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# QUANTIFICATION OF THE RESPIRATORY TIME-SERIES REGULARITY AND COMPLEXITY USING APPROXIMATE ENTROPY AND SAMPLE ENTROPY

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**Abstract** – The objective of this article is an attempt to measure complexity and regularity of the physiological signals during sleep in direction of detection and classification of the sleep apnoea syndrome. We use approximate entropy (*ApEn*) and sample entropy (*SampEn*) to assess diversity of consecutive breathing patterns. Experimental investigations are preceded by the theoretical and computer analysis for the example of stochastic process *MIX*(*P*) and the cardiorespiratory PNEUMA model. Realisation of the research procedure resulted in the statement of the potential of the algorithms to distinction between normal and pathological respiratory conditions during sleep and quantitative evaluation of the observed changes. In conclusion, some important directions were outlined for the future studies.

**Keywords**: complex systems, regularity analysis, sleep apnoea syndrome

## 1. INTRODUCTION

The issue of the evaluation of the complex systems is an area of research interests both from the theory point of view as well as its application [1, 2, 3]. Objects complexity manifests in the complexity of their behaviours, recorded during observation of the output signals. The natural consequence of it is also the systematics, which is based on the evaluation of the regularity or variability of the signals and systems. A good example of such objects is the respiratory systems with its intra-periodic and breath-to-breath variability [4, 5, 6, 7]. There are the reports pointed at classifying complexity of the processes and their association with the normal and pathological regime of work of the system [1, 2, 8, 9]. A quite substantial challenge is the reconstruction of acquired signals as a conglomerate of intermingled processes with various natures (deterministic or stochastic, stationary or non-stationary, with lumped or distributed character) and scales (micro-, macro-world). A respiratory disorder during sleep – sleep apnoea syndrome (SAS) – is interesting also for that reason and still needs the solution [4, 10, 11]. Therefore, one of the question is how can we compare such tracings?

Regularity or its lack can be depicted conceptually adequate to the level of arrangement of the data set. The typical indexes for such formulation are the entropic-like measures [12, 13]. In the paper, the approximate entropy (*ApEn*) and sample entropy (*SampEn*) are explored to assess their usefulness in measurements of occurrence of systematic rules during sleep. The algorithms are located in a range of nonlinear dynamics method, which stands for the front of the modern research in the domain of physiological data processing. After implementation of the theoretical tools, we tested their properties and calibrated them for the application on example of the respiratory signals recorded in the group of subjects: normal, with central and obstructive sleep apnoea syndrome. The core tests were aimed at quantitative identification of the symptoms between the members of the group. Regularity assessment was performed on the set of the signals acquired during the polisomnography.

## 2. METHODS

Approximate entropy and sample entropy was proposed as a tool for finite and noisy time-series analysis. The methods examine the data set for similar epochs: more frequent and more similar epochs lead to lower values of *ApEn* or *SampEn*. Their rigorous definitions and apllication details can be found, e.g. in [14, 15, 16, 17]. Given $N$ points, the family of statistics $ApEn(m, r, N)$ is approximately equal to negative average natural logarithm of the conditional probability that two sequences that are similar for $m$ points remain similar, that is, within a tolerance $r$, at the next point. Thus, a low value of *ApEn* reflects a high degree of regularity [17]. To avoid the occurrence of ln(0) in the calculation, the *ApEn* algorithm counts each sequence as matching itself. This solution makes the approximate entropy the biased estimator.

*SampEn* statistics is free of the bias caused by self-matching. Furthermore, in contrast to $ApEn(m, r, N)$, which calculates probabilities in a template-wise fashion, $SampEn(m, r, N)$ calculates the negative logarithm of a probability associated with the time series as a whole [17].

Both, *ApEn* and *SampEn* were calculated via a short computer code. The advantage of the algorithms is insensitivity to noise and artifacts, by introduction of filtering properties of $r$ and probabilistic form of the comparisons (of $m$-points sequences), respectively.

The correctness of the applied procedures and the properties of the theoretical tools – *ApEn* and *SampEn* –

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were tested with the family of *MIX*(*P*) processes, defined as in [14, 15] (Fig. 1).

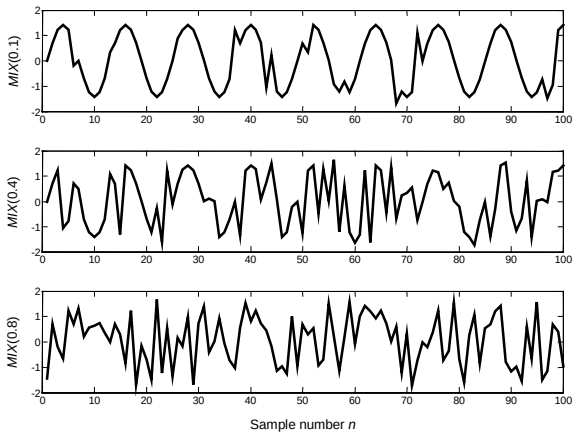


Fig. 1. Family of stochastic processes *MIX*(*P*) with controlled parameter *P* = [0.1, 0.4, 0.8].

Methodological idea of analysis of the complex systems and processes assumes exploitation of models of the undertaken object. Such attempt enables analysis of characteristics difficult to observe/measure during real experiment, giving explanation for 'hidden' properties and its various complex (inter-)realisations. Models and signals generated into them are also useful during designing and calibration of the new theoretical tools for system and data exploration. This attempt was also the part of the reported investigations. During the research the PNEUMA analogue of the cardiorespiratory system interactions was used [18, 19, 20]. Its main structural description was depicted in Fig. 2.

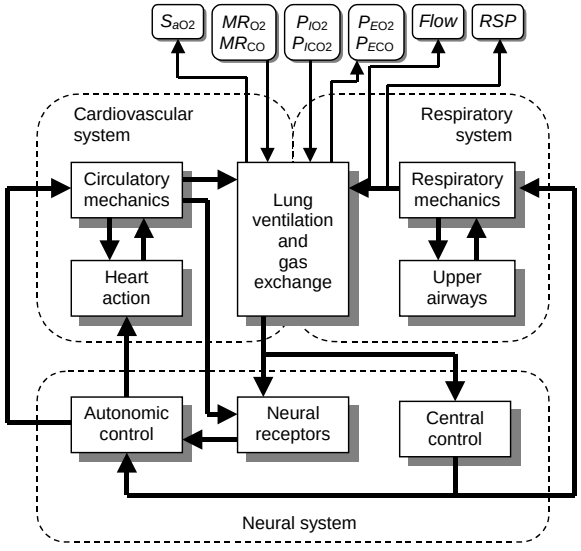


Fig. 2. Architecture of the main flows between the subsystems in the cardiorespiratory PNEUMA model.

In the last stage, the usefulness of the measures for research and/or ambulatory work in the domain of the respiratory measurements were tested in the set of the signals (mouth and nasal flow - *TP*, $SaO_2$, *C*3-*A*1, *O*1-*A*2, *EKG*, *EMG*, thorax movements – *RSP*1, abdomen movements – *RSP*2, body position – *RK*) measured in normal subjects and patients with the symptoms of central and obstructive sleep apnoea syndrome. Trends were acquired with the polisomnograph produced by Elmiko, Poland. Analysis was conducted directly on the signals represented in a regime of recording and after transformation to RRV time-series domain (respiratory rate variability time-series).

## 3. RESULTS

The first step of the investigations was the verification of correctness of application of the *ApEn* and *SampEn* algorithms. The tests were aimed also at exploration of the general properties of the procedures.

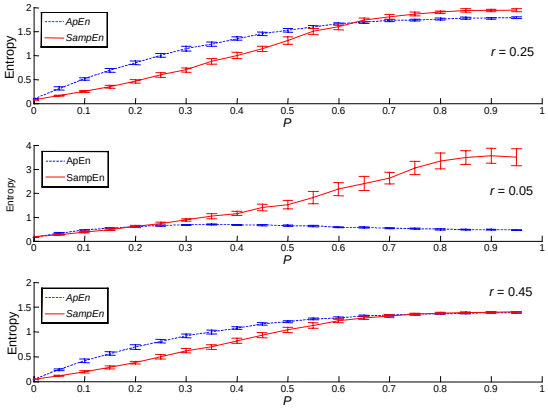


Fig. 3. Detection properties (with *SD*) of *ApEn*(2, *r*, 1000) and *SampEn*(2, *r*, 1000) for the different width of the filter *r* as a function of the level of randomness (*P*) of *MIX*(*P*) process.

Regarding to the assumptions, second activity can be helpful in calibration of the investigated theoretical tools for a case of application to a concrete time-series representation, which was suggested in [14, 15, 21]. The example results were presented in Fig. 3 and Fig. 4.

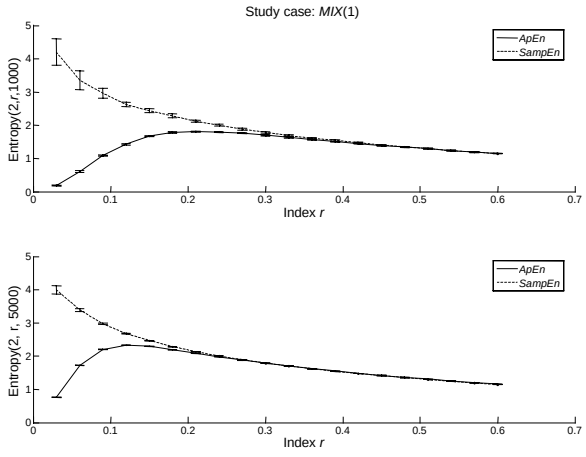


Fig. 4. Relation between *ApEn*(2, *r*, *N*) and *SampEn*(2, *r*, *N*) (with *SD*) for various length *N* of the data and width of the filter *r*; during all simulations parameter *P* in *MIX*(*P*) was fixed as equal to 1.

Simulations show that even for very restrictive properties of the filter *r* assessment of *SampEn* continue to be sensitive and adequate on components of the signal, although *SD* of such estimations rise with *P*. *SampEn* is also more unaffected than *ApEn* in a case of operating on short sets of data. As can be seen in Fig.4, taking the longer time-series under processing can even reduce *SD* of *SampEn*, whereas such action not assures fast and reliable calculations of *ApEn*.

Administering the PNEUMA model we were able to imitate the condition for healthy subject and patient with the symptoms of sleep apnoea, both central and obstructive. Sensitivity and potential of the applied theoretical tools for physiological time-series analysis to differentiate between healthy and pathological patterns are well described (qualitatively and quantitatively) in Fig.5–Fig.8. These example plots for abnormal conditions concern obstructive changes in the system at the level of the upper airways.

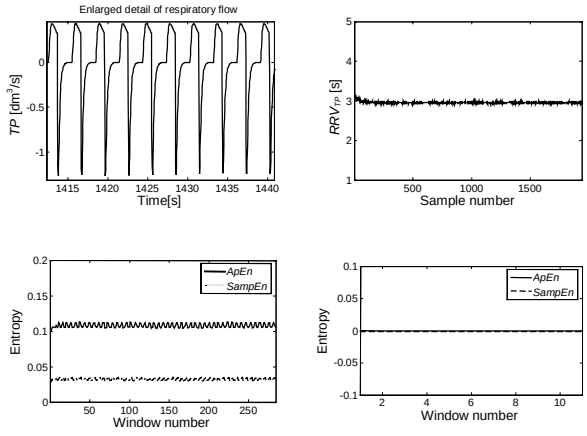


Fig. 5. Respiratory flow *TP*, $RRV_{TP}$ extracted for flow, approximate (*ApEn*) and sample entropy (*SampEn*) during simulations of healthy conditions.

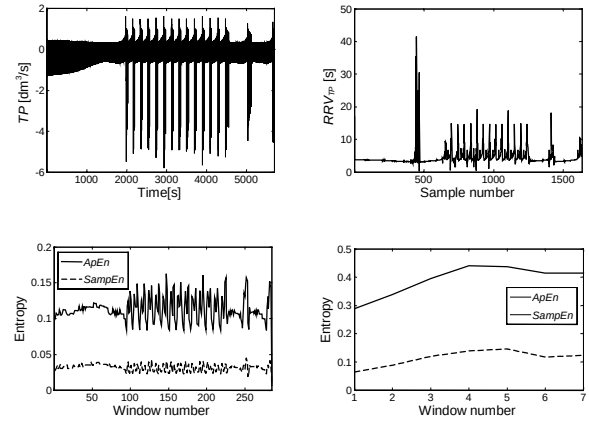


Fig. 6. Respiratory flow *TP*, $RRV_{TP}$ for flow, approximate (*ApEn*) and sample entropy (*SampEn*) during simulations of obstructive sleep apnoea.

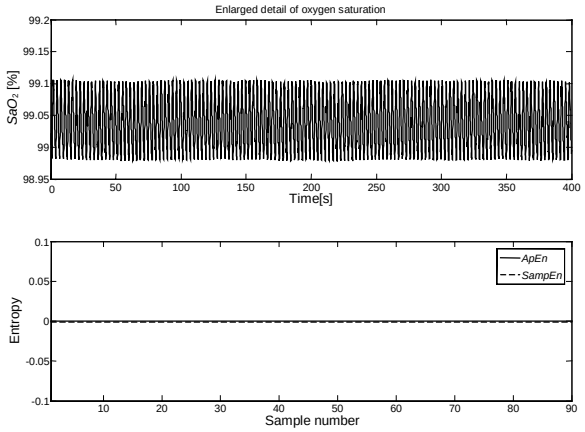


Fig. 7. Oxygen saturation ($SaO_2$) and approximate (*ApEn*) and sample entropy (*SampEn*) calculated during simulations of healthy conditions.

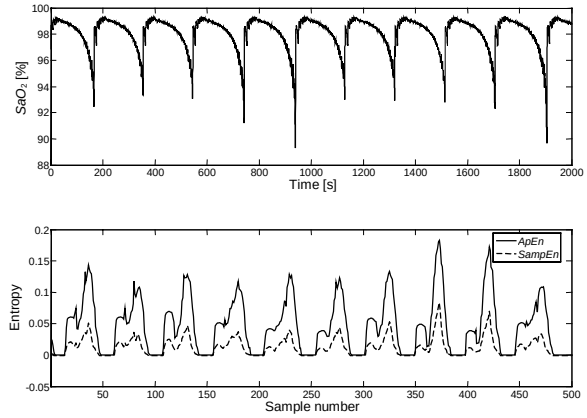


Fig. 8. Oxygen saturation ($SaO_2$) and approximate (*ApEn*) and sample entropy (*SampEn*) calculated during simulations of obstructive sleep apnoea.

There has been proposed the procedure of entropy calculations with the option of moving window. In all cases of analysed signals the input functional parameters for *ApEn*(*m*, *r*, *N*) and *SampEn*(*m*, *r*, *N*) were fixed as: $m = 2$, $r = 0.18 \cdot SD$, $N = 1000$, but there were assumed individual values of window moving steps by *k* samples. Fig. 5 and Fig. 6 depicts the different behaviour of the respiratory system with fluctuation and complexity encoded in simulated signals of the respiratory flow (*TP*). Regularity in amplitude and length of respiration, projected in the time series of raw *TP* data and its transformation $RRV_{TP}$ – characteristic for healthy sleeping subject – was quantified by prepared algorithms for $k$=1000 and $k$ = 100, respectively. The same conditions were applied to the trends (*TP* and $RRV_{TP}$) simulated in PNEUMA for regime of obstructive sleep apnoea syndrome. Both, *ApEn* and *SampEn* were sensitive for variety of data ordering, proving their usefulness for detection and classification of sleep episodes. Regular in amplitude *TP* and almost steady frequency of respiration ($RRV_{TP}$) – when healthy – produces small and almost constant entropy measures, whereas

distinct, artifact-like disturbances in respiration find reflection in similar modulation of the *ApEn* and *SampEn* values (Fig. 6). These observations apply to the trends from Fig. 7 and Fig. 8. In these circumstances arises the question about potential of explored entropy measures to detection of the respiratory temporal disruptions in conditions of mixed composition of time series, i.e. when there are deterministic, periodic, random correlated, random uncorrelated components in data set. It determines the future directions of research in the undertaken domain.

Next, the physiological trends (acquired in 21 subjects: healthy, with the symptoms of central and obstructive apnoea) of respiration were processed for the fixed values of $m$ = 2, $r$ equal to 0.18·*SD* of the signal and $N$ = 1000. Example plots for the chosen, normal subject and the patient with obstructive sleep apnoea were shown in Fig. 9 and Fig. 10, respectively.

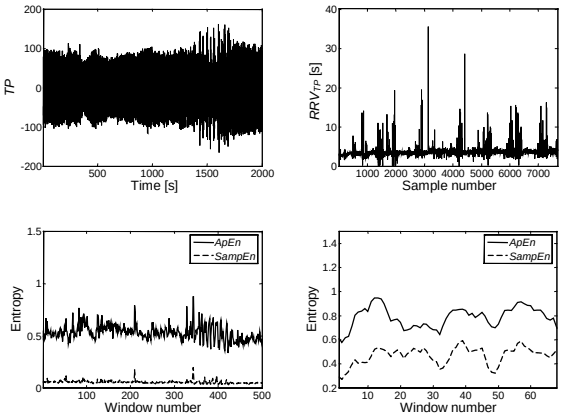


Fig. 9. *ApEn* and *SampEn* for *TP* and $RRV_{TP}$ time series recorded in normal subject.

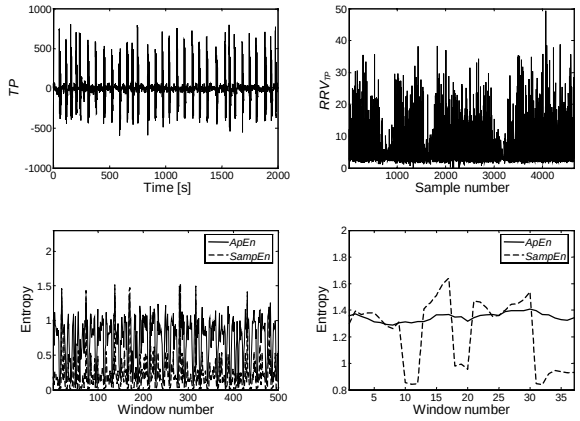


Fig. 10. *ApEn* and *SampEn* for *TP* and $RRV_{TP}$ time series recorded in patient with obstructive sleep apnoea syndromes.

They show general tendencies observed with a model (window coefficient $k$ was set the same as for the synthetic data). It is noticeable rising in entropy measures when the data ordering is disrupted. Interestingly, when a patient showed important pathological symptoms the sensitivity of *SampEn* on detection of respiratory rate changes against *ApEn* was grown (Fig. 10).

Selective studies with the set of accessible data showed also some level of synchronisation between the processes (Fig. 11 – Fig. 12), related in literature as interconnected. In that case, the algorithmic solution with moving window ($k$ = 500) can be direct alternative for entropy measures and long trends with essential local dynamics.

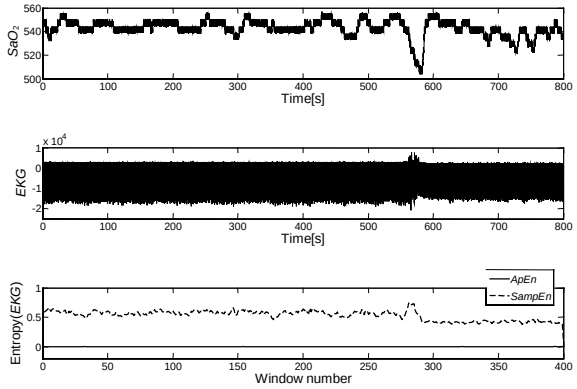


Fig. 11. Synchronisation between $SaO_2$ and *EKG* signal; *ApEn* and *SampEn* calculated for *EKG* time-series.

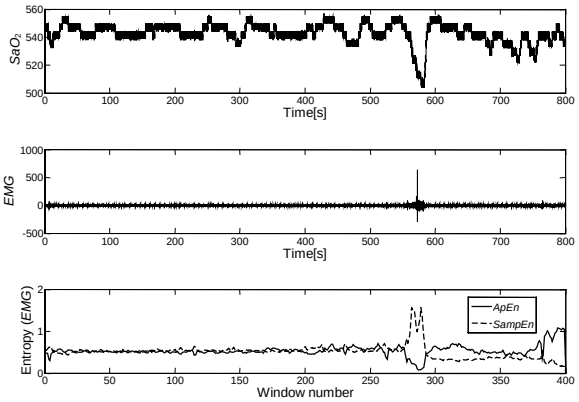


Fig. 12. Synchronisation between $SaO_2$ and *EMG* signal; *ApEn* and *SampEn* calculated for *EMG* time-series.

Awakening in about 580 s was preceded by more disordered work of heart – higher entropy for *EKG* trend, whereas after that point time series became more regular; in this case *SampEn* is again more predictive coefficient than *ApEn*. It should be also highlighted here, that procedures dedicated to qualitative and quantitative description of character and level of such coupling can be important tool in forecasting and interpretation of sleep episodes.

## 4. CONCLUSIONS

Topically, the paper represents the research area connected with description of objects and signals in the systematics of non-linear dynamics. Ambulatory attractive tools of approximate and sample entropy were verified on example of physiological signals which accompany the processes of apnoea during sleep. Tests were preceded by computer analysis of the *ApEn* and *SampEn* properties,

which made it possible to calibrate unambiguously the conditions for the regularity and complexity measurements. It were shown, as a contrast between health subject and patients with SAS, the selective properties of the investigated theoretical tools in quantitative description of the complex processes with different levels of variability.

From the diagnostic strategies points of view (prediction and/or control), it can be valuable to organise broaden studies which could provide fusion of information derived in various techniques. Application of *ApEn* or *SampEn* with moving window of length *N* can bring in valuable information, especially in those sections of the trends where important abnormalities take place, e.g. in the moments of occurrences of Cheyne-Stokes' flow disruptions.

Early stage of investigations, presented by the authors in the paper, will be continued in the direction of mathematical modelling of the complex physiological system. Together with the real experiment, it will enable to test the hypothesis on the object (e.g. on obstructive and central character of SAS), qualitatively and quantitatively measure its properties and depict the processes by the novel techniques of data processing.

From the undertaken object point of view, the issues of time-scaling in properties and behaviour can be an influent components during the future work. The perspective direction can be also description of the cross-correlations between various signals, where approximate entropy and sample entropy seem to be attractive tools, as they offer such variants of analysis – *Cross-ApEn* and *Cross-SampEn* [17].

The main problems and developmental tools for future studies are as follows:

- forecasting, detection and classification (central, obstructive, mixed) of sleep apnoea character,
- advancement of work with the complex model of the system (improvement of description of the respiratory mechanics is planned in the near future),
- inclusion of the other theoretical tools of data analysis (e.g. DFA algorithms, measures typical for description of deterministic chaos – Lyapunov exponent, capacity dimension, correlation dimension, recurrence and cross-recurrence plots, others),
- objectivation of functional input parameters for the used measures of complexity and regularity of data set.

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