Testing for non-linearity in spontaneous pupil signal of health subjects: preliminary approach based on non-stationary surrogate data methods

W.Nowak, A.Hachoł, M. Misiuk-Hojło

Abstract**—**The papers presents investigation on deterministic and stochastic nature of short-term fluctuations in spontaneous pupil size fluctuations signal.. The Small-Shuffle Surrogate (SSS) Test was performed on the set of SPF signals recorded for healthy subjects by dynamic pupillometry. The results of the test obtained for all SPF signals show that there is short-term dynamics in irregular fluctuations of pupil size.

Keywords**—** Spontaneous pupil size fluctuations, Small-Shuffle Surrogate (SSS) Test, short-term dynamics in irregular fluctuations.

I. Introduction

THE spontaneous pupil size fluctuation (SPF) appears even in constant light and accommodation conditions. This complex behavior reflects a dynamical equilibrium modulated by the central nervous system (CNS) and the two branches of the autonomous nervous system (ANS), the sympathetic, which innervate the iris dilator muscle and the parasympathetic, which innervate the iris sphincter muscle [1,2].

The possibility to noninvasive and easy monitoring of nervous systems activity by using SPF signal provokes its intensive research using many analysis approaches/techniques including Fourier Transform [3], Short-Time Fourier Transform [4], Wavelet Transform [5] and Wavelet Entropy [6]. Performed analysis has shown that SPF is nonstationary and its main spectra is below 1 Hz, including respiratory and heart beat components. It has been show that SPF reflect sleepiness, cognitive and affective processes [7,8].

The important question that was not considered so for, is what are the characteristics of the underlying system that generate SPF Signal? (i.e. it is deterministic or stochastic? Linear or nonlinear?).

If the system is deterministic, its future performance can be clearly determine based on its past behaviour. If it is random, then it can be done only with a certain probability. The answer for this question can be obtain only by careful examination of the nature of the signal/system.

The methods used so far, the spectral analysis allows to resolve the determinism in the form of cycles of different lengths, hence they are used to study the periodicity.

New possibilities for this area creates statistical method based on surrogate data [9, 10]. The surrogate data generated with the original data preserve certain properties of the data and destroy others, and is also consistent with a specified null hypothesis. Generically stated, the procedure can be characterized by four steps:

(1) A discriminating statistic is applied to the original data,
(2) Artificial surrogate data that are consistent with some null hypothesis are constructed using the original data,
(3) The discriminating statistic is applied to the surrogates,
(4) The discriminating statistic value for the original data is compared with the ensemble of values estimated for the surrogates.

One of the newest statistical tests using surrogate data is the Small-Shuffle Surrogate (SSS) test. The test identifies the short-term dynamics (determinism) in the time series of irregular fluctuations, including those containing long cycles or trends. Hence, its versatility, with respect to the data is its main advantage.

Small-Shuffle Surrogate data proposed by Nakamura in [11, 12] allows for nonstationary data analysis, as contrary to linear surrogate methods which analyze stationary data.

SSS can investigate whether there is some kind of dynamics in irregular fluctuations, even if they are modulated by long term trends. The null hypothesis addressed by this algorithm is that irregular fluctuations are independently distributed random variables (i.e. there is no short term dynamics or determinism).

In this paper, we apply the Small-Shuffle surrogate method (SSS) to SPF signal. The results and analysis of these results will be presented and discussed.

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II. Material and Methods

A. Database

SPF was recorded using laboratory version of the pupillometr equipment at a sampling rate of 60 Hz [13]. There are 5 records of healthy subjects, 2 men and 3 women, aged 20-38. All participants were in good health, without any eye disease and they were non-smokers.

Before initiating a measurement series, all subjects participated in a training session concerning the pupillometric measuring procedure. At the beginning the measurement started with adapting the subject to darkness (5 min) and calibrating the system to individual characteristics of the subject. A subject was asked to keep her/his eyes open, look at the fixation point, and avoid blinking and head movements during the recording procedure. Subjects were also asked to avoid drinking coffee and alcohol for 24 hours before the measuring session. Measuring sessions were conducted between 9:00 am and 10:00 am hour. Each measurement lasted for 60 seconds, and the signal length used for the analysis contained 3600 samples. For each subject 4 SPF signals were recorded.

B. *Small-Shuffle Surrogate Test and Discriminant Statistic*

Small-Shuffle Surrogate (SSS) data are generated as follows: Let the original data be $x(t)$, let $i(t)$ be the index of $x(t)$ (that is, $i(t)=t$, and so $x(i(t))=x(t)$), let $g(t)$ be Gaussian random numbers and $s(t)$ will be the surrogate data. The procedure can be characterized by three steps:

(1) Obtain $i'(t)=i(t)+Ag(t)$, where A is an amplitude,

(2) Sort $i'(t)$ by the rank-order and let the index of $i'(t)$ be $\bar{i}(t)$

(3) Obtain the surrogate data $s(t)=x(\bar{i}(t))$.

In the SS surrogate data the local structures or correlations in irregular fluctuations (short term variability) are destroyed but the global behaviors (trends) are preserved. The SS surrogate data have the same probability distribution as the original data.

The SSS method changes the flow of information in data. Hence, the average mutual information (AMI) has been chosen as the discriminating statistic for surrogate test. AMI, a general nonlinear version of auto-correlation on a time series, can answer the question: on average, how much does one learn about the future from the past?

After calculation of these statistics, the inspection whether a null hypothesis shall be rejected or not is needed. T-test is employed to check whether estimated statistics of the original data fall within or outside the statistic distribution of the surrogate data.

If estimated statistic of the original data fall within the distribution of the surrogate data, the surrogate null hypothesis may not be rejected (in other words, there is no dynamics in irregular fluctuations). Contrary, the null hypothesis may be rejected (the irregular fluctuations have some kind of dynamics) if estimated statistic of the original data fall outside the distribution of the surrogate data.

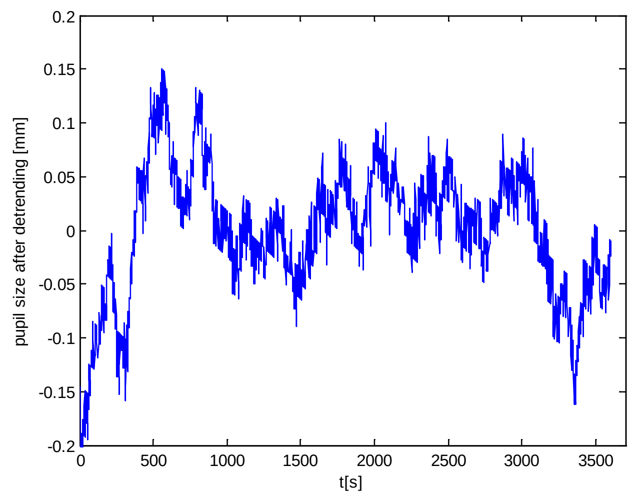
C. *Application of the SSS to SPF data*

For each of 5 signals of 5 subjects, 50 surrogates time series were generated from the original one. To compare the original and the surrogate series, discriminating statistics (AMI) are calculated for both signals. The significance level is 0.05. This information lead us to reject or not the null hypothesis.

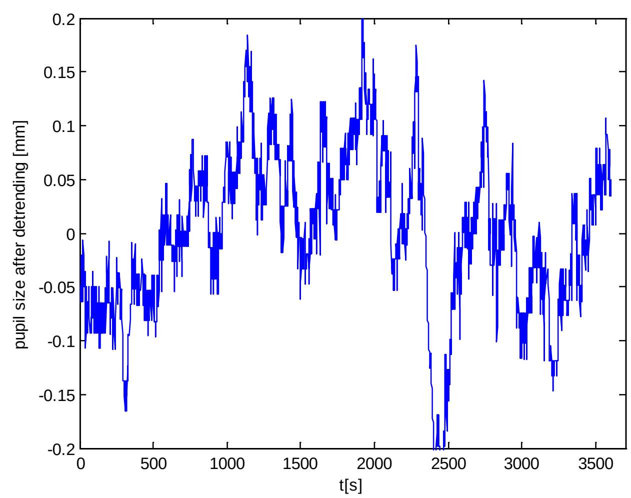
III. Results and Discussion

Fig. 1a. and Fig. 1b. show two examples of the SPF data. Preliminary observation of time variation of the SPF signals presented in Figure 1 reveals that there are only a few high amplitudes and more medium amplitudes as compared with many small amplitudes ones.

In addition, it is difficult to perceive any regularity in the amplitude changes. Generally, based on this observation it is impossible to determine whether the test system generates random or deterministic values.



a)



b)

Fig. 1. SPF examples signals

Fig. 2 shows the enlarged segments of SPF data and one of the SS surrogate data. Comparison of the course of original data and the course of the surrogate data, shows the large similarity of shapes and only slight (hardly noticeable) differences. This confirms the correctness of the applied SSS data generation algorithm (the SS surrogate method generates data in which long term behaviors are preserved and local structures are destroyed).

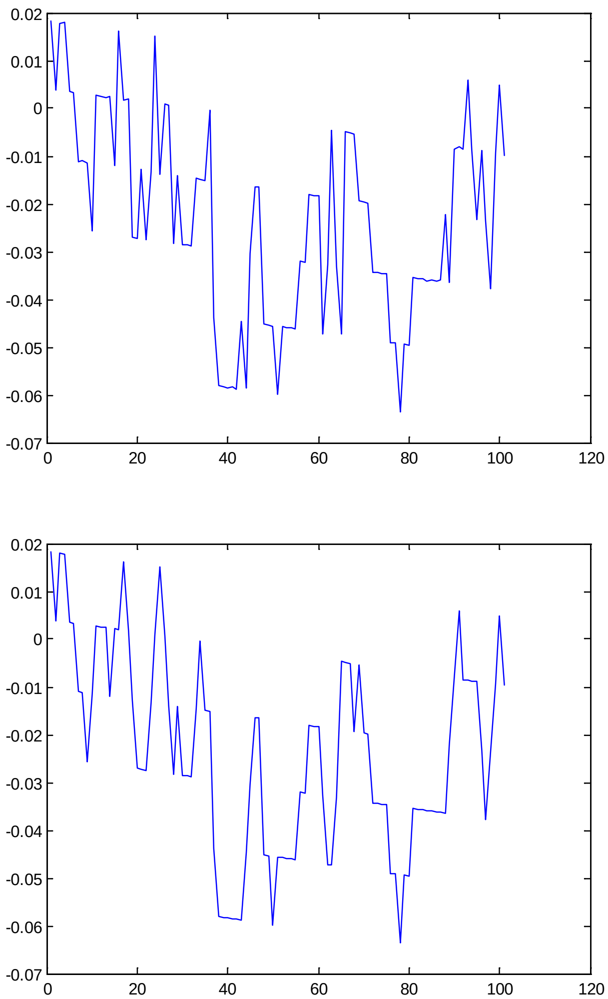


Fig. 2. The enlargement segments of SPF signal (higher panel) and surrogate data (lower panel)

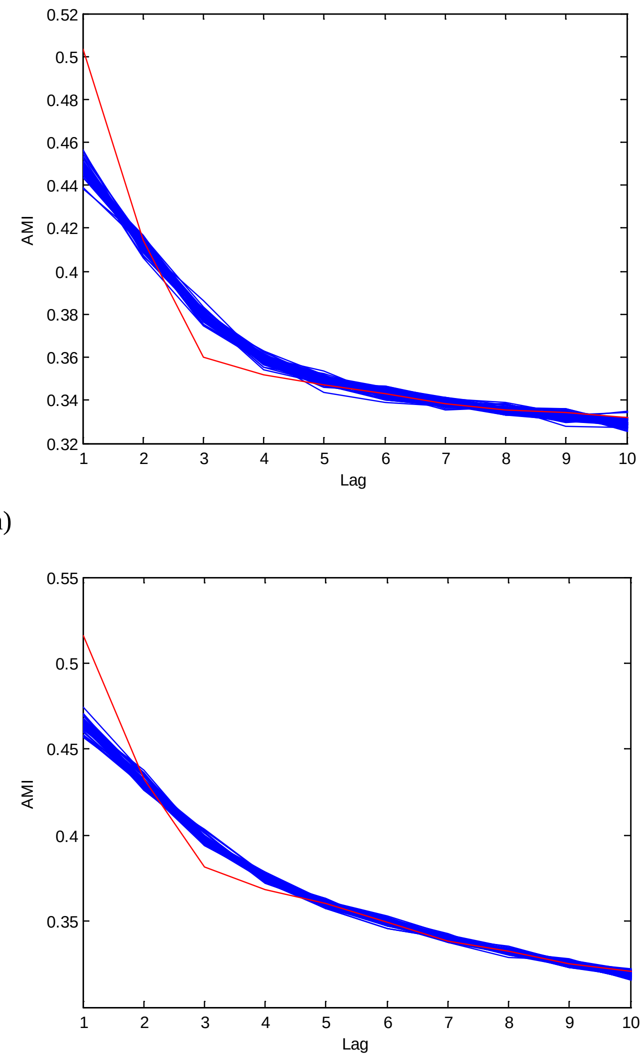
Fig. 3 shows the result of applying the SS surrogate method. The figure shows the AMI estimated for the original data and the AMI distributions of the SS surrogate data.

We noticed that some differences (the original data fall outside the distributions of SS surrogate data) clearly appear when the time lag is relatively small, because the information in the systems is not retained for longer periods of time.

Hence, we conclude that irregular fluctuations in the SPF have some kind of short term (inter second) dynamics.

It is also interesting to note that the course of AMI function for the original data is similar to the course of this function for the surrogate data. This is a confirmation that in the SSS data local structures were destroyed but the global structures were retained.

Tab. 1 shows AMI statistic calculated for all tested subjects.



a)

b)

Fig. 3. The results of SSS test for SPF data presented in Fig.1. Vertical axis of the plot shows the estimated AMI statistic. Horizontal axis shows the lag. The ‘thin‘ line is the original data and ’thick’ lines are the SS data. We use 3600 data points, A=1.0 and 50 surrogate data.

Table 1. AMI Statistics for all subjects

SPF signal		AMI (Lag=1) Original data	AMI (Lag=1) Surrogate data
Subject 1	1	0.50	0.45±0.01
	2	0.53	0.45±0.01
	3	0.58	0.52±0.01
	4	0.51	0.44±0.01
Subject 2	1	0.74	0.70±0.01
	2	0.80	0.76±0.01
	3	0.77	0.72±0.01
	4	0.47	0.41±0.01
Subject 3	1	0.34	0.28±0.01
	2	0.53	0.46±0.01
	3	0.44	0.38±0.01
	4	0.40	0.33±0.01
Subject 4	1	0.60	0.57±0.01
	2	0.58	0.56±0.01
	3	0.75	0.70±0.01
	4	0.46	0.39±0.01
Subject 5	1	0.82	0.79±0.01
	2	0.84	0.80±0.01
	3	0.79	0.75±0.01
	4	0.83	0.78±0.01

IV. CONCLUSIONS

In this study we applied a Small-Shuffle Surrogate (SSS) Test for dynamic testing in spontaneous pupil fluctuation (SPF) signal of health subjects. SSS test is capable of testing against the null hypothesis of irregular fluctuations are independently distributed random variables (in other words, there is no dynamics in irregular fluctuations).

Signals which were analyzed represent complex papillary behavior regulated by the sympathetic and parasympathetic innervations of the iris muscles controlled via neural feedback mechanism. As has been shown in Figures and Table, the SSS test detect that irregular fluctuations in the SPF have some kind of short term (inter second) dynamics. These results suggest possible future treatment and understanding SPF signal.

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