Physica A 422 (2015) 143–152

Contents lists available at ScienceDirect

Physica A

journal homepage: www.elsevier.com/locate/physa

Multiscale entropy-based methods for heart rate variability complexity analysis

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HIGHLIGHTS

- New complexity metrics derived from nonadditive entropy are proposed.
- Proposed metrics are more consistent with physiological complexity concept.
- Proposed metrics outperformed classical multiscale entropy.
- Results reinforce the hypothesis that multiscale mechanisms are degraded in AF.
- Results suggest that low scale mechanisms are the most affected in CHF.

ARTICLE INFO

Article history:
Received 13 August 2014
Received in revised form 3 November 2014
Available online 19 December 2014

Keywords:
Nonadditive statistics
Tsallis entropy
Multiscale entropy
Complexity
Heart rate variability

ABSTRACT

Physiologic complexity is an important concept to characterize time series from biological systems, which associated to multiscale analysis can contribute to comprehension of many complex phenomena. Although multiscale entropy has been applied to physiological time series, it measures irregularity as function of scale. In this study we purpose and evaluate a set of three complexity metrics as function of time scales. Complexity metrics are derived from nonadditive entropy supported by generation of surrogate data, i.e. SDiff$_{q_{max}}$, q_{max} and q_{zero}. In order to access accuracy of proposed complexity metrics, receiver operating characteristic (ROC) curves were built and area under the curves was computed for three physiological situations. Heart rate variability (HRV) time series in normal sinus rhythm, atrial fibrillation, and congestive heart failure data set were analyzed. Results show that proposed metric for complexity is accurate and robust when compared to classic entropic irregularity metrics. Furthermore, SDiff$_{q_{max}}$ is the most accurate for lower scales, whereas q_{max} and q_{zero} are the most accurate when higher time scales are considered. Multiscale complexity analysis described here showed potential to assess complex physiological time series and deserves further investigation in wide context.

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1. Introduction

Although complexity in time series is not formally defined, there are some key concepts involved in the mechanisms of complex systems [1]. Complex systems are composed of many interdependent agents, interacting with each other in a

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http://dx.doi.org/10.1016/j.physa.2014.12.011
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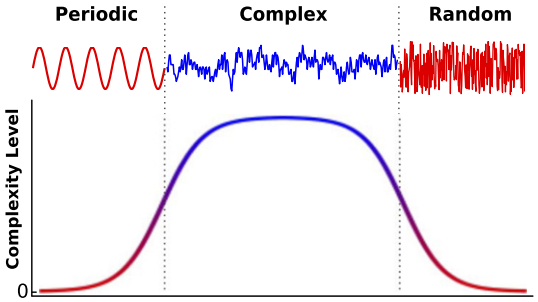

Fig. 1. Illustration for the concept of physiologic complexity measurement. According to the concept, lower values of complexity are associated to periodic and random (red) dynamics and higher values are obtained from self-structured dynamics (blue) occurring between these extreme limits. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

nonlinear fashion. They also present multifractal structures in scales, in time or space. Human body, for example, is composed of several types of tissue, which in turn are composed of cells, and cells are also composed of several other components. Combining components at a given scale results in behavior on scale just above [2].

Physiologic systems are typical examples of complex systems. In physiologic complexity theory [3], healthy systems are assigned as the most complex because of their ability to adapt themselves in response to adverse conditions, exhibiting long-range correlations and complex variability at multiple scales. In contrast, aged and diseased systems present complexity loss, i.e., they lose the capability to adapt to such adverse conditions [3,4].

Some diseases, such as heart failure, tend to show highly periodic heart rate variability (HRV) whereas atrial fibrillation tends to show random variability, with properties similar to white noise [5]. According to this reasoning, a good physiologic complexity measurement is supposed to classify both periodic and random dynamics as low complexity. Consequently, complex physiologic systems are found between these two extremes, as shown in Fig. 1. In addition, such good measurement for complexity must assign higher values to original dynamics than to its shuffled series, where temporal correlations are broken. Therefore, identifying and quantifying complexity in physiological signals becomes a very important and difficult task.

Several efforts have been made to distinguish different physiological conditions through heart rate variability (HRV) analysis [6–11]. Most methods are based on fractal dimensions and entropy measurements [12–14]. Although previous studies are able to distinguish different dynamics and extract important information, no method is able to correctly classify signals according to its physiologic complexity level. The method hereby proposed does not only distinguish different physiological conditions, but also correctly classifies different HRV series according to their physiologic complexity levels.

In a previous study [15] we proposed a generalized form of sample entropy method, namely SampEn_q, based on Tsallis nonadditive statistical mechanics [16]. We also defined SDiff_q, which consists in entropy (SampEn_q) difference between a given time series and its uncorrelated form, the latter represented by surrogate series. Surrogate data was originally proposed to test nonlinearity in time series. One of the simplest null hypotheses considers that the time series can be described by an independent and identically distributed (IID) random variable. Surrogate series, in this case, can be generated by simply shuffling the original time series, resulting in a time series with exactly the same time distribution but broken time correlations [17].

In this study, complexity metrics based on SDiff_q were extended to multiscale domain. We investigated whether physiological complexity is sustained with different time scales, or physiological conditions exist that make complexity changes with time scale. Multiscale q-attributes metrics were compared with classical MSE [18] in order to know whether the multiscale q-attributes are more accurate than traditional MSE and how the accuracy of those measurements behaves with the time scale in discriminating different HRV conditions.

In the next section we discuss detailed features of SDiff_q and q-attributes in physiologic complexity context and also the multiscale analysis for such metrics, searching for complex structures that might be present in HRV time series.

2. SampEn_q and SDiff_q

Sample Entropy (SampEn) is a widely known entropy rate measurement, very useful for short time series analysis [7]. Based on Grassberger and Procaccia's definition [19], SampEn is fundamentally a regularity statistic, an improvement of approximate entropy method, which is known to be biased [20,21]. Therefore, the higher the SampEn value, the more irregular and more unpredictable is the time series.

In previous study [15] we introduced SampEn_q, a generalized form of SampEn based on Tsallis nonadditive statistics [16], and SDiff_q, a measurement which quantifies entropic difference between one signal and its uncorrelated version.

Considering a time series $u(1), u(2), \ldots, u(n)$, let $x_m(i)$ be the set of points u from i to $i+m-1$, i.e., $x_m(i) = [u(i), u(i+1), u(i+2), \ldots, u(i+m-1)]$. SampEn_q is defined by [15]

$$\begin{aligned}\mathrm{SampEn}_q(m, r, N) &= \log_q[U^m(r) \oslash_q U^{m+1}(r)] \\ &= \log_q U^m(r) - \log_q U^{m+1}(r) \end{aligned} \quad (1)$$

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