On multi-scale entropy in laboratory animals exposed to different ambiental conditions

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Abstract— **This paper analyses multi-scale entropy (MScEn) applied to laboratory animals exposed to different ambient temperature – low, normal and high. The effect of reduced length within the scaling steps, in respect to the fixed length series is examined. The results are compared with control data comprising the isodistributional surrogate data (temporally randomized signal samples) and with artificially generated signals with normal distribution.**

Keywords: multiscale entropy, biomedical data

I. INTRODUCTION

Information theory rapidly evolved in 1950's as a study that deals with quantification, storage and communication of information. The key measure to assess system's irregularity is entropy. Depending on the problem complexity, there are several types that are used to describe the system, such as sample entropy, approximate entropy, dispersion entropy etc. [1]. Sample entropy has been commonly used for the analysis of physiological data, although it demonstrates sensitivity to the parameter values, instability for short time series and inability to quantify the irregularity of signals on a multiple scale [2].

Since the complex systems operate on multiple temporal scales, new approach in analyses of their irregularity has been suggested [3]. Multiscale entropy has appeared as most suitable tool for the predictability assessment of healthy physiological systems [4].. Its algorithm is composed from two main steps: i) a "coarse-graining" process is applied to the time series; ii) Sample entropy is calculated for each coarse-grained time series.

Pulse fluctuation (HRV) is a solid impression of the numerous physiological components modulating the ordinary beat of the heart. They give an incredible methods for watching the transaction between the sympathetic and parasympathetic nervous systems [5]. It demonstrates that the structure producing the signal isn't just essentially direct, yet additionally includes nonlinear commitments. Pulse (HR) is a nonstationary signal; its variety may contain markers of ongoing malady, or admonitions about looming cardiovascular diseases. [6].

It is known that thermoregulation and renin vasopressin system are closely linked. Vasopressin is a neuropeptide synthetized in the hypothalamus and secreted from the posterior pituitary. Vasopressin exerts its effects binding to V1a, V1b and V2 receptors. It is shown that vasopressin acts centrally and peripherally to reduce body temperature. As thermoregulation is intimately associated with blood pressure and heart rate regulation, the underlying mechanisms are still not clear [7].

Therefore, the aim of this study was to investigate the effect of different ambient conditions on hart rate regulation of exposed rats. Multiscale entropy was used as quantitative analysis of the complexity of inter-beat intervals (RR) recorded during high, normal and low temperature exposal in order to investigate existence of unique markers for each state.

II. MATERIALS AND METHODS

A. Sample Entropy

The SampEn method is a modified entropy computation from the approximate entropy (ApEn) method. [2] It computes the conditional probability that quantifies that the similarity of two arrays of different length m and m + 1 is maintained. Here, m denotes the length of sequences that are compared to each other. More specifically, the SampEn method consists of four steps: reconstruction, definition of distance, definition of the criterion for similarity, and entropy calculation [1]. In general, r is selected in the range of $[0.1\sigma, 0.25\sigma]$, where σ represents the standard deviation of original time series x_N. Finally, SampEn is defined by:

$$SampEn(m, r, N) = -\ln \frac{A^m(r)}{B^m(r)}. \quad (1)$$

where A is the total number of forward matches of length m + 1 whereas B is the total number of templates matches of length m. SampEn is a "regularity statistic." It "looks for patterns" in a time series and quantifies its degree of predictability or regularity.

B. Multiscale Entropy

For a given time series, multiple coarse-grained time series are constructed by averaging the data points within non-overlapping windows of increasing length, t in order to reduce the high frequency components (Fig. 1) [4].

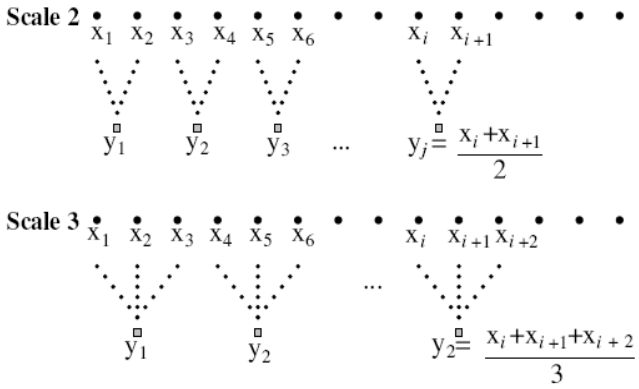

Figure 1. Schematic representation of the coarse-graining technique for scale 2 and 3.

Eeach component of the coarse-grained time arrangement, y(τ) j, is calculated according to the equation:

$$y_j^t = \frac{1}{t} \sum_{(j-1)t+1}^{jt} x(i) \quad 1 \le j \le \frac{N}{t} \quad (2)$$

where τ represents the scale factor and 1⩽ j ⩽ N/ τ . The length of each coarse-grained time series is N/ τ . For scale 1, the coarse-grained time series is simply the original time series.

SampEn is determined for each coarse-grained time series, and after that plotted as an element of the scale factor.

Two types of MSC entropy were examined, one gained in previously explained manner and other with identical length for each time series (MSC N1=1000). That means that for each scale N/N1/t times entropy was calculated (e.g. for τ =1, 17 entropy were calculated and their average value was taken into count for current scale and so on)

C. Evaluation Data

1.1 Synthetic Data

To verify the efficiency of the MSE methods with respect to the length of data, we first employed entropy calculation on synthetic data. The synthetic data used in this work are isodistributional (ID) surrogates and white Gaussian noise (or simply white noise). ID surrogates are generated by randomly permuting the temporal order of the original signal samples; the samples of the obtained stochastic process are independent and identically distributed (i.i.d.) with the same mean, variance, and distribution as the original time series [8]. The way toward creating surrogate information wrecks the relationships and corrupts the data substance of the original signal. Finally, white noise is that the values at any pair of times are identically distributed and statistically independent and it is the case of uncorrelated noise. For each signal, 10 realizations were randomly generated and then averaged.

1.2 Real ECG Data

All experimental procedures confirmed to ECC Directive 86/609. Experiments were performed in adult male Wistar outbred rats, weighing 300–350g housed under control laboratory conditions (temperature - 23±1ºC; relative humidity: 60–70%; lighting: 12:12h light-dark cycle) with food (0.2% NaCl) and tap water ad libitum. At the end of the experiments rats were sacrificed by a lethal dose of thiopental sodium (150 mg/kg, i.p.).

On the day of surgery rats were treated with gentamicin (25 mg/kg i.m.) with carprofen (5 mg/kg, s.c.). Sutured skin was sprayed with a combination of local antibiotics (bacitracin and neomycin). Under ketamine and xylasine anesthesia (0.3 ml of 10% ketamine i.p. and 0.1 ml of 2% xylazine i.p.) TL11M2-PA-C50-PXT DSI implant was introduced in abdominal aorta for concomitant measurement of blood pressure (BP) wavecorms and body temperature (Tb). [7]

Arterial BP and Tb were digitalized at 1000Hz. Systolic BP (SBP), diastolic BP (DBP) and pulse interval (PI) were derived from the arterial BP as maximum, minimum and interval between the steepest local rises of BP waveforms, respectively. Experiments were performed at decreased ambient temperature (12°C ± 2), at neutral ambient temperature (22°C ± 2) and at increased ambient temperature (34°C ± 2). The number of exposed rats was 4,9 and 10

The artifacts were removed using a filter designed specifically for RR (or PI) time series [9], while the signal stationarity was assured by removing the slow-varying trend using another filter, also designed for RR (PI) time series [10].

III. RESULTS

From the TABLE I, smooth gradation across mean RR values from three groups of experimental rats can be seen, whereas HT stands for high temperature, NT for natural temperature and LT for low temperature. Experimental setup was divided into three steps.

TABLE I. Mean RR values, their standard deviation and standard error calculated for ten HT, nine NT and four LT rats

	Mean value	Standard deviation	Standard error
HT	188.6192	8.950637	2.83044
NT	171.6282	24.34851	8.11617
LT	164.5468	24.31278	3.473254

A. *Experiment I-Synthetic Data*

SampEn, MScEn and MScEn (N1=1000) were calculated from synthetically generated data for each group of rats and plotted simultaneously on each figure (Fig2., Fig3., F4.,).

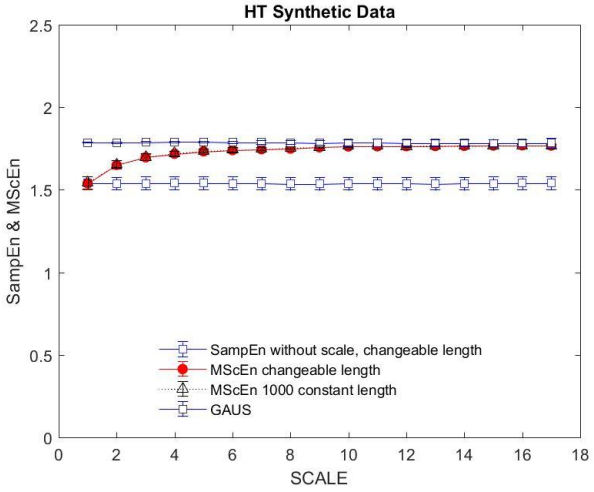

Figure 2. Representation of three entropies for HT group (synthetic data)

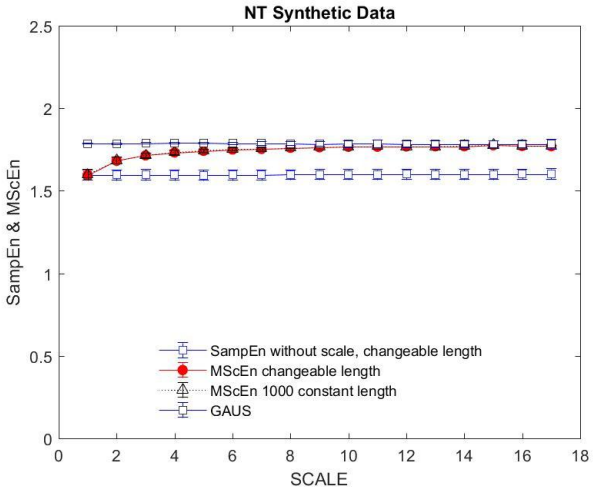

Figure 3. Representation of three entropies for NT group (synthetic data)

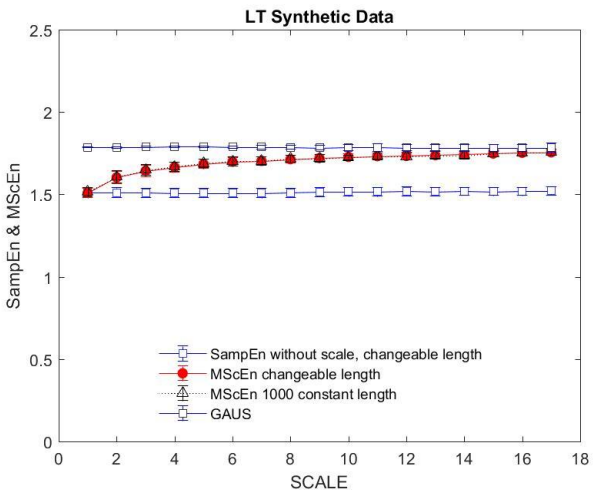

Figure 4. Representation of three entropies for LT group (synthetic data)

B. *Experiment II-Real ECG Data*

SampEn, MScEn and MScEn (N1=1000) were calculated from real data for each group of rats and plotted simultaneously on each figure (Fig5.,Fig6.,Fig7.,)

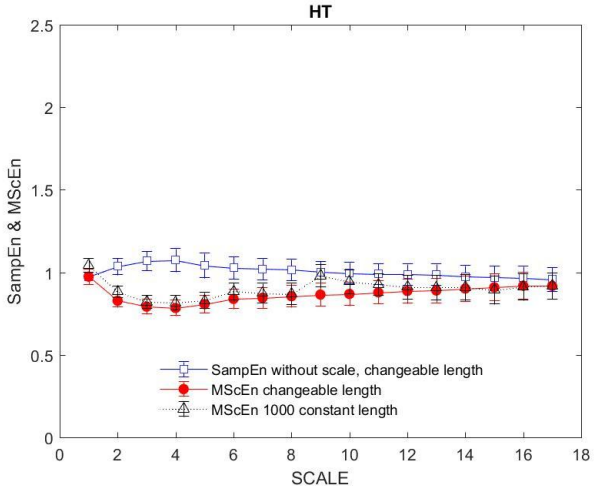

Figure 5. Representation of three entropies for HT group (real data)

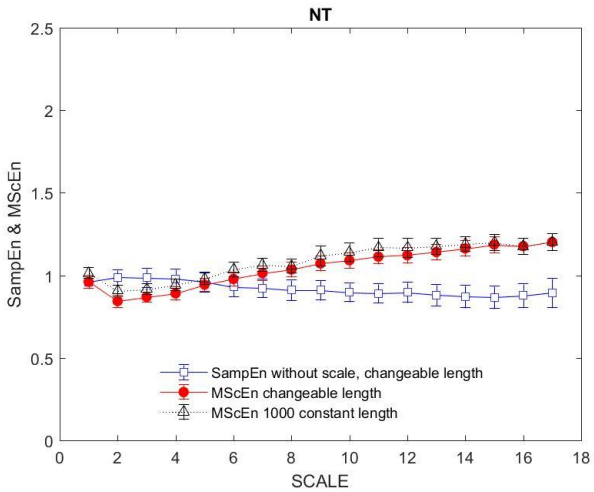

Figure 6. Representation of three entropies for NT group (real data)

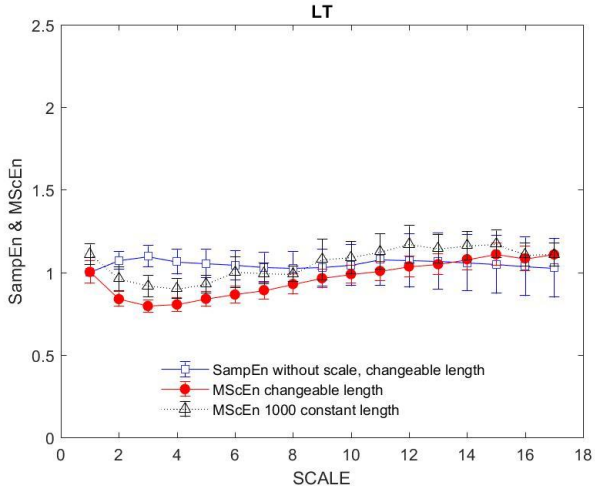

Figure 7. Representation of three entropies for LT group (real data)

C. *Experiment III*

SampEn, MScEn and MScEn (N1=1000) are displayed on separate figures, where for each of them simulations comparison of real data and synthetic is showed. For SampEn only NT group is presented since HT, NT and LT express similar behavior (Fig.8). MScEn with changeable length is represented with Fig 9., Fig10., Fig11., for each group, as well as MScEn (N1=1000) with Fig12., Fig13. and Fig14.

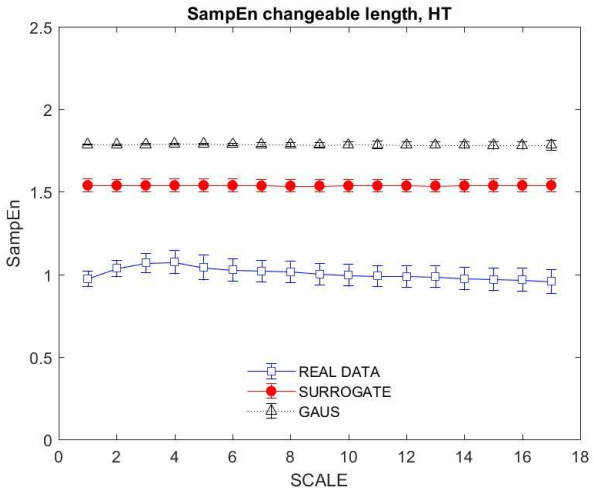

Figure 8. Representation of SampEn based on different types of data

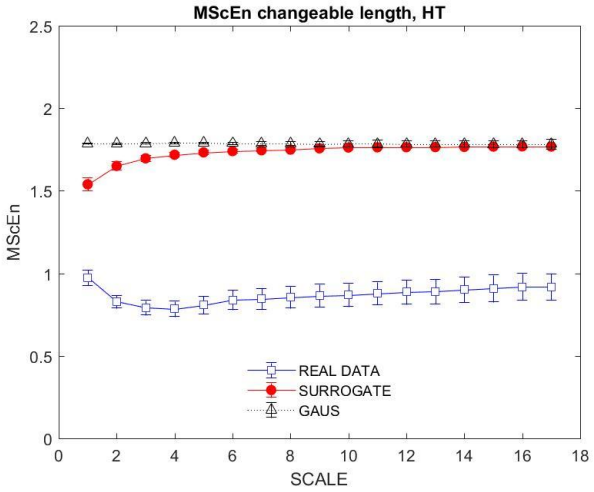

Figure 9. Representation of MScEn for HT

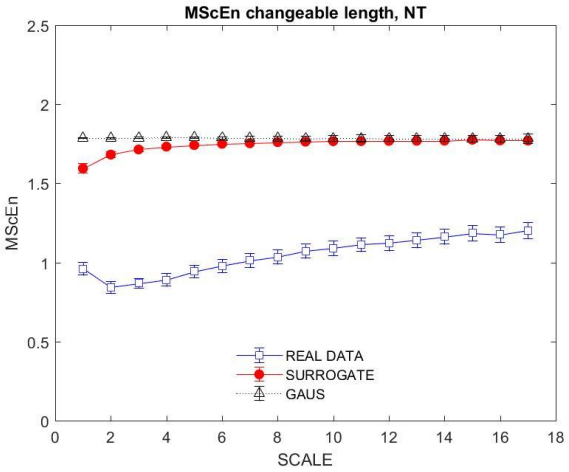

Figure 10. Representation of MScEn for NT

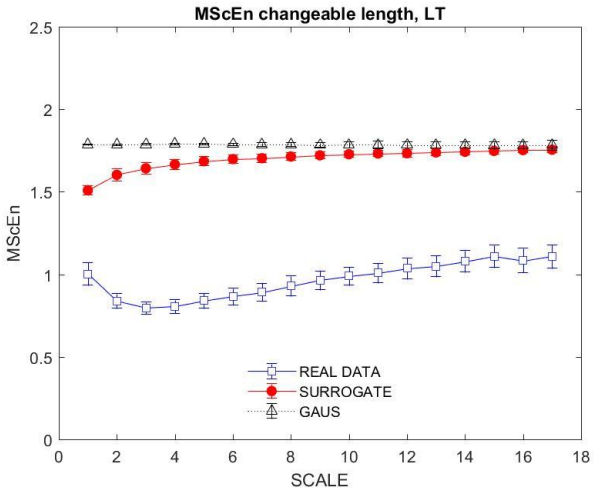

Figure 11. Representation of MScEn for LT

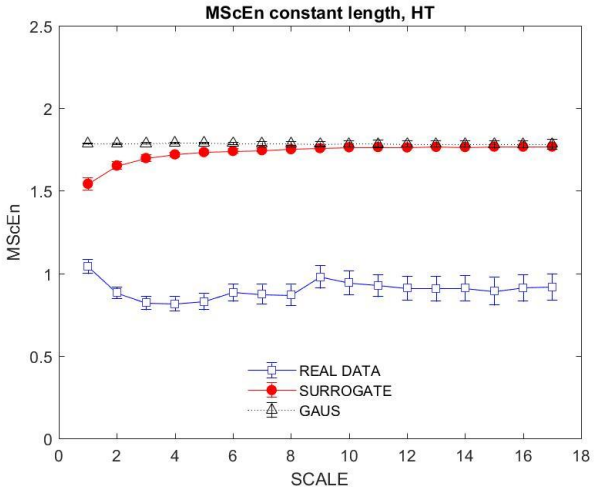

Figure 12. Representation of MScEn (N1=1000) for HT

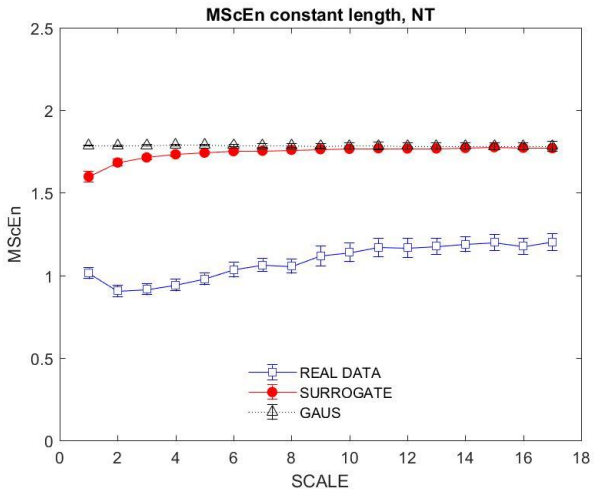

Figure 13. Representation of MScEn (N1=1000) for NT

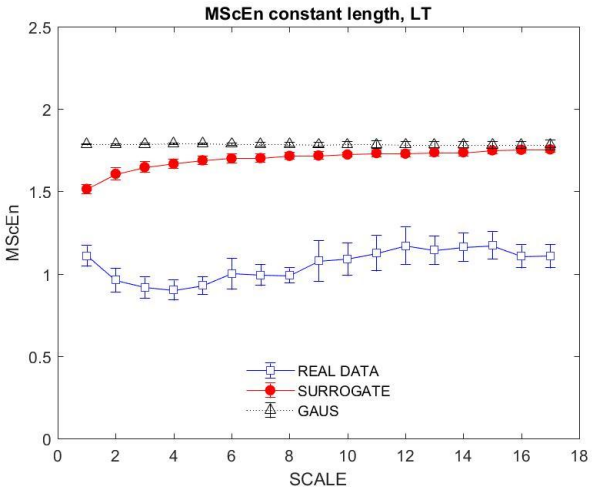

Fig1ure 14. Representation of MScEn (N1=1000) for LT

IV. DISUCSSION

From Experiment I and Experiment II it could be observed that MScEn with changeable and MScEn with constant length of time series demonstrate same behavior, which mainly differs between HT from NT(LT) groups (Experiment III).

Customary single-scale entropy measures will in general yield lower entropy in time series of physiologic information, for example, between beat (RR) interval series than in surrogate arrangement framed by shuffling the original physiologic information. This happens on the grounds that the shuffled information are more sporadic and less unsurprising than the first arrangement, which regularly contain connections at many time scales. It shows same example of appearance for HT, NT and LT gathering.

The MSE techniques demonstrates that the original time series are more unpredictable than the surrogate ones, by uncovering the reliance of entropy measures on scale. MScEn express same example of appearance for HT, NT and LT gathering of rodents.

V. CONCLUSSION

The aim of this study was to analyze RR intervals extracted from ECG data recorded from rats exposed to different ambiental conditions in order to find possible hallmark of each condition. Methods applied for this purpose were SampEn, MScEn and MScEn with constant length for each time series. It is found that SampEn is same for each temperature condition. MScEn exhibits same pattern for LT and NT group but for HT is different. This may be due to the fact that rats have adaptive behavior to high environmental temperature which fallows demonstrated higher pulse interval. It is shown that ambient air temperatures of under 6°C or more prominent than 29°C initiate substantial changes in blood vessel circulatory strain and pulse in homeotherms, such as, rodents [11].

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