similarity across time.

Complexity has been shown to exist in many physiological systems, most notably in heart-rate variability (HRV) [10, 11, 12] and has been shown to decline in patients with cardiac diseases [13]. Further, Lipsitz and Goldberger [2] proposed that there is a reduction in the complexity of a physiological or behavioural system with the onset of age or disease. High complexity is often found in systems in which fluctuations are paramount to healthy behaviour, for example heart rate variability. Goldberger suggested that a high level of complexity could imply variance with a continuous adaptability to the subject's environment [14].

### 3.1. Detrended Fluctuation Analysis

DFA was first introduced by Peng *et al* [15] to analyse long-range correlations in DNA sequences. In the literature, such correlations are also known as $1/f$-scaling. This type of analysis has been

used to show that the complexity of heart rate dynamics increased after 8 weeks of aerobic training [16] and has been applied to HRV to quantify sleep [17].

DFA is a method of determining, statistically, the self-affinity of a signal. The exponent gained quantifies the correlation properties of the signal in order to identify complex behaviour. The algorithm works by first integrating a time series, then splitting the signal into equally sized boxes. A least squares line is then fit to the data in each box in order to detrend the series. The root-mean-squared deviation is calculated to show the typical fluctuations of the series, $F(n)$,

$$F(n) = \sqrt{\frac{1}{N}\sum_{k=1}^{N}[y(k) - y_n(k)]^2}, \tag{2}$$

where $N$ denotes the length of the data, $n$ is the box size, $y(k)$ is the integrated time series and $y_n(k)$ is the local trend. This algorithm is then repeated for every box to provide a relationship between the average local fluctuations, $F(n)$, and the box size, $n$. For our studies, $F(n)$ was calculated for box sizes of 5-420 minutes. A log-log plot is then used to deduce whether there is a linear relationship, indicating the presence of self-similar scaling, denoted by the $\alpha$ parameter. The correlations of the time series are then presented as $n^{-\alpha}$, where the parameter $\alpha$ estimates the type of correlation present.

An exponent between $0.75 \leq \alpha \leq 1.25$ is indicative of $1/f$-type scaling. This signifies the presence of long-range correlations and hidden-hierarchical structures such as self-organised criticality.

DFA has previously been applied to investigate the heart rate dynamics of patients during sleep to distinguish sleep stages [18], and has been shown to have applications for the detection of obstructive sleep apnea [19, 20]. Ivanov *et al* [21] applied DFA to investigate the correlations present in the heart beat dynamics during sleep and wake periods for three groups: healthy individuals, individuals having suffered heart-failure, and cosmonauts. The results in [21] illustrated a clear decline in complexity during sleep for the healthy individuals and cosmonauts, and an increase in complexity during sleep for the individuals who have suffered heart-failure, compared with the healthy controls.

*3.2. Magnitude and Sign Analysis*

Any long-range correlated time-series can be divided into two sub-series formed by the magnitude and sign of each increment [22, 23]. The DFA quantifies the linear fractal characteristics related to two-point correlations, while the magnitude and sign analyses (MSA) method is applied to investigate the long-range nonlinear properties that may exist in the data [22]. The MSA consists of the following steps: (i) calculation of the incremental value between successive values; (ii) decomposition of this incremental series into a magnitude series and sign series; (iii) subtraction of the magnitude and sign series from their respective means in order to avoid artificial trends; (iv) integration of the magnitude and sign series in order to allow for a more accurate calculation of the DFA exponent; and (v) DFA analysis to obtain $\alpha$ for both series.

The DFA exponents obtained from the magnitude and sign series are denoted $\alpha^{mag}$ and $\alpha^{sign}$ respectively. Fig 1 illustrates the MSA method for one night of actigraphy.

Positive correlations in the magnitude series ($\alpha^{mag} > 0.5$) indicate that an increment with a large magnitude is more likely to be followed by an increment with a large magnitude, and similarly for increments with small magnitudes. They could also be a reliable marker of long-term nonlinear properties [24]. Anti-correlation in the sign series indicates that a positive increment is more likely to be followed by a negative increment and vice versa. MSA is a complementary method to DFA as it distinguishes long-range correlations (similar to DFA) but also quantifies the nonlinear properties as well as the temporal organisation of the series.
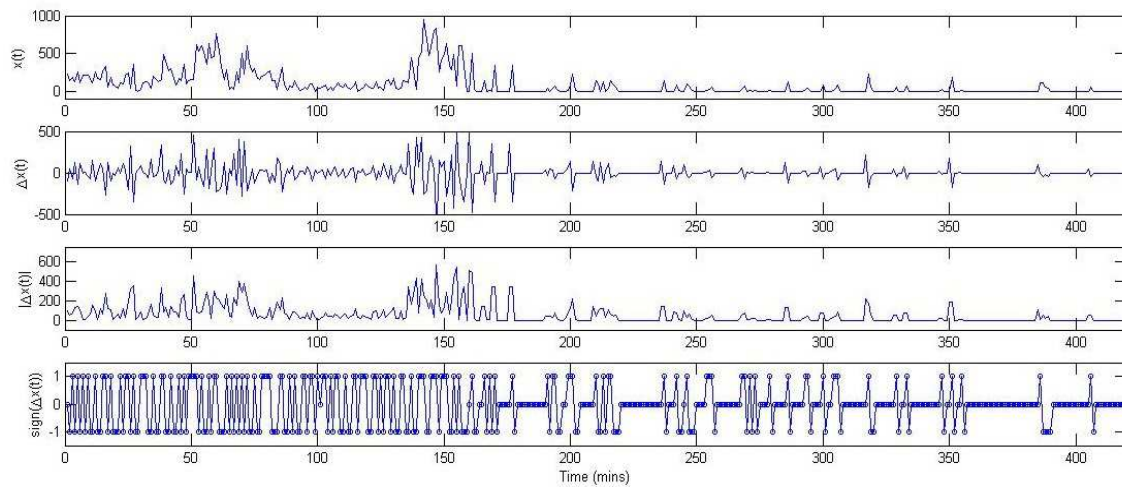
**Figure 1.** A typical time-series for one night of actigraphy (top), the incremental series of the original signal (second), the magnitude of the increments (third), and the sign series of the increments (bottom).

*3.3. Power Spectral Analysis*
Power Spectral Analysis (PSA) is another method used to study time series. It is based on power spectrum calculation from the data (3.3), then logarithms are taken of both the frequency and the power to produce a linear relationship, the slope of which can indicate the presence of scaling or self-similarity, $\beta$. Both parameters $\beta$ and $\alpha$ are used to calculate the correlations in a time series, and are linearly related [26],

$$\beta = 2\alpha - 1. \tag{3}$$

Random uncorrelated white noise does not have long-range correlations resulting in $\beta \simeq 0$. A random-walk process which only has short-range correlations between successive points has a $\beta$ parameter of around 2. Similar to DFA, $\beta \simeq 1$ identifies the presence of long-range correlations. Table 1 illustrates the relationship between DFA and PSA scaling exponents, $\alpha$, and, $\beta$, as well as the type of noise each value represents.

| Correlation | DFA ($\alpha$) | PSA ($\beta$) |
|---|---|---|
| White noise | 1/2 | 0 |
| Pink noise | 1 | 1 |
| Brownian noise | 3/2 | 2 |

**Table 1.** Scaling exponents $\alpha$ and $\beta$ for different type of noise.

Both DFA and PSA have been proven useful in the study of physiologic complexity with a loss in complexity shown in cases with heart conditions [13, 11]. Both methods have also very recently been implemented to study the transition of scaling behaviour across sleep and wake periods, also using actigraphy data, concluding that both methods could be exploited to detect sleep/wake transitions [27]. Here, DFA is primarily used to analyse the complexity of actigraphy during night-time hours via the $\alpha$-scaling exponent. The $\beta$ exponent is used to verify the results.

### 3.4. Recurrence Quantitative Analysis

Recurrence Quantitative Analysis (RQA) contains small and large scale structures which can be used as a qualitative measure on the dynamics of the system. Single, isolated recurrence points can occur if states are rare. A diagonal line (running parallel to the main diagonal) occurs when a segment of the trajectory runs parallel to another segment. The greater the percentage of these diagonals suggests a higher determinism in the system (Fig. 2).
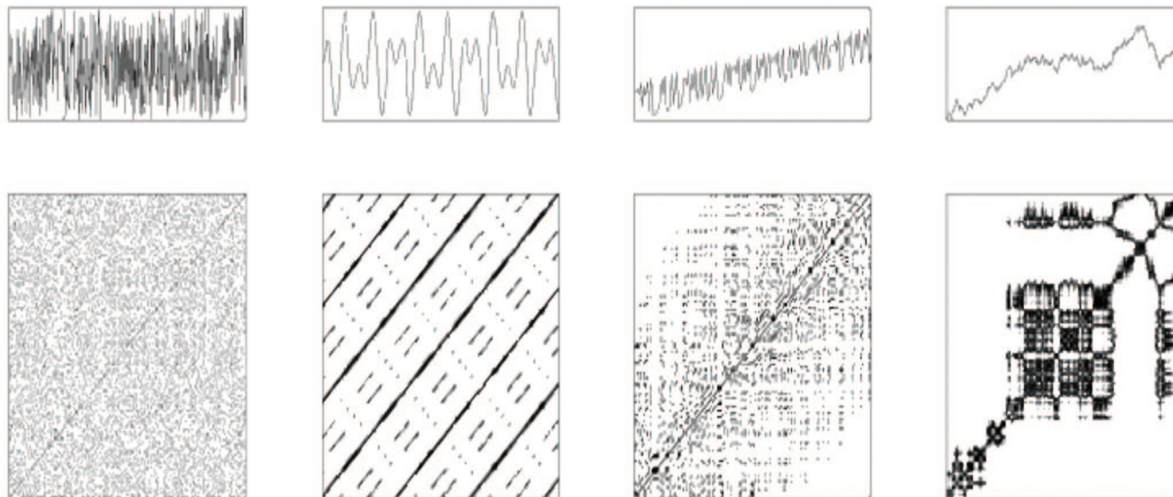


**Figure 2.** Illustration of the steps in RQA analysis.

### 3.5. Variability Analysis

Variability measures the extent to which data points in a series diverge from their mean value. Common measures of variability include range, variance and standard deviation. The most common use of variability in physiology is in the quantification of HRV, where a high degree of variability reflects healthy system function. Here a standard deviation (std) is used as a crude method of finding the activity of an individual during the night. High std value is considered as a sign of more activity during the night. Therefore, similar to calculating complexity, a lower variability is expected in those who do not suffer adverse health related events, such as insomnia.

For the purpose of this study, it is important to show that there is a correlation between the complexity and variability of night-time movements. Lipsitz [7] highlighted that there is a difference between the two. A relationship does often exist between complexity and variability, one key example being the complexity and HRV of heart beat dynamics, both of which decline with age and disease.

## 4. Results

### 4.1. Sleep Study

Activity distributions were constructed using the raw actigraph data for two case studies: (a) healthy sleepers and acute insomniacs and (b) healthy individuals from age groups 20-90 to investigate their mobility function. These indicate the distribution of the number of movements made in a given minute. Healthy sleepers tend much closer to zero movements per minute with quite a small tail-off whereas acute insomniacs show far greater dispersion towards a higher number of movements per minute.

The DFA parameter $\alpha$ was calculated for each night for every individual from both groups, these were then averaged to give each person a score. Variability was calculated alongside

DFA in order to examine whether a linear relationship exists between the two. The results are presented in Fig 3. A linear regression line is fit to the data and a positive correlation can be seen between the DFA exponent and the variability of the time-series thus justifying our hypothesis that a more complex signal would be indicative of a disturbed night's sleep. The $R^2$ value, known as the coefficient of determination, represents how well the regression line fits the data. For the healthy individuals (black circles), the regression line fits 70% of the data showing good correlation between the $\alpha$-exponent from DFA and the variability. Thus, a positive linear relationship exists for the group. However, the group with acute insomnia showed more dispersion around their regression line, but a positive correlation between the complexity and variability of the night-time movements was still observed.
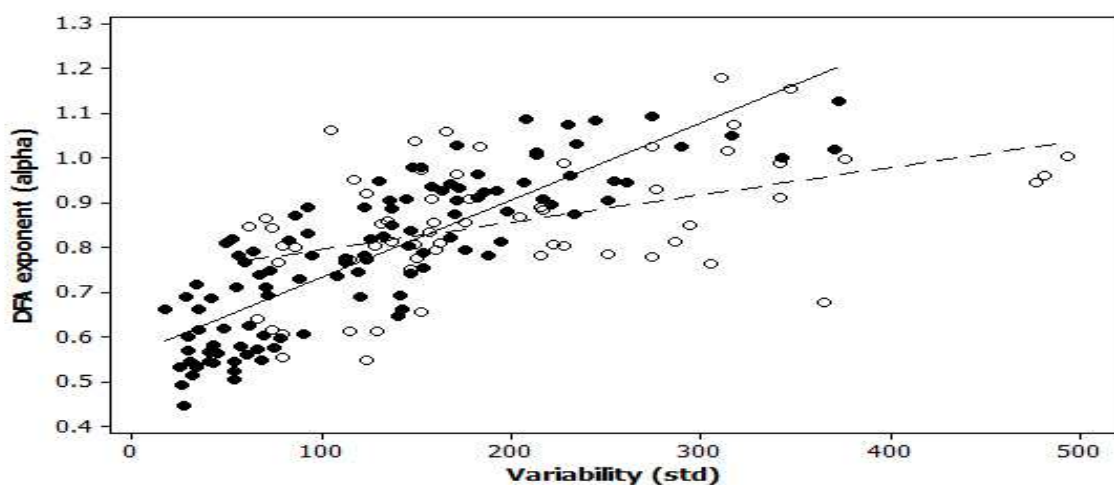


**Figure 3.** Scatter plot to show the linear relationship between the DFA parameter $\alpha$ and variability, calculated for each night, for both healthy sleepers (solid circles) and acute insomniacs (hollow circles). The solid and broken lines illustrate a correlation between the DFA parameter and the variability measures respectively.

Fig 4 shows the results gained from DFA analysis for a typical night of actigraphy from a healthy individual and one with acute insomnia, both individuals aged 25. A clear difference can be seen in the scaling parameter $\alpha$, with a higher correlation seen in the individual with acute insomnia.

Figure 5 refers to a 25 year old female suffering from insomnia. It demonstrates a high complexity with a $\beta$ value of 1.08. The results show similar findings to those gained from power spectral analysis.

These results are consistent across the whole dataset with those with acute insomnia exhibiting higher correlations during sleep than healthy subjects. From our data, 73% of all individuals with acute insomnia fell within the complex ($1/f$-scaling) region, $0.75 \leq \alpha \leq 1.25$, compared with just 33% of normal, healthy sleepers. Also, out of every individual who fell within this region, over 70% suffered from acute insomnia. In addition, significance testing was carried out on the two groups to look for significant differences in the complexity scores. A Mann-Whitney U test gave a p-value of 0.0015 indicating a highly significant difference between the complexities of healthy sleepers (mean 0.73) and acute insomniacs (mean 0.84).

The night-to-night variability of sleep complexity was calculated for both healthy sleepers and those with insomnia. These results demonstrate slight night-to-night fluctuations in the complexity for both groups, however none of these fluctuations are significant.
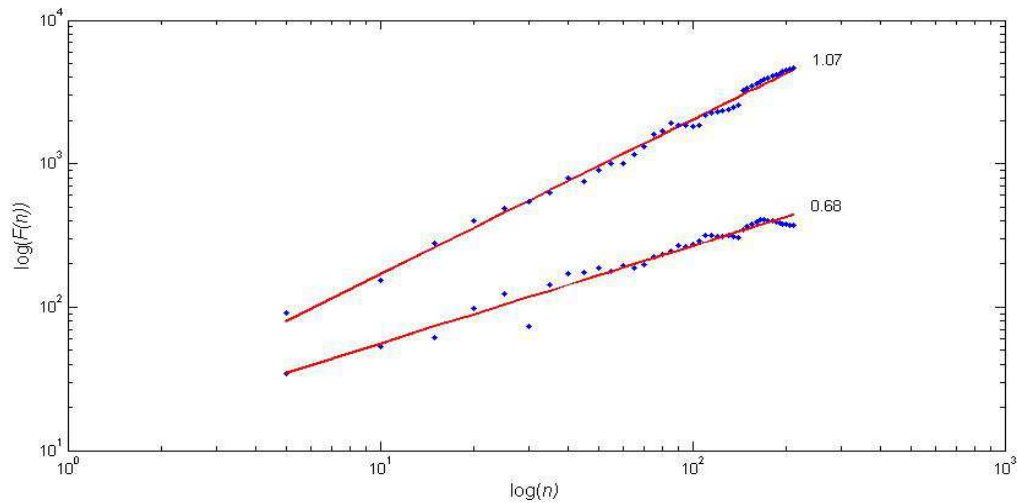
**Figure 4.** Log-log plot of the root-mean squared deviation, $F(n)$, versus the box size, $n$ (5-420 mins) for a healthy sleeper, $\alpha = 0.68$, and an individual with acute insomnia, $\alpha = 1.07$.
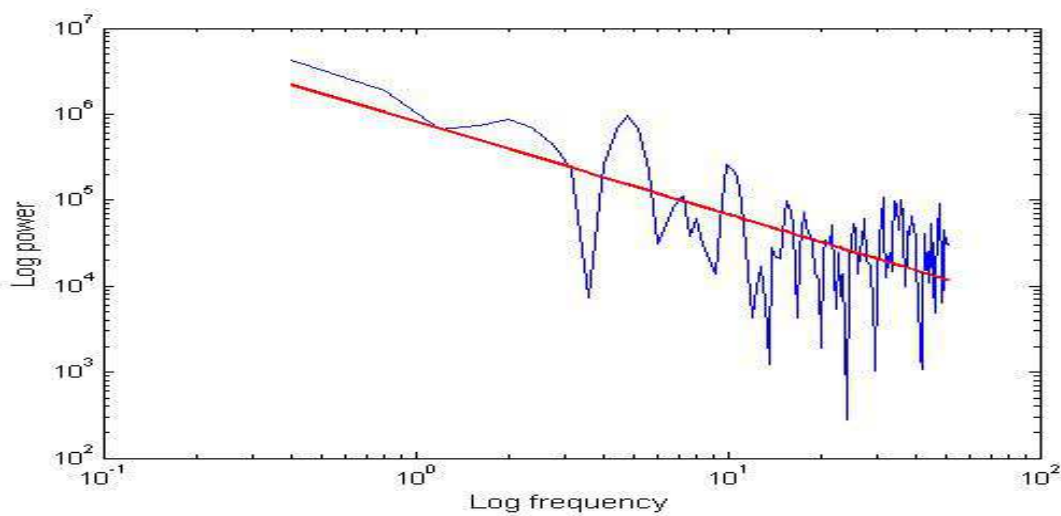


**Figure 5.** Log-transformed PS from one night of actigraphy for female, aged 25, with acute insomnia, $\beta = 1.08, \alpha = 1.04$, indicating high complexity.

*4.2. Mobility Study*

The second case study investigated PS, DFA and RQA for healthy individuals aged from 20 to 90. It showed that a threshold is apparent in many of the analyses present in the 60-70 group. A dynamical RQA measure, the determinism of the activity, is shown on Fig 6. The results for complexity metrics, obtained by RQA for the mobility case study, are shown in Table 2. The peak levels of the activity and trapping time show sharp change in value in the 60-70 age group region. Thus, the second case study also shows that complexity could prove to be a very good tool for the analysis of change of physiological function with age.
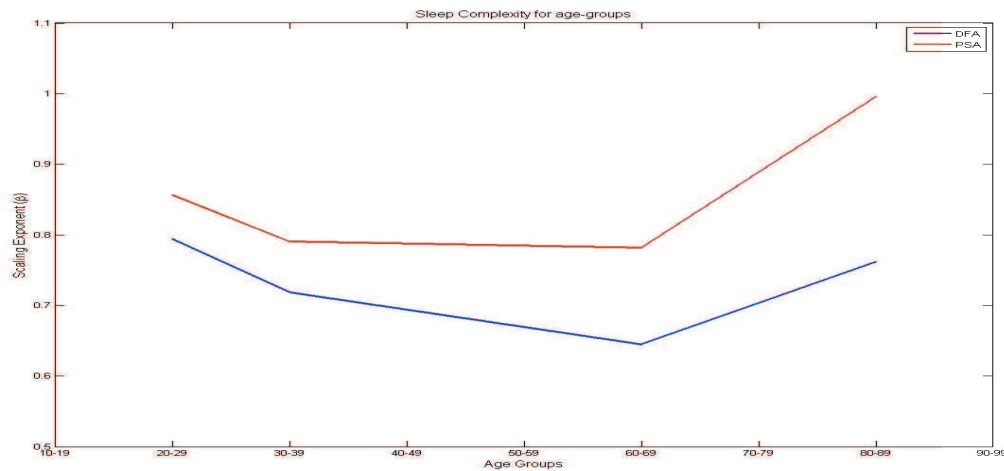
**Figure 6.** RQA plots showing treshold values for complexity metrics.

|  | 20-30 | 30-40 | 60-70 | 80-90 |
|---|---|---|---|---|
| Determinism | 69.76 | 68.11 | 66.15 | 70.69 |
| LMAX | 6.34 | 6.15 | 5 | 4.26 |
| TT | 10.29 | 9.15 | 7.70 | 6.51 |

**Table 2.** Complexity measures for mobility study obtained by RQA

## 5. Discussion and Conclusions

This study showed that complexity analysis, applied to actigraphy data, can differentiate between individuals with healthy functions and the onset of health-related events. In the first case study, our results suggest that this is the case with normal sleepers demonstrating significantly less complexity (with less correlation) in night-time movements than those with acute insomnia. In the second case study our results showed a clear treshold in change of physiological functions for the 60-70 age group.

Due to the nature of the data within these studies, each time-series may contain a considerable amount of zero-recordings - resulting from no movement made within a one minute epoch. This could potentially affect the accuracy of the DFA parameter $\alpha$. Chen *et al* [33] investigated the effect of nonstationarities on DFA and in particular the effects of a segmented time-series with different local properties. It was reported that for nonstationary time-series, segments with high positive correlations will dominate. Therefore, there is a possibility that the results discussed here are a slight exaggeration of the true correlations that exist, especially in the case of the healthy group who had a higher degree of zero-movements. We also cannot ignore the probability that some of the activity seen during the night could be the result of conscious movements.

Fractal techniques such as DFA, PSA and RQA have never been applied to actigraphy of sleep before with the hypothesis of high correlations being a marker of sleep-related health issues (in this case, acute insomnia), despite some studies showing an apparent increase in night-time movement complexity with other health problems, e.g. previous heart-failure [21]. The results gained are very promising and could provide a useful non-invasive markers for the identification of of health-related conditions.

## Acknowledgments

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