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Article

Amplitude- and Fluctuation-based Dispersion Entropy

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Abstract: Dispersion entropy (DispEn) is a recently introduced entropy metric to quantify the uncertainty of time series. It is fast and so far, it has demonstrated very good performance in the characterisation of time series. It includes a mapping step but the effect of different mappings has not been studied yet. Here, we investigate the effect of linear and nonlinear mapping approaches in DispEn. We also inspect the sensitivity of different parameters of DispEn to noise. Moreover, we develop fluctuation-based DispEn (FDispEn) as a measure to deal with only the fluctuations of time series. Furthermore, the original and fluctuation-based forbidden dispersion patterns are introduced to discriminate deterministic from stochastic time series. Finally, we compare the performance of DispEn, FDispEn, permutation entropy, sample entropy, and Lempel-Ziv complexity on two physiological datasets. The results show that DispEn is the most consistent technique to distinguish various dynamics of the biomedical signals. Due to their advantages over existing entropy methods, DispEn and FDispEn are expected to be broadly used for the characterization of a wide variety of real-world time series.

Keywords: Nonlinear analysis; permutation entropy; dispersion entropy; fluctuation-based dispersion entropy; forbidden patterns

1. Introduction

Searching for patterns in signals and images is a fundamental problem and has a long history [1]. A pattern denotes an ordered set of numbers, shapes, or other mathematical objects, arranged based on a rule. Elements of a given set are usually arranged by the concepts of permutation and combination [2]. Combination means a way of selecting elements or objects of a given set in which the order of selection does not matter. However, the order of objects is usually a crucial characteristic of a pattern [1,2]. In contrast, the concept of permutation pattern indicates an arrangement of the distinct elements or objects of a given set into some sequences or orders [2–5]. Permutation patterns have been studied occasionally, often implicitly, for over a century, although this area has grown significantly in the last three decades [6].

However, the concept of permutation pattern does not consider repetition. Repetition is an unavoidable phenomenon in digitized signals. Furthermore, permutation considers only the order of amplitude values and so, some information regarding the amplitudes may be ignored [7,8]. To deal with these issues, we have recently introduced dispersion patterns, taking into account repetitions [9].

The probability of occurrence of each potential dispersion or permutation pattern makes a key role to define the entropy of signals [9–11]. Entropy is a powerful measure to quantify the uncertainty of time series [9,11]. Assume we have a probability distribution \mathbf{s} with N potential patterns $\{s_1, s_2, \dots, s_N\}$. Based on the Shannon's definition, the entropy of the distribution \mathbf{s} is $-\sum_{k=1}^N Pr\{s_k\} \log(Pr\{s_k\})$,

34 where $Pr\{s_k\}$ is the probability of occurrence of pattern s_k [11]. When all the probability values are
35 equal, the maximum entropy occurs, while if one probability is certain and the others are impossible,
36 the minimum entropy is achieved [9,11].

37 Over the past three decades, a number of entropy methods have been introduced based on
38 Shannon entropy (ShEn) and conditional entropy (ConEn), respectively denoted the amount of
39 information and the rate of information production [9,12–14]. The widely-used sample entropy
40 (SampEn) [14] is based on ConEn [14], whereas popular permutation entropy (PerEn) and newly
41 developed dispersion entropy (DispEn) [9] are based on ShEn [10] (we compare these methods and
42 also evaluate the relationship between the parameters of DispEn and SampEn in Section 6).

43 SampEn denotes the negative natural logarithm of the conditional probability that two series
44 similar for m sample points remain similar at the next sample, where self-matches are not considered
45 in calculating the probability [14]. For detailed information, please refer to [14]. SampEn leads to
46 undefined or unreliable entropy values for short time series and is not fast enough for long signals
47 [15,16].

48 PerEn, which is based on the permutation patterns or order relations among amplitudes of a
49 time series, is a widely-used entropy method [10]. For detailed information about the algorithm of
50 PerEn please see [10]. PerEn is conceptually simple and computationally quick. Nevertheless, it has
51 three main problems directly derived from the fact that it considers permutation patterns. First, the
52 original PerEn assumes a signal has a continuous distribution, therefore equal values are rare and
53 can be ignored by ranking them based on the order of their emergence. However, while dealing with
54 digitized signals with coarse quantization levels, it may not be appropriate to simply ignore them
55 [17,18]. Second, when a time series is symbolized based on the permutation patterns (Bandt-Pompe
56 procedure), only the order of amplitude values is taken into account and some information with regard
57 to the amplitudes may be ignored [8]. Third, it is sensitive to noise (for further information, please see
58 Section 6).

59 To deal with the aforementioned shortcomings of PerEn and SampEn at the same time, we have
60 very recently developed DispEn based on symbolic dynamics or patterns (here, dispersion patterns)
61 and Shannon entropy to quantify the uncertainty of time series [9]. The concept of symbolic dynamics
62 arises from a coarse-graining of the measurements, that is, the data are transformed into a new signal
63 with only a few different elements. Thus, the study of the dynamics of time series is simplified
64 to a distribution of symbol sequences. Although some of detailed information may be lost, some
65 of the invariant, robust properties of the dynamics may be kept [19–21]. Of note is that since the
66 original DispEn is based on the amplitude-based symbols of signals [9], it might also be referred to as
67 amplitude-based DispEn. Nevertheless, we will only use the term DispEn for conciseness.

68 The results showed that DispEn, unlike PerEn, is sensitive to change in simultaneous frequency
69 and amplitude values and bandwidth of time series and that DispEn outperformed PerEn in terms of
70 discrimination of diverse biomedical and mechanical states [9]. As DispEn needs to neither sort the
71 amplitude values of each embedding vector nor calculate every distance between any two composite
72 delay vectors with embedding dimensions m and $m + 1$, it is fast [9]. The good performance of DispEn
73 to distinguish different dynamics of real time series was also shown in [22–24].

74 In this article, we investigate the effect of different parameters and mapping algorithms on the
75 ability of DispEn to quantify the uncertainty of signals for the first time. Note that these issues were not
76 the scope of our last paper, which developed DispEn [9]. Furthermore, herein, we also develop for the
77 first time fluctuation-based DispEn (FDispEn) taking into account the fluctuations of signals. FDispEn
78 is based on Shannon entropy and the differences between adjacent elements of dispersion patterns,
79 named fluctuation-based dispersion patterns. We also introduce the concepts of forbidden amplitude-
80 and fluctuation-based dispersion patterns and show that they can be used to distinguish deterministic
81 from stochastic time series. Additionally, we compare both DispEn and FDispEn with commonly used
82 metrics (SampEn, PerEn, and Lempel-Ziv complexity) in the analysis of two real-world datasets.

83 2. Methods

84 In this section, we describe DispEn and FDispEn in detail.

85 2.1. Dispersion Entropy (DispEn) with Different Mapping Techniques

86 Given a univariate signal $\mathbf{x} = \{x_1, x_2, \dots, x_N\}$ with length N , the DispEn algorithm is as follows:

87 1) First, $x_j (j = 1, 2, \dots, N)$ are mapped to c classes with integer indices from 1 to c . The classified
88 signal is $u_j (j = 1, 2, \dots, N)$. A number of linear and nonlinear mapping techniques, introduced in
89 Subsection 2.3, can be used in this step.

90 2) Time series $\mathbf{u}_i^{m,c}$ are made with embedding dimension m and time delay d according to $\mathbf{u}_i^{m,c} =$
91 $\{u_i^c, u_{i+d}^c, \dots, u_{i+(m-1)d}^c\}$, $i = 1, 2, \dots, N - (m-1)d$ [9,10]. Each time series $\mathbf{u}_i^{m,c}$ is mapped to a
92 dispersion pattern $\pi_{v_0 v_1 \dots v_{m-1}}$, where $u_i^c = v_0$, $u_{i+d}^c = v_1, \dots, u_{i+(m-1)d}^c = v_{m-1}$. The number of
93 possible dispersion patterns assigned to each vector $\mathbf{u}_i^{m,c}$ is equal to c^m , since the signal $\mathbf{u}_i^{m,c}$ has m
94 elements and each can be one of the integers from 1 to c [9].

3) For each of c^m potential dispersion patterns $\pi_{v_0 \dots v_{m-1}}$, relative frequency is obtained as follows:

$$p(\pi_{v_0 \dots v_{m-1}}) = \frac{\#\{i \mid i \leq N - (m-1)d, \mathbf{u}_i^{m,c} \text{ has type } \pi_{v_0 \dots v_{m-1}}\}}{N - (m-1)d} \quad (1)$$

95 where # means cardinality. In fact, $p(\pi_{v_0 \dots v_{m-1}})$ shows the number of dispersion patterns of $\pi_{v_0 \dots v_{m-1}}$
96 that is assigned to $\mathbf{u}_i^{m,c}$, divided by the total number of embedded signals with embedding dimension
97 m .

4) Finally, based on the Shannon's definition of entropy, the DispEn value is calculated as follows:

$$DispEn(\mathbf{x}, m, c, d) = - \sum_{\pi=1}^{c^m} p(\pi_{v_0 \dots v_{m-1}}) \cdot \ln(p(\pi_{v_0 \dots v_{m-1}})) \quad (2)$$

98 As an example, let's have a series $\mathbf{x} = \{3.6, 4.2, 1.2, 3.1, 4.2, 2.1, 3.3, 4.6, 6.8, 8.4\}$, shown on the top
99 left of Figure 1. We want to calculate the DispEn value of \mathbf{x} . For simplicity, we set $d = 1$, $m = 2$, and
100 $c = 3$. The $3^2 = 9$ potential dispersion patterns are depicted on the right of Figure 1. $x_j (j = 1, 2, \dots, 10)$
101 are linearly mapped into 3 classes with integer indices from 1 to 3, as can be seen in Figure 1. Next,
102 a window with length 2 (embedding dimension) moves along the signal and the number of each of
103 dispersion patterns is counted. The relative frequency is shown on the bottom left of Figure 1. Finally,
104 using Eq. 2, the DispEn value of \mathbf{x} is equal to $-(\frac{2}{9} \ln(\frac{2}{9}) + \frac{2}{9} \ln(\frac{2}{9}) + \frac{2}{9} \ln(\frac{2}{9}) + \frac{1}{9} \ln(\frac{1}{9}) + \frac{1}{9} \ln(\frac{1}{9}) +$
105 $\frac{1}{9} \ln(\frac{1}{9})) = 1.7351$.

106 If all possible dispersion patterns have equal probability value, the DispEn reaches to its highest
107 value, which has a value of $\ln(c^m)$. In contrast, when there is only one $p(\pi_{v_0 \dots v_{m-1}})$ different from zero,
108 which demonstrates a completely certain/regular time series, the smallest value of DispEn is obtained
109 [9]. Note that we use the normalized DispEn as $\frac{DispEn}{\ln(c^m)}$ in this study [9].

110 2.2. Fluctuation-based Dispersion Entropy (FDispEn)

111 In some applications (e.g., in computing the correlation function and in spectral analysis), it is needed
112 to remove the (local or global) trend from the data [25,26]. In this kind of algorithms, after detrending
113 the local or global trends of a signal, the fluctuations are evaluated [25,26]. For example, in the popular
114 detrended fluctuation analysis technique, the local trends of a signal are first removed [27].

115 When only the fluctuations of a signal is relevant or local trends of a time series are irrelevant [25–27],
116 there is no difference between dispersion patterns $\{1, 3, 4\}$ and $\{2, 4, 5\}$ or $\{1, 1, 1\}$ and $\{3, 3, 3\}$. That is,
117 the fluctuations of $\{1, 3, 4\}$ and $\{2, 4, 5\}$ or $\{1, 1, 1\}$ and $\{3, 3, 3\}$ are equal. Accordingly, we introduce
118 FDispEn in this article.

119 In fact, FDispEn considers the differences between adjacent elements of dispersion patterns, termed
120 fluctuation-based dispersion patterns. In this way, we have vectors with length $m - 1$ which each of

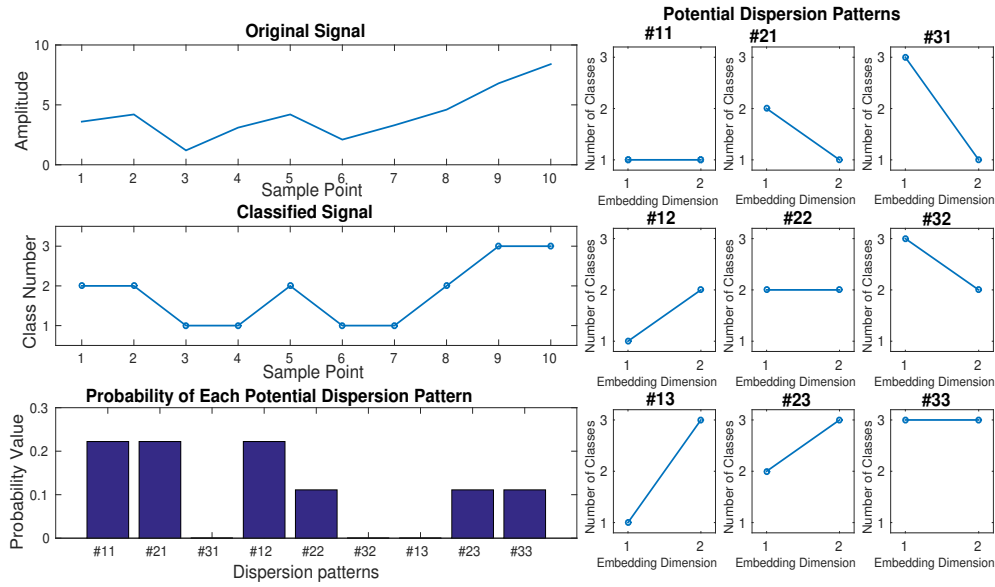


Figure 1. Illustration of the DispEn algorithm using linear mapping of $\mathbf{x} = \{3.6, 4.2, 1.2, 3.1, 4.2, 2.1, 3.3, 4.6, 6.8, 8.4\}$ with the number of classes 3 and embedding dimension 2.

121 their elements changes from $-c + 1$ to $c - 1$. Thus, there are $(2c - 1)^{m-1}$ potential fluctuation-based
 122 dispersion patterns. The only difference between DispEn and FDispEn algorithms is the potential
 123 patterns used in these two approaches. Note that we use the normalized FDispEn as $\frac{FDispEn}{\ln((2c-1)^{m-1})}$
 124 herein.

125 As an example, let's have a signal $\mathbf{x} = \{3, 4.5, 6.2, 5.1, 3.2, 1.2, 3.5, 5.6, 4.9, 8.4\}$. We set $d = 1$,
 126 $m = 3$, and $c = 2$, leading to have $3^2 = 9$ potential fluctuation-based dispersion patterns
 127 ($\{(-1, -1), (-1, 0), (-1, 1), (0, -1), (0, 0), (0, 1), (1, -1), (1, 0), (1, 1)\}$). Then, x_j ($j = 1, 2, \dots, 10$) are
 128 linearly mapped into 2 classes with integer indices from 1 to 2 ($\{1, 1, 2, 2, 1, 1, 1, 2, 2, 2\}$). Afterwards, a
 129 window with length 3 moves along the time series and the differences between adjacent elements are
 130 calculated ($\{(0, 1), (1, 0), (0, -1), (-1, 0), (0, 0), (0, 1), (1, 0), (0, 0)\}$). Afterwards, the number of each
 131 fluctuation-based dispersion pattern is counted. Finally, using Eq. 2, the DispEn value of \mathbf{x} is equal to
 132 $-\left(\frac{1}{8} \ln\left(\frac{1}{8}\right) + \frac{1}{8} \ln\left(\frac{1}{8}\right) + \frac{2}{8} \ln\left(\frac{2}{8}\right) + \frac{2}{8} \ln\left(\frac{2}{8}\right) + \frac{2}{8} \ln\left(\frac{2}{8}\right)\right) = 1.5596$.

133 2.3. Mapping Approaches used in DispEn and FDispEn

134 A number of linear and nonlinear methods can be used to map the original signal x_j ($j = 1, 2, \dots, N$)
 135 to the classified signal u_j ($j = 1, 2, \dots, N$). The simplest and fastest algorithm is the linear mapping.
 136 However, when maximum or minimum values are noticeably larger or smaller than the mean/median
 137 value of the signal, the majority of x_j are mapped to only few classes. To alleviate the problem, we
 138 can sort x_j ($j = 1, 2, \dots, N$) and then divide them into c classes in which each of them includes equal
 139 number of x_j (DispEn or FDispEn with sorting method).

140 We also use several nonlinear mapping techniques. Many natural processes show a progression from
 141 small beginnings that accelerates and approaches a climax over time (e.g., a sigmoid function) [28,29].
 142 When there is not a detailed description, a sigmoid function is frequently used [29–31]. Well-known
 143 log-sigmoid (logsig) and tan-sigmoid (tansig) transfer functions are respectively defined as:

$$y_j = \frac{1}{e^{-\frac{x_j - \mu}{\sigma}} + 1} \quad (3)$$

$$y_j = \frac{2}{1 + e^{-2\frac{x_j - \mu}{\sigma}}} - 1 \quad (4)$$

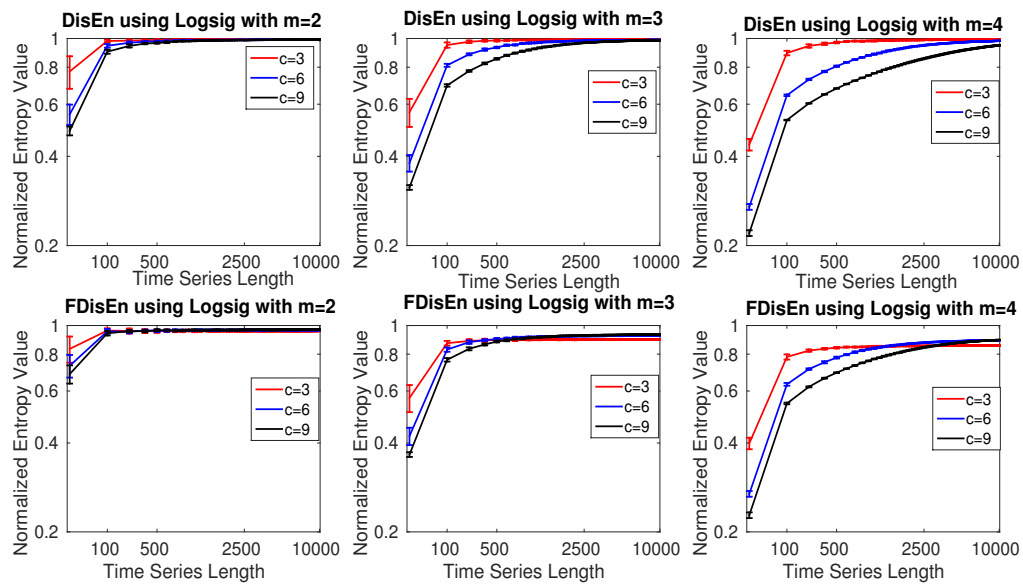


Figure 2. Mean and SD of results obtained by the DispEn and FDispEn with logsig and different values of embedding dimension and number of classes for 40 realizations of univariate white noise. Logarithm scale for both the axis is used.

144 where σ and μ are the standard deviation (SD) and mean of time series \mathbf{x} , respectively.

145 The cumulative distribution functions (CDFs) for many common probability distributions are
 146 sigmoidal. The most well-known such example is the error function, which is related to the CDF of a
 147 normal distribution, termed normal CDF (NCDF). NCDF of \mathbf{x} is calculated as follows:

$$y_j = \frac{1}{\sigma\sqrt{2\pi}} \int_{-\infty}^{x_j} e^{-\frac{(t-\mu)^2}{2\sigma^2}} dt \quad (5)$$

148 Each of the aforementioned techniques maps \mathbf{x} into $\mathbf{y} = \{y_1, y_2, \dots, y_N\}$, ranged from α to β . Then,
 149 we use a linear algorithm to assign each y_j to a real number z_j from 0.5 to $c + 0.5$. Next, for each
 150 element of the mapped signal, we use $u_j^c = \text{round}(z_j)$, where u_j^c denotes the j^{th} element of the classified
 151 signal and rounding involves either increasing or decreasing a number to the next digit [9]. It is worth
 152 noting that DispEn with NCDF and DispEn with linear mapping were compared by the use of several
 153 synthetic time series and four biomedical and mechanical datasets [9]. The results illustrated the
 154 superiority of DispEn with NCDF over DispEn with linear mapping.

155 3. Parameters of DispEn and FDispEn

156 3.1. Effect of Number of Classes, Embedding Dimension, and Signal Length on DispEn and FDispEn

157 To assess the sensitivity of DispEn and FDispEn with logsig, and PerEn to the signal length,
 158 embedding dimension m , and number of classes c , we use 40 realizations of univariate white noise.
 159 Note that we will show why logsig is an appropriate mapping technique for DispEn and FDispEn
 160 to characterize signals. The mean and SD of results, depicted in Figure 2, show that DispEn and
 161 FDispEn need a smaller number of sample points to reach their maximum values for a smaller number
 162 of classes or smaller embedding dimension. This is in agreement with the fact that we need at least
 163 $\ln(c^m)$ [9] and $\ln((2c - 1)^{m-1})$ sample points to reach the maximum value of DispEn and FDispEn,
 164 respectively. The profiles also suggest that the greater the number of sample points, the more robust
 165 DispEn estimates, as seen from the errorbars.

166 3.2. Effect of Number of Classes and Noise Power on DispEn and FDispEn

167 We also inspect the relationship between noise power levels and DispEn with different number
 168 of classes. To this end, we use a logistic map added with different levels of noise power. Signals
 169 created by biological systems are usually nonlinear and most likely include deterministic and stochastic
 170 components [13,32–34]. The reason why the logistic map is very popular in this field (e.g., [10,14,35,36])
 171 is that its behavior changes from periodicity to non-periodic nonlinearity when α changes from 3.5
 172 to 4 [37–39]. We then added white Gaussian noise (WGN) to the signal since real signals, especially
 173 physiological recordings, are frequently corrupted by different kinds of noise [40]. Additive WGN is
 174 also considered as a basic statistical model used in information theory to mimic the effect of random
 175 processes that occur in nature [41].

176 This analysis is dependent on the model parameter α as: $x_j = \alpha x_{j-1}(1 - x_{j-1})$, where the signal x
 177 was generated with the different values α (e.g., 3.5, 3.6, 3.7, 3.8, 3.9, and 4). The length and sampling
 178 frequency of the signal are respectively 500 sample points and 150 Hz. In case α equals to 3.5, the
 179 time series oscillates among four values. For $3.57 \leq \alpha \leq 4$, the series is chaotic, albeit it has segments
 180 with periodic behaviour (e.g., $\alpha \approx 3.8$) [39,42,43]. We added 40 independent realizations of WGN with
 181 different signal-to-noise-ratios (SNRs) per sample, ranging from 0 to 30 dB, to the logistic map.

182 To compare the sensitivity of each method to WGN, we calculate $NrmEntN$ as the entropy value of
 183 each signal with noise over the entropy value of its corresponding signal without noise ($NrmEntN =$
 184 $\frac{\text{entropy of a series with noise}}{\text{entropy of a series without noise}}$).

185 The average and SD values of results obtained by the DispEn using logsig with different number of
 186 classes computed from the logistic map whose parameter (α) is equal to 3.5, 3.6, 3.7, 3.8, 3.9, or 4 with
 187 additive 40 independent realizations of WGN with SNR 0, 10, 20, 30 dB are shown in Figure 3(a), (b),
 188 (c), and (d), respectively. We set $m = 2$ for DispEn [9]. Figure 3 suggests that the SD values for $c = 6$
 189 are considerably smaller than those for $c = 5, 4$, and 3. Moreover, the average of $NrmEntN$ values for
 190 $c = 6$ is smaller than those for $c = 7$, and 8, showing less sensitivity to noise for $c = 6$. Thus, we set
 191 $c = 6$ for all the simulations below.

192 Compared with DispEn, in the FDispEn algorithm, we have vectors with length $m - 1$ where each of
 193 their elements changes from $-c + 1$ to $c - 1$. Thus, we set $m = 3$ here. Like what we did for DispEn,
 194 we changed c from 4 to 9 for FDispEn. We found that $c = 5$ leads to stable results when dealing with
 195 noise (results are not shown herein). Thus, we set $c = 5$ for all simulations using FDispEn, although
 196 the range $3 < c < 9$ results in similar profiles.

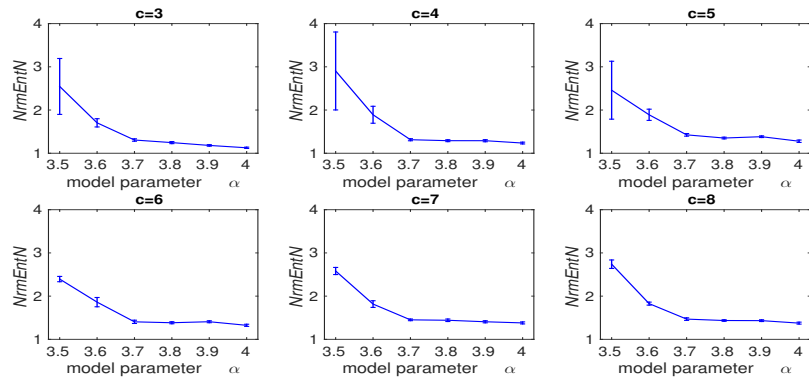
197 Overall, the parameter c is chosen to balance the quantity of entropy estimates with the loss of signal
 198 information. To avoid the impact of noise on signals, a small c is recommended. In contrast, for a small
 199 c , too much detailed data information is lost, leading to poor probability estimates. Thus, a trade-off
 200 between large and small c values is needed.

201 4. Evaluation of Mapping Approaches for DispEn and FDispEn

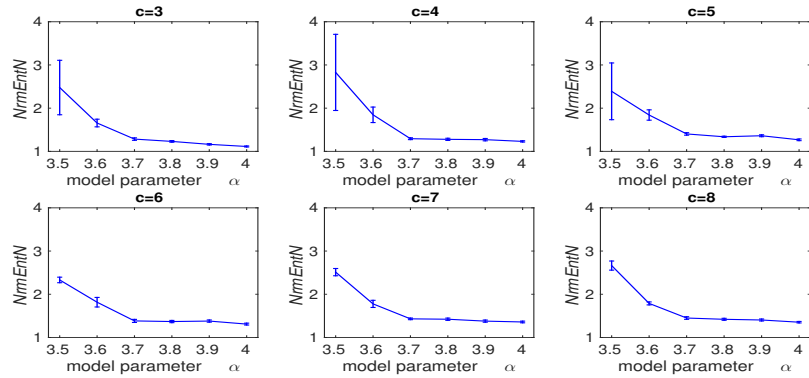
202 To evaluate the ability of DispEn and FDispEn with different mapping techniques to distinguish
 203 changes from periodicity to non-periodic nonlinearity with different levels of noise, the described
 204 logistic map with additive noise is used. The average and SD of results obtained by the DispEn and
 205 FDispEn with different mapping techniques, and PerEn are depicted in Figure 4. The entropy values
 206 of the logistic map generally increase along the signal, except for the segments of periodic behavior
 207 (e.g., for $\alpha = 3.8$), in agreement with Figure 4.10 (page 87 in [39]) and previous studies [43,44]. We set
 208 $m = 2$ and $m = 3$ for DispEn and FDispEn, respectively.

209 As noise affects more on periodic oscillations, $NrmEntN$ is larger for a small α . The range of mean
 210 values show that DispEn and FDispEn with different mapping algorithms, and PerEn are similar,
 211 while dealing with the different levels of noise power. The SD values suggest that when all signals
 212 have equal SNR values, the DispEn and PerEn values are stable for all the methods.

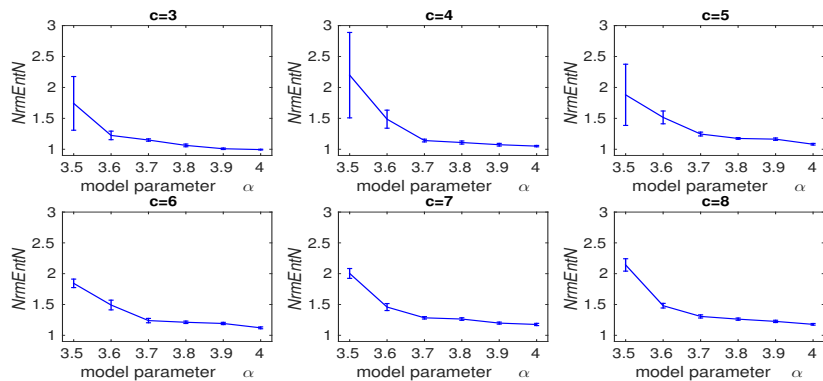
213 The ranges of mean values show that DispEn with sorting method and linear mapping lead to the
 214 most stable results. Although DispEn with sorting method, unlike PerEn, takes into account repetitions,



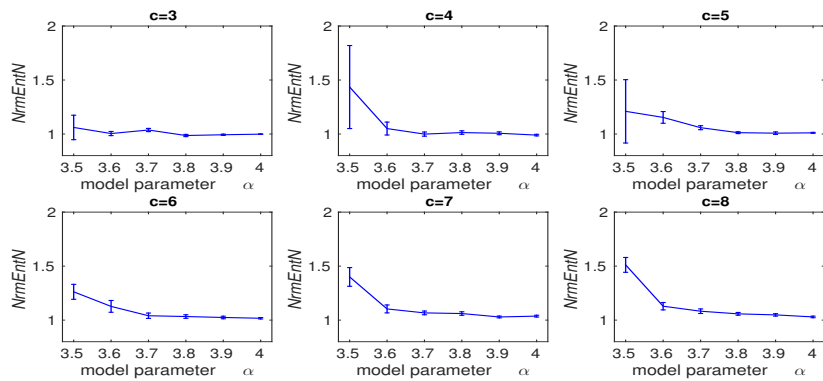
(a) SNR=0 dB



(b) SNR=10 dB



(c) SNR=20 dB



(d) SNR=30 dB

Figure 3. Average and SD of $NrmEntN = \frac{\text{entropy of a series with noise}}{\text{entropy of a series without noise}}$ values obtained by the DispEn using logsig with different number of classes computed from the logistic map with additive 40 independent realizations of WGN with different noise power. $NrmEntN$ compares the sensitivity of DispEn to WGN with different SNRs.

215 it considers only the order of amplitude values and thus, some information regarding the amplitudes
 216 may be discarded. For instance, DispEn with sorting method cannot detect the outliers or spikes which
 217 is noticeably larger or smaller than their adjacent values. For DispEn with linear mapping, when
 218 maximum or minimum values are noticeably larger or smaller than the mean/median value of the
 219 signal, the majority of x_j are mapped to only few classes [9]. Thus, for simplicity, we use DispEn and
 220 FDispEn with logsig for all the simulations below.

221 Noise is frequently considered as an unwanted component or disturbance to a system or data,
 222 whereas recent studies have shown that noise can play a beneficial role in systems [45,46]. In any case,
 223 it has been evidenced that noise is an essential ingredient in the systems and has a noticeable effect on
 224 many aspects of science and technology, such as engineering, medicine, and biology [45,46]. White,
 225 pink, and brown noise are three well-known kinds of noise signals in the real world. White noise is a
 226 random signal having equal energy across all frequencies. The power spectral density of white noise is
 227 as $S(f) = C_w$, where C_w is a constant [46]. Pink and brown noise are random processes suitable for
 228 modelling evolutionary or developmental systems [47]. The power spectral density $S(f)$ of pink and
 229 brown noise are as $\frac{C_p}{f}$ and $\frac{C_b}{f^2}$, respectively, where C_p and C_b are constants [46,47].

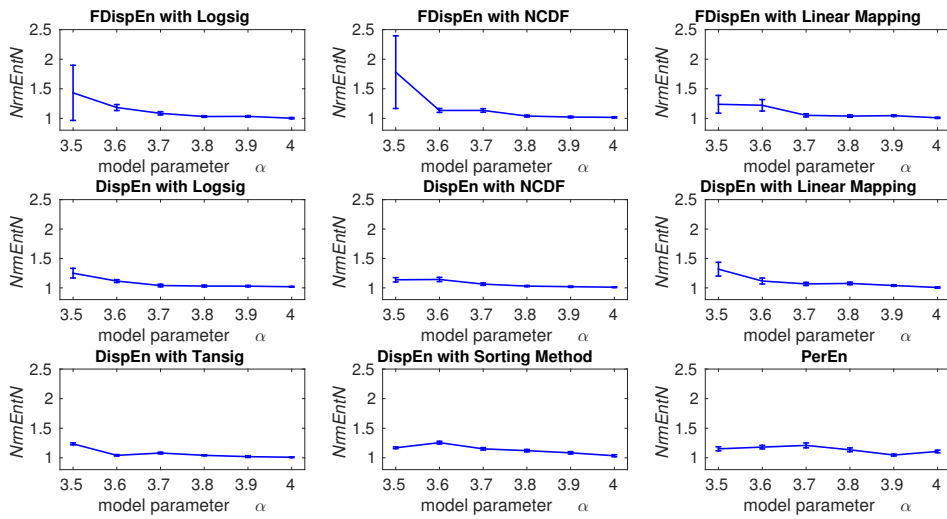
230 To evaluate the ability of DispEn and FDispEn methods with different mapping algorithms, and
 231 PerEn to distinguish the dynamics of different noise signals, we created 40 realizations of white, brown,
 232 and pink noise signals with different lengths changing from 10 to 1000 sample points. Note that, as the
 233 maximum value of PerEn is $\ln(m!)$ [48], we use normalized PerEn as $\frac{PerEn}{\ln(m!)}$ in this study. We set $m = 4$
 234 for PerEn [49], $m = 2$ and $c = 6$ for DispEn [9], and $m = 3$ and $c = 5$ for FDispEn as recommended
 235 before.

236 Figure 5 shows that DispEn and FDispEn with different mapping approaches distinguish brown,
 237 pink, and white noise series with different lengths. Their results are in agreement with the fact that
 238 white noise is the most irregular signal, followed by pink and brown noise, in that order, based
 239 on the power spectral density of white, pink, and brown noise [45,46]. However, there are some
 240 overlaps between the DispEn with tansig, and PerEn values for short pink and white noise time series,
 241 suggesting a superiority of DispEn and FDispEn with different mapping approaches, except tansig,
 242 over PerEn.

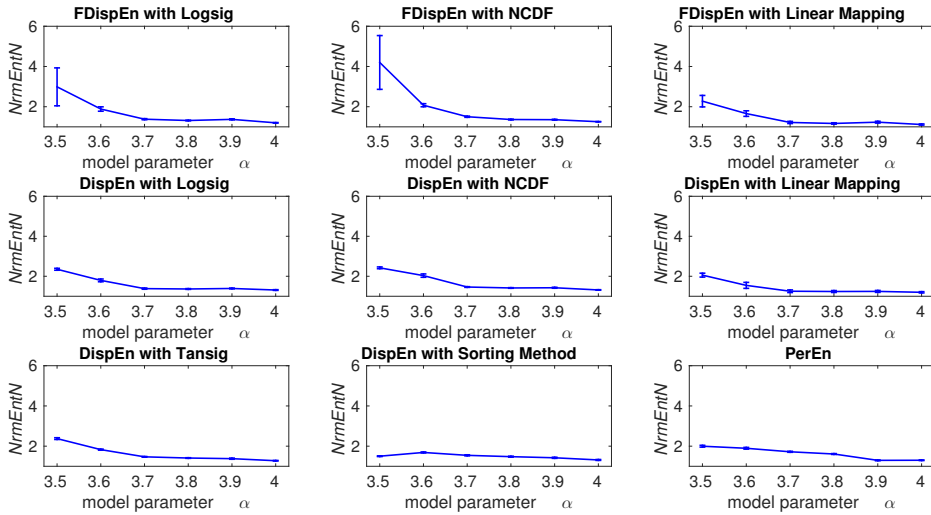
243 5. Univariate Entropy Methods vs. Changes from Periodicity to Non-periodic Nonlinearity

244 Studies on physiological time series frequently involve relatively short epochs of signals containing
 245 informative periodic or quasi-periodic components [13,50,51]. Moreover, empirical evidence identifies
 246 nonlinear, in addition to linear, behavior in some biomedical signals [32,52,53]. Therefore, to find
 247 the dependence of univariate entropy approaches with changes from periodicity to non-periodic
 248 nonlinearity, a logistic map is used herein. This analysis is relevant to the model parameter α :
 249 $x_j = \alpha x_{j-1}(1 - x_{j-1})$, where the signal $\mathbf{x} = x_j$ ($j = 1, \dots, N$) was generated varying the parameter α
 250 from 3.5 to 3.99. We employed a sliding window of 60 sample points with 80% overlap moves along
 251 the signal with a sampling frequency of 150 Hz and a length of 100 s (15,000 sample points). The signal
 252 is depicted in Figure 6. We set $m = 2$ for SampEn, DispEn, and FDispEn, and $m = 3$ for PerEn, as
 253 advised before.

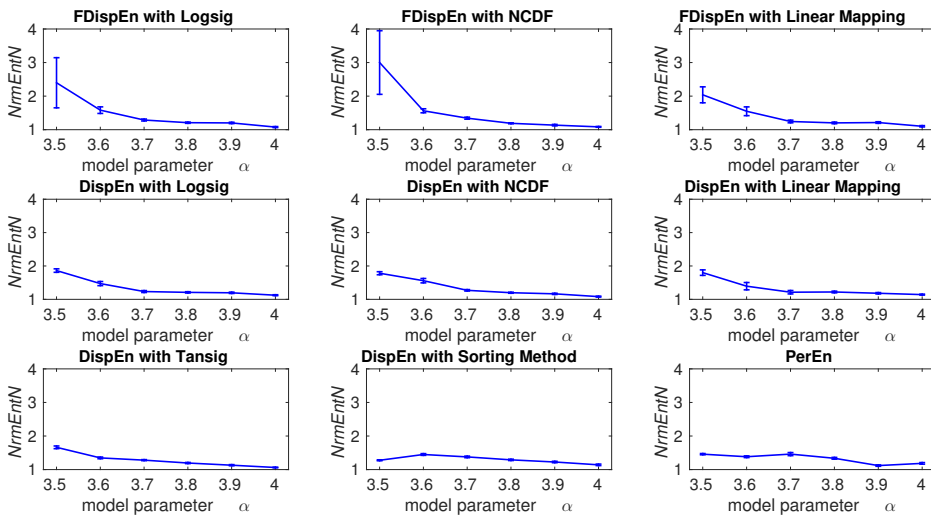
254 The results obtained by FDispEn, DispEn, PerEn, and SampEn for the logistic map are shown in
 255 Figure 6. For each of the methods, when $3.5 < \alpha < 3.57$ (periodic series), the entropy values are
 256 smaller than those for $3.57 < \alpha < 3.99$ (chaotic series), except those epochs that include periodic
 257 components (e.g., $\alpha \approx 3.8$) [39,42,43]. As expected, the entropy values, obtained by the entropy
 258 techniques generally increase along the signal, except for the downward spikes in the windows of
 259 periodic behavior ($\alpha \approx 3.8$). This fact is in agreement with Figure 4.10 (page 87 in [39]) and the other
 260 previous studies [10,16].



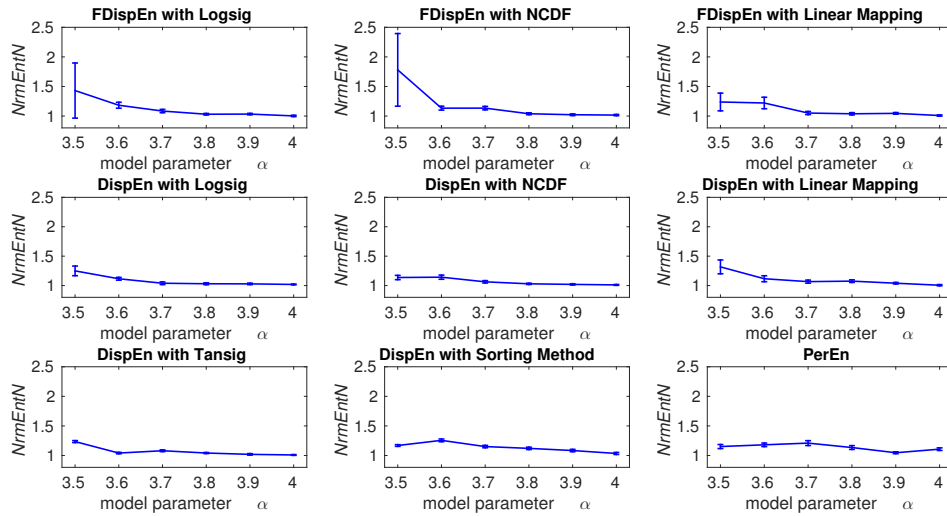
(a) SNR=0 dB



(b) SNR=10 dB



(c) SNR=20 dB



(d) SNR=30 dB

Figure 4. Average and SD of $NrmEntN = \frac{\text{entropy of a series with noise}}{\text{entropy of a series without noise}}$ values obtained by the PerEn, and DispEn and FDispEn with different mapping techniques computed from the logistic map with additive 40 independent realizations of WGN with different noise power. $NrmEntN$ compares the sensitivity of each method to WGN with different SNRs.

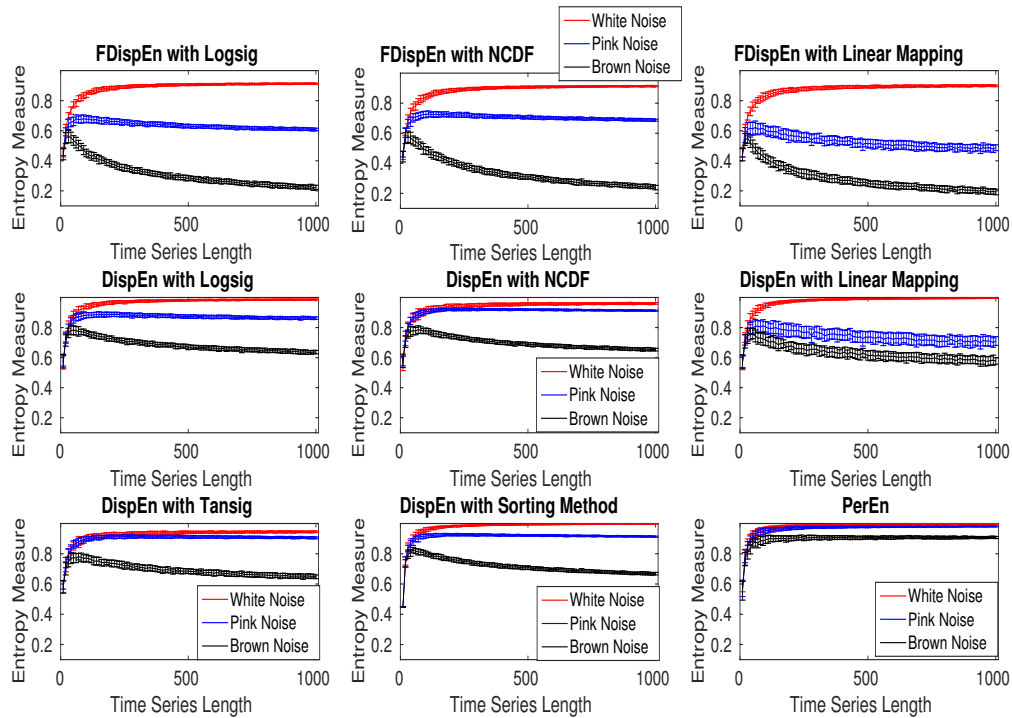


Figure 5. Mean and SD of entropy values obtained by DispEn and FDispEn with different mapping techniques and PerEn, computed from 40 different white, brown, and pink noise signals.

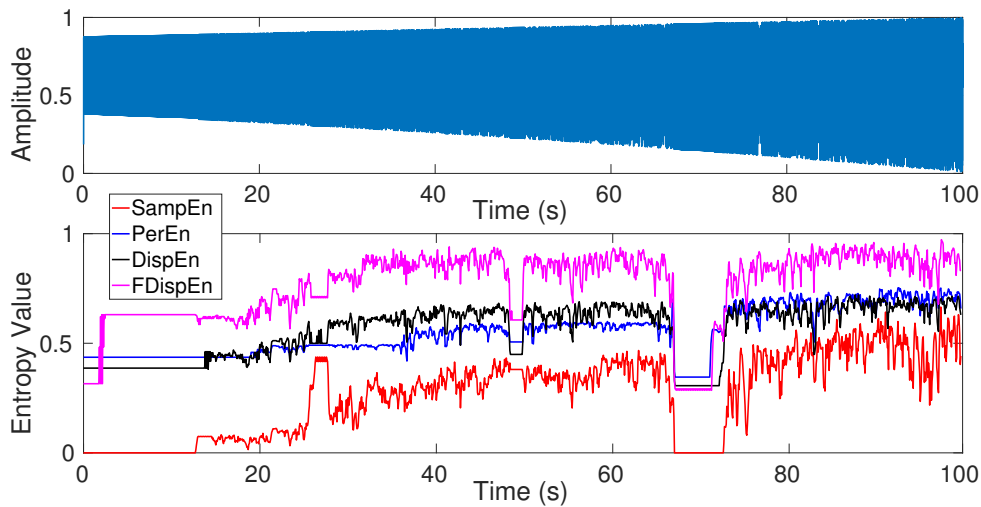


Figure 6. (a) Logistic map with parameter α changing from 3.5 to 3.99 and (b) entropy values of the logistic map to understand better SampEn, PerEn, DispEn, and FDispEn.

261 6. Comparison Between SampEn, PerEn and its Improvements, and Newly Developed DispEn 262 and FDispEn

263 In this Section, we compare the DispEn and FDispEn algorithms with the SampEn and PerEn-based
264 methods.

265 6.1. SampEn vs. DispEn and FDispEn

266 In addition, DispEn, FDispEn, and SampEn have similar behavior when dealing with noise. In
267 SampEn, only the number of matches whose differences are smaller than a defined threshold is counted.
268 Accordingly, a small change in the signal amplitude due to noise is unlike to modify the SampEn value.
269 Similarly, in DispEn and FDispEn, a small change will probably not alter the index of class and so, the
270 entropy value will not change. Therefore, SampEn, DispEn, and FDispEn are relatively robust to noise
271 (especially for signals with high SNR).

The relationship between the number of classes c (DispEn and FDispEn) and threshold r (SampEn) is inspected by the use of a MIX process evolving from randomness to periodic oscillations as follows [35,43]:

$$MIX_k = (1 - z_k)x_k + z_k y_k \quad (6)$$

272 where $\mathbf{z} = \{z_1, z_2, \dots, z_N\}$ is a random variable which equals to 1 with probability p and equals
273 to 0 with probability $1 - p$, $\mathbf{x} = \{x_1, x_2, \dots, x_N\}$ denotes a periodic synthetic time series created by
274 $x_k = \sqrt{2} \sin(\frac{2\pi k}{12})$, and $\mathbf{y} = \{y_1, y_2, \dots, y_N\}$ is a uniformly distributed variable on $[-\sqrt{3}, \sqrt{3}]$ [35,43].
275 The time series was based on a MIX process whose parameter linearly varied between 0.99 and 0.01.
276 Therefore, this series evolved from randomness to orderliness. The signal has a sampling frequency of
277 150 Hz and a length of 100 s (15000 samples). The techniques are applied to 20 realizations of the MIX
278 process using a moving window of 1500 samples (10 s) with 50% overlap. We used different threshold
279 values $r = 0.1, 0.2, 0.3, 0.4$, and 0.5 of SD of the signal [14] for SampEn, and $c = 2, 4, 6, 8$ and 10 for
280 DispEn and FDispEn.

281 The results, depicted in Figure 7, show that the mean entropy values are the lowest in higher
282 temporal windows, in agreement with the previous studies [35,43]. The results also show that the
283 number of classes (c) in DispEn and FDispEn is inversely related to the threshold value r used in the
284 SampEn algorithm. It is worth noting that SampEn, unlike DispEn and FDispEn, is not consistent as

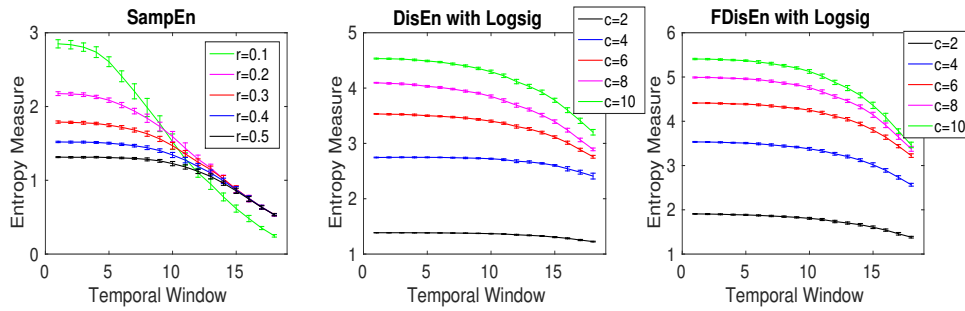


Figure 7. (a) Average and SD of entropy values obtained by the DispEn, FDispEn, and SampEn with different number of classes (for DispEn and FDispEn) and different threshold values (SampEn) using a MIX process evolving from randomness to periodic oscillations. We used a window with length 1500 samples moving along the MIX process (temporal window).

Table 1. CVs of DispEn and FDispEn with logsig, and SampEn values for the MIX process with $p = 0.5$ and length 1000 samples.

| Method | $c = 2$ | $c = 4$ | $c = 6$ | $c = 8$ | $c = 10$ |
|---------|----------------------------|----------------------------|----------------------------|----------------------------|----------------------------|
| DispEn | 0.0021 | 0.0034 | 0.0045 | 0.0041 | 0.0048 |
| FDispEn | 0.0078 | 0.0064 | 0.0040 | 0.0043 | 0.0049 |
| SampEn | $r = 0.1 \times \text{SD}$ | $r = 0.2 \times \text{SD}$ | $r = 0.3 \times \text{SD}$ | $r = 0.4 \times \text{SD}$ | $r = 0.5 \times \text{SD}$ |
| | 0.0604 | 0.0342 | 0.0224 | 0.0174 | 0.0150 |

285 $r = 0.1$ crosses the lines for other values of r . We set $m = 2, 2$, and 3 , for respectively SampEn, DispEn,
 286 and FDispEn, as recommended before.

287 To compare the results obtained by the entropy algorithms, we used the coefficient of variation (CV)
 288 defined as the SD divided by the mean. We use such a metric as the SDs of signals may increase or
 289 decrease proportionally to the mean. We inspect the MIX process with length 1500 samples and $p = 0.5$
 290 as a trade-off between random ($p = 1$) and periodic oscillations ($p = 0$). The CV values, depicted in
 291 Table 1, show that DispEn- and FDispEn results for different number of classes are noticeably smaller
 292 than those for SampEn with different threshold values, showing another advantage of DispEn and
 293 FDispEn over SampEn.

294 In spite of its power to detect dynamics of signals, SampEn has two key deficiencies. They are
 295 discussed as follows:

- 296 1. SampEn values for short signals are either undefined or unreliable, as in its algorithm, the
 297 number of matches whose differences are smaller than a defined threshold is counted. When
 298 the time series length is too small, this number may be 0, leading to undefined values [16,54].
 299 However, the results obtained by DispEn, FDispEn, and PerEn are always defined. To illustrate
 300 this issue, we created 40 realizations of white noise with length 50 sample points. The mean
 301 and median of DispEn, FDispEn, PerEn, and SampEn values for the 40 realizations are shown in
 302 Figure 8. The results show that SampEn, unlike DispEn, FDispEn, and PerEn, yield undefined
 303 values. Note that we set $m = 2$ for SampEn, DispEn, and FDispEn, and $m = 3$ for PerEn, as
 304 advised before.
- 305 2. SampEn is not fast enough for real time applications and has a computation cost of $O(N^2)$ [55].
 306 In contrast, the computation cost of PerEn, DispEn, and FDispEn is $O(N)$ [9,56].

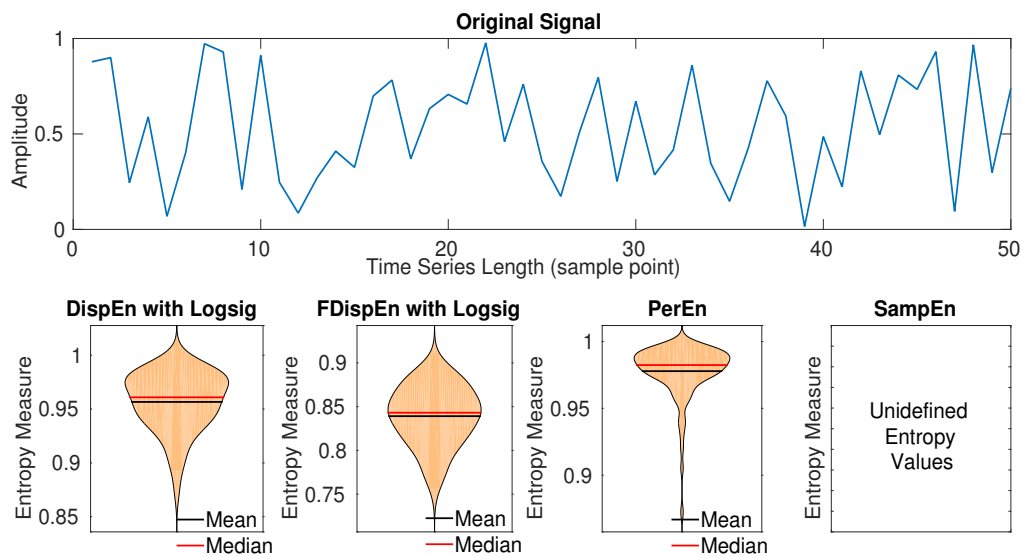


Figure 8. Mean and median of results obtained by PerEn, SampEn, and DispEn and FDispEn with logsig for 40 realization of white noise.

307 6.2. PerEn and its Improvements vs. DispEn and FDispEn

308 PerEn, DispEn, and FDispEn are based on the Shannon's definition of entropy, reflecting the average
 309 uncertainty of a random variable [11,12]. Nevertheless, these techniques have the following main
 310 differences:

- 311 1. PerEn considers only the order of amplitude values, and thus, some information regarding the
 312 amplitude values themselves may be ignored [18]. For example, the embedded vectors $\{1, 10, 2\}$
 313 and $\{1, 3, 2\}$ have similar permutations, leading to the same motif $(0,2,1)$ ($m = 3$) because the
 314 extent of the differences between sequential samples is not considered in the original definition
 315 of PerEn. To alleviate this deficiency, modified PerEn (MPerEn) based on mapping equal values
 316 into the same symbol was developed [17]. However, the second and third shortcomings were not
 317 addressed by MPerEn. Amplitude-aware PerEn (AAPerEn) deals with the problem with adding
 318 a variable contribution, depending on amplitude, instead of a constant number to each level in
 319 the histogram representing the probability of each motif [7]. It was also addressed by the use of
 320 modified ordinal patterns [57]. Mapping data to a number of classes based on their amplitude
 321 values makes DispEn and FDispEn deal with this issue as well.
- 322 2. When there are equal values in the embedded vector, Bandt and Pompe [10] proposed ranking the
 323 possible equalities based on their order of emergence or solving this condition by adding noise.
 324 Considering the first alternative, for instance, the permutation pattern for both the embedded
 325 vectors $\{1, 2, 4\}$ and $\{1, 4, 4\}$ are $(0,1,2)$ ($m = 3$). As another example, assume $\mathbf{z1} = \{1, 2, 2, 2\}$
 326 and $\mathbf{z2} = \{1, 2, 3, 4\}$. The PerEn with $m = 3$ of $\mathbf{z1}$ is exactly the same as $\mathbf{z2}$, both equalling 0
 327 although, unlike $\mathbf{z1}$, $\mathbf{z2}$ is strictly ascending. Adding noise may not lead to a precise answer
 328 because, for example, the embedded vector $\{1, 5, 5\}$ has two possible permutation patterns as
 329 $(0,1,2)$ and $(0,2,1)$ and there are not any differences between them. It should be noted that this
 330 issue is particularly relevant for digitized signals with large quantization steps. Fadlallah *et*
 331 *al.*, have recently proposed weighted PerEn (WPerEn) to weight the motif counts by statistics
 332 derived from the time series patterns [8]. However, WPerEn does not take into account the
 333 first and third alleviations of PerEn. It was addressed in AAPerEn [7] as well. Assigning close
 334 amplitude values to an equal class, FDispEn and DispEn deal with this deficiency.

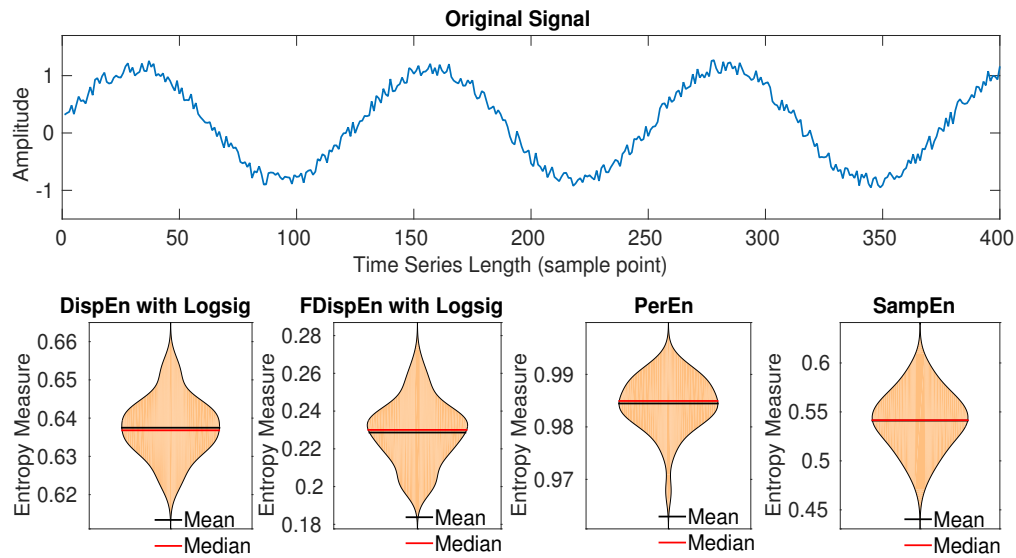


Figure 9. Mean and median of results obtained by PerEn, SampEn, and DispEn and FDispEn with logsig for 20 realization of $x_i = \sin(i/20) + 0.3\eta$.

Table 2. Comparison between DispEn and FDispEn and SampEn, PerEn, and AAPerEn in terms of ability to characterize short signals, sensitivity to noise, type of entropy, and computational cost.

| Characteristics | DispEn | FDispEn | AAPerEn | PerEn | SampEn |
|----------------------|----------|----------|----------|----------|-----------|
| Short signals | reliable | reliable | reliable | reliable | undefined |
| Sensitivity to noise | no | no | yes | yes | no |
| Type of entropy | ShEn | ShEn | ShEn | ShEn | ConEn |
| Computational cost | $O(N)$ | $O(N)$ | $O(N)$ | $O(N)$ | $O(N^2)$ |

335 3. PerEn is sensitive to noise (even when the SNR of a signal is high), since a small change in
 336 amplitude value may vary the order relations among amplitudes. For instance, noise on $\mathbf{z3} =$
 337 $\{1, 2, 2.01\}$ may alter the motif from (0,1,2) to (0,2,1). This problem is present for WPerEn,
 338 MPerEn, AAPerEn, and the approach developed in [57]. However, DispEn and FDispEn address
 339 the problem with mapping data into a few classes and thus, a small change in amplitude will
 340 probably not alter the (index of) class.

341 To demonstrate this issue, let's have twenty realizations of the signal $x_i = \sin(i/20) + 0.3\eta$ with
 342 length 400 sample points, where η denotes a uniform random variable between 0 to 1. The
 343 original signal, and the mean and median of DispEn, FDispEn, PerEn, and SampEn values for
 344 the twenty time series are depicted in Figure 9. The results show that the mean PerEn of these
 345 realizations is close to the PerEn of a random signal (i.e. both are close to 1). In contrast, for the
 346 other entropy methods, there is a considerable difference between the entropy values and their
 347 corresponding maximum entropy. Of note is that we set $m = 3$ for DispEn and FDispEn, $m = 2$
 348 for SampEn, and $m = 4$ for PerEn.

349 To summarize, the characteristics and limitations of DispEn [9], FDispEn, SampEn [14], AAPerEn
 350 [7], and PerEn [10] are illustrated in Table 2.

Table 3. Computational time of DispEn and FDispEn with logsig, SampEn, and PerEn with different embedding dimension values and signal lengths.

| Number of samples \rightarrow | 300 | 1,000 | 3,000 | 10,000 | 30,000 | 100,000 |
|---------------------------------|----------|----------|----------|----------|-----------|------------|
| DispEn ($m = 2$) | 0.0022 s | 0.0022 s | 0.0025 s | 0.0057 s | 0.0080 s | 0.0225 s |
| DispEn ($m = 3$) | 0.0028 s | 0.0035 s | 0.0076 s | 0.0115 s | 0.0284 s | 0.0888 s |
| DispEn ($m = 4$) | 0.0084 s | 0.0094 s | 0.0205 s | 0.0505 s | 0.1422 s | 0.4752 s |
| FDispEn ($m = 2$) | 0.0022 s | 0.0025 s | 0.0028 s | 0.0034 s | 0.0062 s | 0.0175 s |
| FDispEn ($m = 3$) | 0.0025 s | 0.0031 s | 0.0038 s | 0.0062 s | 0.0150 s | 0.0490 s |
| FDispEn ($m = 4$) | 0.0054 s | 0.0064 s | 0.0120 s | 0.0284 s | 0.0699 s | 0.2535 s |
| SampEn ($m = 2$) | 0.0023 s | 0.0208 s | 0.1841 s | 1.8478 s | 16.8394 s | 193.1970 s |
| SampEn ($m = 3$) | 0.0022 s | 0.0206 s | 0.1808 s | 1.8337 s | 16.9200 s | 189.4041 s |
| SampEn ($m = 4$) | 0.0019 s | 0.0193 s | 0.1631 s | 1.8322 s | 16.5596 s | 189.1037 s |
| PerEn ($m = 2$) | 0.0014 s | 0.0015 s | 0.0016 s | 0.0020 s | 0.0034 s | 0.0099 s |
| PerEn ($m = 3$) | 0.0014 s | 0.0016 s | 0.0016 s | 0.0024 s | 0.0043 s | 0.0115 s |
| PerEn ($m = 4$) | 0.0015 s | 0.0016 s | 0.0019 s | 0.0026 s | 0.0054 s | 0.0113 s |

351 7. Computation Cost of DispEn, FDispEn, and PerEn

352 In order to assess the computational time of DispEn and FDispEn with logsig, compared with PerEn,
 353 we use random time series with different lengths, changing from 300 to 100,000 sample points. The
 354 results are depicted in Table 3. The simulations have been carried out using a PC with Intel (R) Xeon
 355 (R) CPU, E5420, 2.5 GHz and 8-GB RAM by MATLAB R2015a. The number of classes for FDispEn and
 356 DispEn was 6. Additionally, DispEn and FDispEn with logsig were used for all the simulations.

357 The results show that the computation times of SampEn with different m are very close, while for
 358 DispEn, FDispEn, and PerEn, the larger the m value, the higher the computation time. PerEn is the
 359 fastest algorithm. For long signals and $m = 2, 3$, and 4, FDispEn is relatively faster than DispEn.
 360 For long time series, the running times of SampEn are considerably higher than those for DispEn,
 361 FDispEn, and PerEn. This is in agreement with the fact that the computation costs of DispEn, FDispEn,
 362 PerEn, and SampEn are respectively $O(N)$, $O(N)$, $O(N)$, and $O(N^2)$ [9,55]. Of note is that the optimised
 363 implementation of PerEn was used in this article [57], whereas the straightforward implementations of
 364 DispEn and FDispEn were utilized.

365 8. Forbidden Amplitude- and Fluctuation-based Dispersion Patterns

366 In this section, we introduce forbidden amplitude- and fluctuation-based dispersion patterns and
 367 explore the use of these concepts to discriminate deterministic from stochastic time series. Forbidden
 368 patterns denote those patterns that do not appear at all in the analysed signal [18,58]. There are two
 369 reasons behind the existence of forbidden patterns. First, a signal with finite length does not have a
 370 number of potential patterns (false forbidden patterns). For example, the time series $\{1, 2, 3, 2.1, 1, 4\}$
 371 has only 4 permutations from 6 potential permutation patterns with $m = 3$. Thus, the permutations
 372 $\{231\}$ and $\{312\}$ can be considered as false forbidden patterns. The second reason is based on the
 373 dynamical nature of the systems creating a signal. When signals made by an unconstrained stochastic
 374 process, all possible permutation patterns are appeared and there is no forbidden pattern. In contrast,
 375 it was evidenced that deterministic one-dimensional maps always have forbidden permutation or
 376 ordinal patterns [58,59].

377 Based on a null hypothesis, we illustrate that it is impossible that, for the embedding dimension m ,
 378 we have all the dispersion patterns, but not all the permutation patterns.

- 379 • Step 1: Null hypothesis. We have all the dispersion patterns, while the permutation pattern
 380 $(\ell_1, \ell_2, \dots, \ell_m)$ does not exist for the signal \mathbf{x} .
- 381 • Step 2: Rejection of null hypothesis. As the permutation pattern $(\ell_1, \ell_2, \dots, \ell_m)$ does not exist,
 382 we do not have any dispersion patterns sorted as $(\ell_1, \ell_2, \dots, \ell_m)$. This is in contradiction with
 383 the fact that we have all the dispersion patterns for \mathbf{x} . Hence, the null hypothesis is rejected.

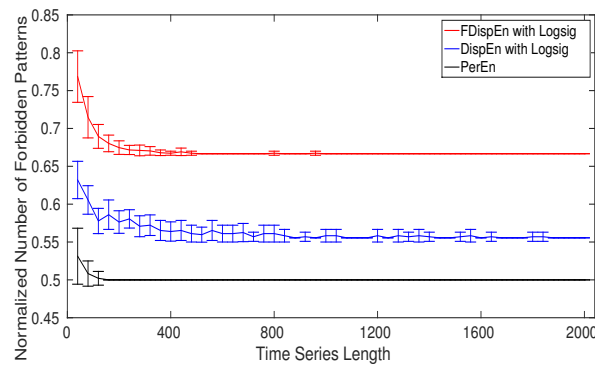


Figure 10. Mean and SD of the normalized number of forbidden amplitude- and fluctuation-based dispersion and permutation patterns ($\frac{\text{number of forbidden patterns}}{\text{potential number of patterns}}$) as functions of the signal length.

- 384 • Step 3: Conclusion. When we have all the dispersion patterns, all the permutation patterns are
 385 present too. It confirms the fact that a forbidden permutation pattern leads to several forbidden
 386 dispersion patterns. Thus, if a signal is deterministic, and so, does not have several permutation
 387 patterns, there are a number of forbidden dispersion patterns. Consequently, lack of dispersion
 388 patterns, like permutation patterns [58,59], reflects the deterministic behavior of a signal.

389 Conversely, when there is a forbidden dispersion pattern or fluctuation-based dispersion pattern for
 390 a signal, the time series is not stochastic. Thus, there is at least one forbidden permutation pattern as
 391 well. It is worth noting that the null hypothesis for FDispEn is similar.

392 To illustrate this issue, an example is provided: we set $m = 3$ for DispEn, FDispEn and PerEn and
 393 $c = 6$ for DispEn and FDispEn. If the permutation pattern (2,3,1) does not exist for the signal x , we
 394 do not have the following dispersion patterns: (2,3,1), (2,4,1), (2,5,1), (2,6,1), (3,4,1), (3,5,1), (3,6,1),
 395 (4,5,1), (4,6,1), (5,6,1), (3,4,2), (3,5,2), (3,6,2), (4,5,2), (4,6,2), (5,6,2), (4,5,3), (4,6,3), (5,6,3), and (5,6,4); and
 396 fluctuation-based dispersion patterns: (1,-2), (2,-3), (3,-4), (4,-5), (1,-3), (2,-4), (3,-5), (1,-4), (2,-5), (1,-5),
 397 (1,-2), (2,-3), (3,-4), (1,-3), (2,-4), (1,-4), (1,-2), (2,-3), (1,-3), and (1,-2). This demonstrates that lack of a
 398 permutation pattern results in lack of several dispersion and fluctuation-based dispersion patterns.
 399 Accordingly, as permutation patterns are used to discriminate deterministic from stochastic series
 400 based on lack of permutation patterns [58,59], dispersion and fluctuation-based patterns are able to be
 401 utilized as well.

402 The normalized number of forbidden (missing) dispersion and permutation patterns as a function of
 403 the signal length using the logistic map $x_{t+1} = 4x_t(1 - x_t)$ [59] for DispEn and FDispEn with logsig,
 404 and PerEn are shown in Figure 10. Note that the normalized number of forbidden patterns is equal to
 405 the number of forbidden patterns over the potential number of patterns ($m!$, c^m , and $(2c - 1)^{m-1}$ for
 406 respectively PerEn, DispEn, and FDispEn). As can be seen in Figure 10, for short signals we have a
 407 number of false forbidden patterns. The results evidence that more than half of the dispersion and
 408 permutation patterns are forbidden. On the whole, the results show that both the amplitude- and
 409 fluctuation-based dispersion patterns can be used to differentiate deterministic from stochastic time
 410 series.

411 9. Applications of DispEn and FDispEn to Biomedical Time Series

412 Physiologists and clinicians are often confronted with the problem of distinguishing different kinds
 413 of dynamics of biomedical signals, such as heart rate tracings from infants who had an aborted sudden
 414 infant death syndrome versus control infants [32], and electroencephalogram (EEG) signals from
 415 young versus elderly people [60]. A number of physiological time series, such as cardiovascular,
 416 blood pressure, and brain activity recordings, show a nonlinear in addition to linear behaviour [61–63].
 417 Moreover, several studies suggested that physiological recordings from healthy subjects have nonlinear

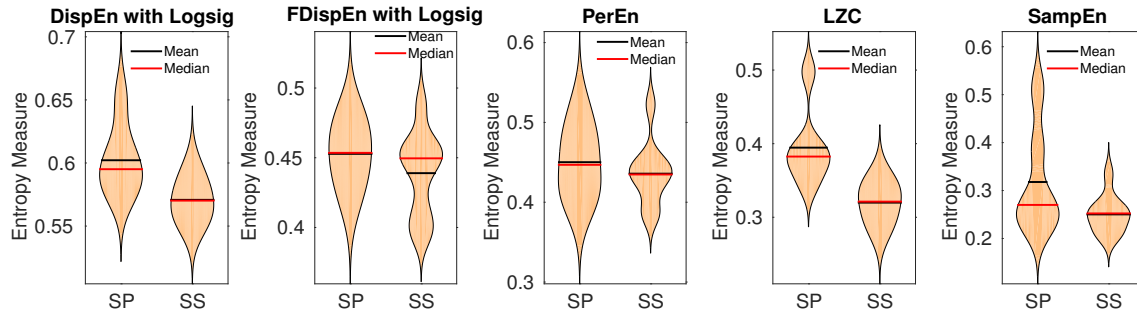


Figure 11. Mean and median of results obtained by PerEn, LZC, SampEn, and DispEn and FDispEn with logsig from salt-sensitive (SS) vs. salt protected (SP) rats' blood pressure signals.

Table 4. Differences between results for SS vs. SSBN13 Dahl rats (blood pressure data), and for elderly vs. young children (gait maturation dataset) obtained by DispEn and FDispEn with logsig, LZC, SampEn, and PerEn based on the Hedges' g effect size.

| Dataset | DispEn | FDispEn | PerEn | LZC | SampEn |
|-----------------|-------------------|---------------|---------------|-------------|--------------|
| Blood pressure | 1.35 (very large) | 0.46 (medium) | 0.31 (small) | 1.74 (huge) | 0.84 (large) |
| Gait maturation | 0.74 (large) | 0.75 (large) | 0.63 (medium) | 0.16 small | 0.79 (large) |

418 complex relationships with ageing and disease [13]. Thus, there is an increasing interest in nonlinear
 419 techniques, especially entropy-based metrics, to analyse the dynamics of physiological signals. To
 420 this end, to evaluate the DispEn and FDispEn methods to quantify the degree of the uncertainty of
 421 biomedical signals, we use two publicly-available datasets from <http://www.physionet.org>. The
 422 proposed methods are compared with PerEn, Lempel-Ziv complexity (LZC), and SampEn.

423 9.1. Blood Pressure in Rats

424 We evaluate the ability of entropy methods and LZC on the non-invasive blood pressure signals
 425 from nine salt-sensitive hypertensive (SS) Dahl rats and six rats protected (SP) from high-salt-induced
 426 hypertension (SSBN13) on a high-salt diet (8% salt) for 2 weeks [34,64]. Each blood pressure signal was
 427 recorded using radiotelemetry for two minutes with sampling frequency of 100 Hz. The study
 428 was approved by the Institutional Animal Care and Use Committee of the Medical College of
 429 Wisconsin-Madison, US [34,64]. Further information can be found in [34,64].

430 As the entropy approaches are used for stationary signals [10,14], we separated each signal into
 431 epochs with length 4 s (400 sample points) and applied the methods to each of them. Next, the average
 432 entropy value of all the epochs was calculated for each signal. The results, illustrated in Figure 11,
 433 show a loss of uncertainty with the salt-sensitive rats, in agreement with [64]. We set $m = 4$ for PerEn
 434 [49], $m = 2$ and $r = 0.2$ multiplied by SD of each epoch for SampEn, and $m = 3$ for both DispEn and
 435 FDispEn. The Hedges' g effect size [65] was employed to assess the differences between results for
 436 SS versus SSBN13 Dahl rats. The differences, illustrated in Table 4, show that the best algorithm to
 437 discriminate the SS from SSBN13 Dahl rats is LZC, followed by DispEn, SampEn, FDispEn, and PerEn,
 438 in that order.

439 9.2. Gait Maturation Database

440 We also used the gait maturation database to assess the entropy methods to distinguish the effect
 441 of age on the intrinsic stride-to-stride dynamics [66]. A subset including 23 healthy boys and girls
 442 is considered in this study. The children were classified into two age groups: 3 and 4 years old (11
 443 subjects) and 11 to 14 years old children (12 subjects). Height and weight of the young and elderly
 444 groups were 105 ± 2 cm and 155 ± 10 cm, and 17.3 ± 0.7 kg, and 44.4 ± 2.7 kg, respectively. The time

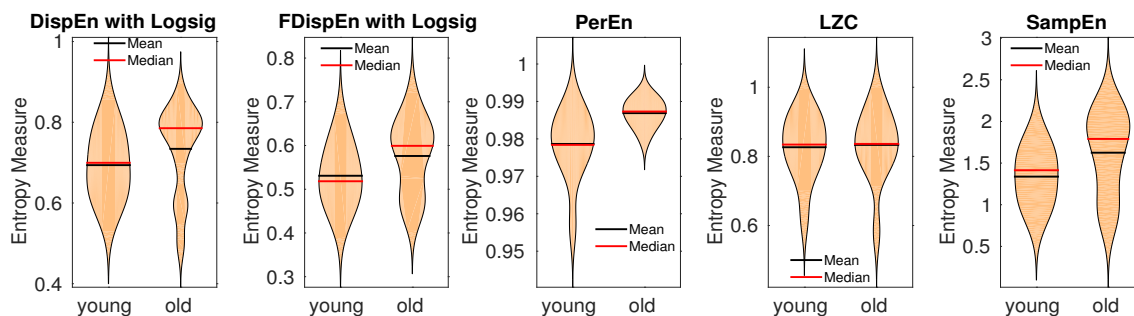


Figure 12. Mean and median of results obtained by PerEn, LZC, SampEn, and DispEn and FDispEn with logsig for young and elderly children's stride-to-stride recordings.

445 series recorded from the subjects walking at their normal pace have the lengths of about 400-500
 446 sample points. For more information, please see [66].

447 The results, depicted in Figure 12, show that the average entropy values obtained by DispEn and
 448 FDispEn with logsig, SampEn, and PerEn for the elderly children are larger than those for the young
 449 children, in agreement with previous studies [67,68]. The parameters values for the entropy methods
 450 are equal to those used for the blood pressure in rats. The differences for the elderly vs. young children
 451 based on Hedges' g effect size are shown in Table 4. The results demonstrate that DispEn, FDispEn, and
 452 SampEn outperform PerEn and LZC to distinguish various dynamics of the stride-to-stride recordings.

453 Overall, the results for the two real datasets demonstrate an advantage of DispEn and FDispEn with
 454 logsig over PerEn to distinguish different types of dynamics of the biomedical recordings. However,
 455 we acknowledge that there may be other datasets where PerEn outperforms DispEn and FDispEn. In
 456 any case, our results show the potential of DispEn and FDispEn for characterization of biomedical
 457 signals. Furthermore, the differences for the blood pressure and gait maturation datasets are shown
 458 that DispEn is the most consistent algorithm to distinguish the dynamics of signals for the real datasets.
 459 In spite of the promising findings and results for different applications aforementioned in this pilot
 460 study, further investigations on potential applications of DispEn and FDispEn are recommended.

461 10. Conclusions

462 In this paper, we carried out an investigation aimed at gaining a better understanding of our recently
 463 developed DispEn, especially regarding the parameters and mapping techniques used in DispEn. We
 464 also introduced FDispEn to quantify the uncertainty of time series in this article. The basis of this
 465 technique lies in taking into account only the local fluctuations of signals. The concepts of forbidden
 466 amplitude- and fluctuation-based dispersion patterns were also introduced in this study.

467 The work done here has the following implications for uncertainty or irregularity estimation. Firstly,
 468 we showed that DispEn and FDispEn with logsig are appropriate approaches when dealing with noise.
 469 We also found that the forbidden amplitude- and fluctuation-based dispersion patterns are suitable
 470 to distinguish deterministic from stochastic time series. Additionally, the results showed that both
 471 DispEn and FDispEn with logsig distinguish various physiological states of the two biomedical time
 472 series better than PerEn. Finally, the most consistent method to distinguish the different states of
 473 physiological signals was DispEn with logsig, compared with FDispEn with logsig, LZC, PerEn, and
 474 SampEn.

475 Due to their low computational cost and ability to detect dynamics of signals, we hope DispEn and
 476 FDispEn can be used for the analysis of a wide range of physiological and even non-physiological
 477 signals.

478 **Author Contributions:** Hamed Azami and Javier Escudero conceived and designed the methodology. Hamed
 479 Azami was responsible for analysing and writing the paper. Both the authors contributed critically to revise the
 480 results and discussed them and have read and approved the final manuscript.

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