Modified permutation-entropy analysis of heartbeat dynamics

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Heart rate variability (HRV) contains important information about the modulation of the cardiovascular system. Various methods of nonlinear dynamics (e.g., estimating Lyapunov exponents) and complexity measures (e.g., correlation dimension or entropies) have been applied to HRV analysis. Permutation entropy, which was proposed recently, has been widely used in many fields due to its conceptual and computational simplicity. It maps a time series onto a symbolic sequence of permutation ranks. The original permutation entropy assumes the time series under study has a continuous distribution, thus equal values are rare and can be ignored by ranking them according to their order of emergence, or broken by adding small random perturbations to ensure every symbol in a sequence is different. However, when the observed time series is digitized with lower resolution leading to a greater number of equal values, or the equalities represent certain characteristic sequential patterns of the system, it may not be rational to simply ignore or break them. In the present paper, a modified permutation entropy is proposed that, by mapping the equal value onto the same symbol (rank), allows for a more accurate characterization of system states. The application of the modified permutation entropy to the analysis of HRV is investigated using clinically collected data. Results show that modified permutation entropy can greatly improve the ability to distinguish the HRV signals under different physiological and pathological conditions. It can characterize the complexity of HRV more effectively than the original permutation entropy.

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I. INTRODUCTION

The beat rhythm of a healthy heart is not stable but rather is constantly changing, and it is affected by many internal and external factors. This results in heart rate variability (HRV), which is defined as tiny time differences between successive heartbeat periods. HRV contains important information about the modulation of the cardiovascular system [1]. Many studies show that two branches of the autonomic nervous system, namely sympathetic and parasympathetic, have a significant relationship with HRV. When the sympathetic branch is enhanced or the function of the parasympathetic branch is impaired, heart rate variability is reduced. This is likely to cause heart diseases such as myocardial ischemia, cardiac disorders, or even death [2–4]. HRV is affected by many other factors, such as exercise, breathing, blood pressure, body temperature, and mental stress. Circadian biological rhythms and the renin-angiotensin system are also involved in the modulation [5]. Because of these factors, the series of heart rate variability exhibits properties of high nonstationarity and complexity. Therefore, in addition to conventional linear analysis, many methods of nonlinear dynamics (e.g., estimating Lyapunov exponents [6–10]) and complexity measures (e.g., correlation dimension [11–14], fractal dimension [15–18], and entropies [19–21]) are also used for the analysis of HRV series. These studies have greatly advanced the research to reveal the underlying law and physical nature of heart rate variability and cardiovascular regulation.

Entropy is an effective measure to characterize the complexity of time series. To distinguish regular (e.g., periodic) signals, random signals, and chaotic signals and to quantify their complexity, many entropy measures have been proposed in recent years, such as Kolmogorov (or metric) [22,23] entropy, approximate entropy (ApEn) [24,25], and entropy of symbolic dynamics (SymDyn) [26]. The permutation entropy (PE) recently proposed by Bandt *et al.* [27] is widely used in many fields due to its conceptual and computational simplicity.

The PE algorithm assumes that the time series under study has a continuous distribution, thus equal values in the sequence are rare and can be ignored. Bandt *et al.* proposed to rank the equalities according to their order of emergence or to eliminate them by adding random noise to the original series [27]. Bandt's method has been successfully used in many studies [28–32]. In HRV series, the case of equal values appears very frequently due to limited sampling frequency of electrocardiogram (ECG) from which the HRV series (RR intervals, i.e. the interval from the peak of one QRS complex to the peak of next one as shown on an electrocardiogram) are derived. RR intervals obtained are discrete, and the resolution is limited to the sampling intervals of ECG, e.g., the resolution of an RR interval is 4 ms when ECG is sampled at a frequency of 250 Hz. Due to the high frequency of equal values in HRV series, Bandt's method of dealing with equal values might miss some important information embedded in HRV series. Therefore, we propose the modified permutation-entropy (mPE) method to deal with this situation. In the mPE algorithm, we utilize another method to process the equal values, i.e., by mapping the equal RR interval with the same symbol (rank) during the symbolizing procedure. Experiments show that the modification proposed in this paper can greatly improve the efficiency of permutation-entropy analysis of the complexity of heartbeat dynamics.

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II. METHOD

A. Permutation-entropy algorithm

For a given time series $\{x(i)\}_{i=1}^{N}$, we can embed the time series in the m-dimensional space and get reconstruction vectors $X(i)$,

$$X(i) = [x(i), x(i+l), \ldots, x[i+(m-1)l]], \tag{1}$$

where m is the embedding dimension and l is the delay time. Then each $X(i)$ can be arranged in increasing order,

$$x[i+(j_1-1)l] \leqslant x[i+(j_2-1)l] \leqslant \cdots \leqslant x[i+(j_m-1)l], \tag{2}$$

where j_* is the (time) index of the element in the reconstruction vector. If $x[i+(j_{k1}-1)l] = x[i+(j_{k2}-1)l]$, arrange it according to the index j_*. That is, $x[i+(j_{k1}-1)l] \leqslant x[i+(j_{k2}-1)l]$ when $j_{k1} < j_{k2}$.

Therefore, we can get a symbol series $A(i)$ for each $X(i)$,

$$A(i) = [j_1, j_2, \ldots, j_m]. \tag{3}$$

There are m different symbols in $[j_1, j_2, \ldots, j_m]$ and thus there are $m!$ different permutations, or $m!$ different symbol sequences. One can estimate the probability distribution for each symbol sequence and denote them as $P_1, P_2, \ldots, P_k$, where $k \leqslant m!$. Then the permutation entropy of k different symbol sequences for the time series $\{x(i)\}$ is defined as the Shannon entropy,

$$H_p(m) = -\sum_{v=1}^{k} P_v ln P_v. \tag{4}$$

Note that the maximum value of $H_p(m)$ is reached for a uniform distribution on all permutations, i.e., $H_p(m) = ln(m!)$ when $P_v = 1/m!$ and $k = m!$. Hence $H_p(m)$ is often normalized as

$$h_p = H_p(m)/ln(m!), \tag{5}$$

where $0 \leqslant h_p \leqslant 1$. Note that, for regular (periodic, quasiperiodic) and chaotic signals, they would get $\lim_{m\to\infty} h_p = 0$. The value of h_p quantifies the randomness of time series $\{x(i)\}$. The smaller h_p is, the more regular is the time series; otherwise, the series is more random.

B. Modified permutation-entropy algorithm

As is described above, the original permutation-entropy algorithm maps the equal values in the sequence to different symbols according to their sequential orders in the original series. Bandt *et al.* [27] also proposed to break equalities by adding small random perturbations. These two methods are valid when the values in the time series are continuous or discrete but with a high resolution, since the possibility of having equal values is very small when the resolution is high. However, the possibility of equal values may be very high when the resolution is much lower, or the equal values may represent a feature state of the system, such as the heart rate variability sequence in this study. If we ignore or eliminate the equivalent states, it is probable that we cannot accurately describe the complexity of the system. Therefore, we propose to map the equal values onto the same symbols in a modified permutation-entropy algorithm.

TABLE I. Upper bound of k for different m.

m	3	4	5	6	7
k_m	13	73	501	4051	37633

First, like the original permutation-entropy algorithm, one can sort the reconstruction components of $X(i)$ in increasing order:

$$x[i+(j_1-1)l] < x[i+(j_2-1)l] < \cdots < x[i+(j_{k1}-1)l] = x[i+(j_{k2}-1)l] < \cdots < x[i+(j_m-1)l]. \tag{6}$$

Normally, when there is no equality, $x[i+(j_*-1)l]$ is represented by j_*. However, when equality happens, we map the equal values onto the same symbol, which is the smallest indice j_* of these equal values, e.g., if $x[i+(j_{k1}-1)l] = x[i+(j_{k2}-1)l]$ and $j_{k1} < j_{k2}$, both $x[i+(j_{k1}-1)l]$ and $x[i+(j_{k2}-1)l]$ are represented by j_{k1} in the symbol sequence. Thus, the corresponding permutation sequence of $X(i)$ is defined as

$$A'(i) = [j_1, j_2, \ldots, j_{k1}, j_{k1}, \ldots, j_m]. \tag{7}$$

For example, considering two vectors $X(1) = [0.2,0.5,0.1,0.2,0.7]$ and $X(2) = [0.2,0.5,0.1,0.4,0.7]$, the original PE method ranks the equalities with their sequential orders and attains the same symbol vectors $A(1) = A(2) = [3,1,4,2,5]$ for $X(1)$ and $X(2)$. Our modified PE method maps the equalities to the same symbols and attains different symbol vectors $A'(1) = [3,1,1,2,5]$ and $A'(2) = [3,1,4,2,5]$ instead. When there is no equality in the embedded vectors, the original and modified PE methods are equivalent. However, when a lot of equalities occur, the mPE method is expected to perform better since it characterizes more system states than the original PE method. Then one can compute the probability distribution for each symbol sequence obtained using mPE and denote them as $P'_1, P'_2, \ldots P'_k$, where $k \leqslant k_m(m)$. The upper bound of k $[k_m(m)]$ can be calculated with a recursive method, which is demonstrated in the Appendix, and the upper bound of k for $m = 3$–7 is listed in Table I. The modified PE is defined in the same way as the original PE:

$$H'_p(m) = -\sum_{v=1}^{k} P'_v ln P'_v. \tag{8}$$

$H'_p(m)$ can also be normalized with maximum entropy as

$$h'_p = \frac{H'_p(m)}{ln[k_m(m)]}. \tag{9}$$

C. Experimental data

We test the mPE algorithm using the publicly available PhysioNet database. The heart rate variability signals are obtained from the MIT-BIH Fantasia database and the BIDMC congestive heart failure (CHF) database [33–35].

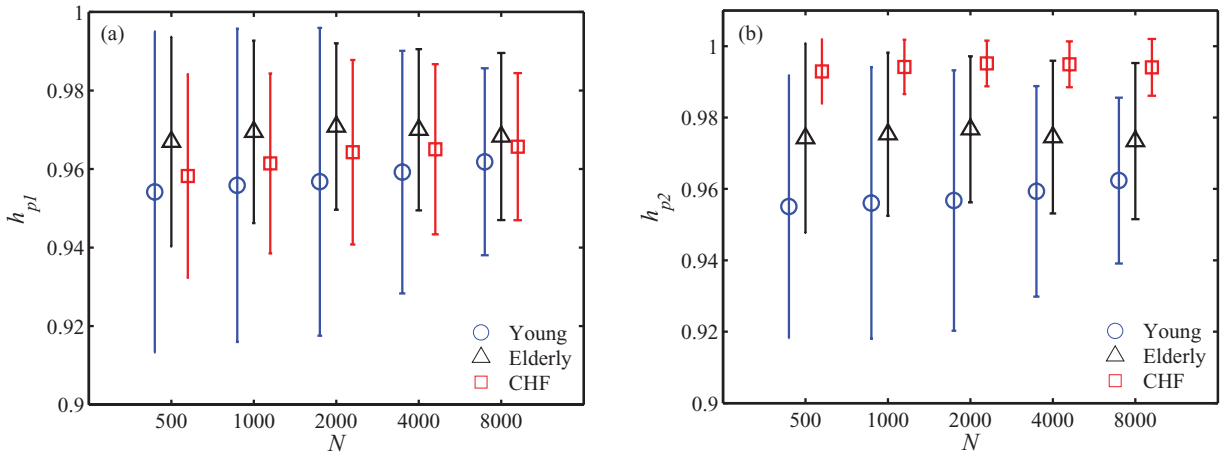

FIG. 1. (Color online) Permutation-entropy analysis of heart rate variability data from healthy young subjects, healthy elderly subjects, and congestive heart failure (CHF) patients using (a) PE1 and (b) PE2 methods with embedding dimension $m = 3$ and delay time $l = 1$ (see text for details). N indicates the length of data under analysis. The symbols and error bars indicate the average values and the standard deviations, respectively. We note that the normalized entropies should vary in [0, 1]; while some of the error bars go slightly beyond 1, which is caused by algebraic calculation, this does not mean the normalized entropies could actually have values larger than 1.

The Fantasia database includes long-term ECG recordings from 40 healthy subjects (20 healthy young subjects, aged 21 to 34, and 20 healthy elderly subjects, aged 68 to 85). All subjects remained in a resting state in sinus rhythm while watching the movie Fantasia (Disney, 1940) to help maintain wakefulness. The ECG signals were sampled at 250 Hz (the corresponding resolution of heart rate variability is 4 ms) for 120 min. The time marks of R-wave peaks automatically detected from continuous ECG signals after manual inspection and correction are given in the database, from which we can obtain the time sequence of heartbeat intervals.

The BIDMC CHF database includes long-term ECG recordings from 15 subjects with severe congestive heart failure (NYHA class 3-4). The individual recordings are each about 20 h in duration, sampled at 250 Hz. It also provides automatically detected R-wave markers after manual inspection and correction [35].

D. Statistical analysis

We use one-way analysis of variance (ANOVA) to test for differences among two or more independent groups. Its null hypothesis H_0 is that all samples have the same mean and variance, which means all samples come from the same population and there is no difference between groups. The statistic used is

$$F = \frac{\sigma_B^2}{\sigma_W^2}, \tag{10}$$

where σ_B^2 and σ_W^2 denote the variances between and within groups, respectively. If variance between groups is far greater than variance within groups, i.e., F is far greater than 1, the null hypothesis H_0 is rejected, and it demonstrates that the samples are from different populations or significant differences exist between groups. Otherwise, the null hypothesis is accepted, which means no significant difference exists between groups. The larger F is, the higher the probability that there is variation between groups.

The t test is used to test whether the means of two groups are statistically different from each other. The formula for the

TABLE II. One-way analysis of variance of PE1, PE2, and mPE analysis results.

	PE1		PE2		mPE	
N	F	p	F	p	F	p
500	0.64	0.53	7.39	0.0017	64.41	6.23×10^{-14}
1000	0.81	0.45	7.76	0.0013	69.28	1.83×10^{-14}
2000	0.92	0.41	8.63	0.0007	86.14	4.11×10^{-16}
4000	0.76	0.47	10.36	0.0002	99.48	3.04×10^{-17}
8000	0.38	0.68	10.52	0.0002	102.65	1.71×10^{-17}

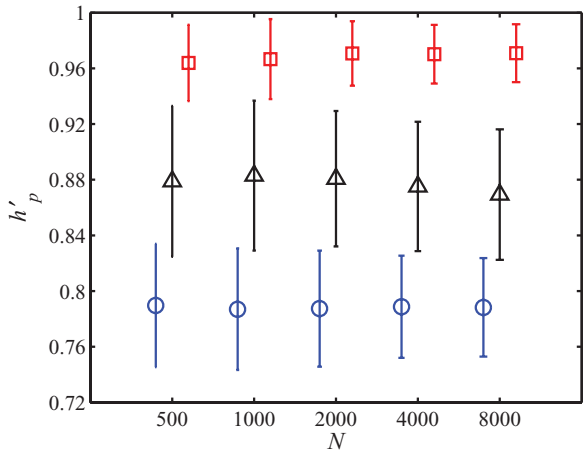

FIG. 2. (Color online) Modified permutation-entropy analysis of heart rate variability data in three groups with embedding dimension $m = 3$ and delay time $l = 1$ (the same symbols are used for groups as in Fig. 1).

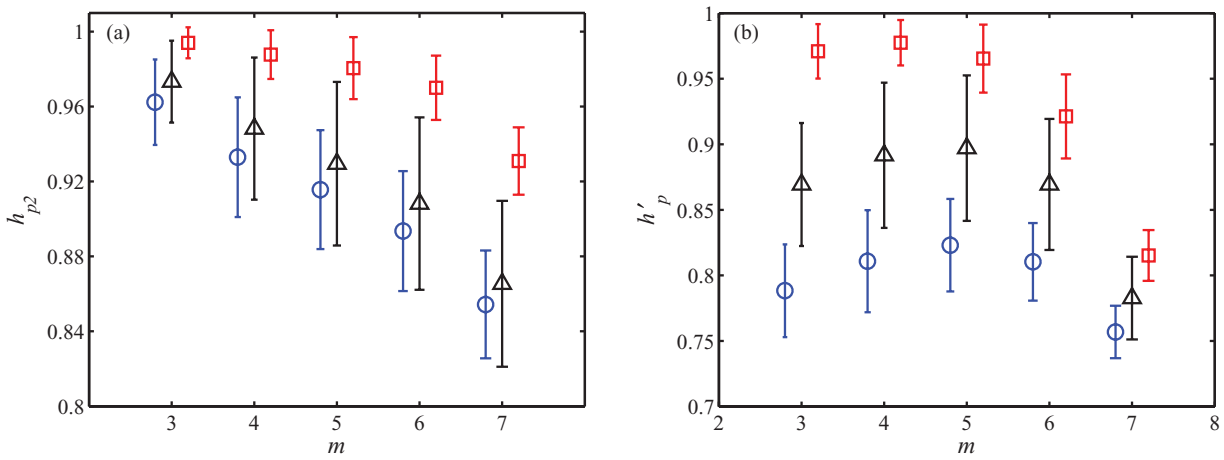

FIG. 3. (Color online) Results of (a) permutation-entropy and (b) modified permutation-entropy analysis with various embedding dimensions m. Here, delay time $l = 1$ and length of time series $N = 8000$ (the same symbols are used for groups as in Fig. 1).

one-sample t-test statistic is

$$t = \frac{\bar{x} - \mu_0}{s/\sqrt{n}}, \tag{11}$$

where $\bar{x}$ is the sample mean, μ_0 is the population mean, s is the sample standard deviation, and n is the sample size. The smaller t is, the more significant is the variation between two groups. Actually, the two-group ANOVA and t test are equivalent when $F = t^2$.

In hypothesis testing, p-value stands for the probability that we will make a mistake when we reject the null hypothesis. In the t test here, the smaller p is, the more likely it is that a statistical difference exists between the two groups. Generally, if $p > 0.05$, it is believed that the difference has no statistical meaning and just results from sampling error; if $p < 0.05$, it is believed that a substantial difference exists between groups.

III. RESULTS

First, we analyzed the data using the PE algorithm. As mentioned in Sec. II B, one method to deal with equalities in the series is to map the equal values to different symbols according to their sequential orders in the original series. We denote this method as PE1 and the entropy value as h_{p1}. From the results [see Fig. 1(a)], we can intuitively see that this method does not distinguish between different pathophysiology states. Another method (denoted as PE2, h_{p2}) is to add random Gaussian white noise (with $\mu = 0$ and $\sigma^2 = 0.1$) in order to break the equalities. The results [see Fig. 1(b)] show that PE2 performs better than PE1 in distinguishing different states, but it is still not sensitive enough.

The results of these two methods are analyzed using one-way ANOVA (see Table II). As expected, PE1 has no discrimination power for all three groups, while the ANOVA test for PE2 shows $p < 0.01$, indicating a certain discrimination between three groups. We further perform a t test between each group, and we find that PE2 has discrimination power between elderly and CHF groups ($p < 0.01$), but not between young and elderly groups ($p > 0.05$).

Then, we analyzed the data using the mPE algorithm (Fig. 2). The results show that mPE can effectively distinguish between young, elderly, and CHF groups and the discrimination power increases with the increase of data length. The result of mPE is also analyzed using ANOVA (see Table II). Comparing PE1 and PE2, the difference between three groups is statistically significant when using mPE (also confirmed by a t test between each group).

TABLE III. One-way analysis of variance of various embedding dimensions.

	PE2		mPE	
m	F	p	F	p
3	10.68	0.0002	102.65	1.17×10^{-17}
4	13.35	2.80×10^{-5}	68.25	2.36×10^{-14}
5	16.65	3.87×10^{-6}	50.05	3.63×10^{-12}
6	22.39	1.78×10^{-7}	35.32	5.98×10^{-10}
7	25.47	4.01×10^{-8}	23.76	9.07×10^{-8}

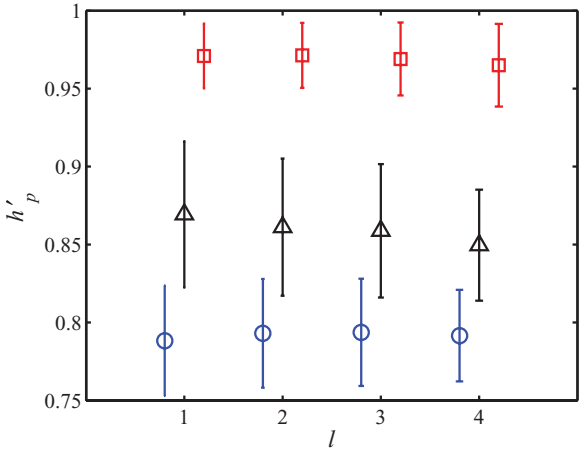

FIG. 4. (Color online) Results of modified permutation-entropy analysis with various delay times l. Here, the embedding dimension $m = 3$ and the length of the time series $N = 8000$ (the same symbols are used for groups as in Fig. 1).

TABLE IV. Probability (%) of tied ranks of the three databases (young, elderly, and CHF).

m	3	4	5	6	7
Young	8.6	15.8	23.9	32.1	33.8
Elderly	17.0	30.0	42.5	53.2	61.7
CHF	43.3	67.3	83.5	92.1	96.2

To investigate the influence of embedding dimensions, we calculated permutation entropy and modified permutation entropy with different embedding dimensions ($m = 3$–7) (see Fig. 3). The PE2 algorithm cannot effectively distinguish three groups regardless of the tested embedding dimensions. The discrimination power of the mPE algorithm decreases with the increase of embedding dimension, but it still shows a significant difference between groups for all the embedding dimensions tested. The result of the ANOVA test is shown in Table III.

The influence of delay time (l) is also analyzed and the result of mPE with different l ($l = 1 \sim 4$) is displayed in Fig. 4. It can be seen that l has only a small influence on the mean value and standard deviation of mPE results.

Finally, we test the probability of tied ranks for different embedding dimensions and delay times. The probability of tied ranks in the three databases (young, elderly, and CHF) is calculated and the statistical result is displayed in Table IV. One can see that the probability of tied ranks increases proportionally with the increase of m. This is easy to understand because the probability of equalities in a word with a length of 6 letters ($m = 6$) is certainly far greater than that of 3 letters ($m = 3$).

On the other hand, the probability of tied ranks only has a slight decline trend with the increase of delay time l. When $l = 1$, the values in one word are selected successively from the sequence, while when $l = 3$, they are selected every other two values from the sequence, which reduces the original relevance between successive values. This is also one reason why we set $l = 1$ instead of other longer delay times.

IV. DISCUSSION

Heart rate variability (HRV) contains important information about the modulation of the cardiovascular system. Various nonlinear dynamics methods and complexity measures have been used for HRV analysis. The complexity of HRV reflects the influence of physiological and pathological conditions on cardiovascular systems, and entropy measures are one of the most useful tools for complexity analysis. Manually and subjectively set parameters are required in the process of symbolization in most entropy measures, and the parameters have to be adjusted for different samples. This creates difficulties for practical applications. For example, Steuer *et al.* studied how the partition methods may lead to spurious results for the estimated entropy, and they proposed an optimal partition method [36]. However, their method introduced an extra parameter that complicated the process when determining the parameter.

In contrast, the recently proposed permutation entropy, a new complexity measure with the advantages of conceptual and computational simplicity, symbolizes time series according to their amplitude without any need to set parameters. Therefore, it is more robust and has been widely used in many fields.

In the studies and applications of permutation entropy, the probability of equal values is often assumed to be very small and its influence on the analysis results is assumed to be negligible. Equal values are often processed using two methods proposed by Bandt *et al.* [27]: (i) ranking the equal values according to their order of emergence in the sequence, or (ii) eliminating equal values by adding random noise. In practical applications, the probability of equal values is sometimes very high due to the limited sampling rate. Bandt's methods may lead to a non-negligible deviation between the analysis result and the actual state of the system.

We tested three groups of HRV data from an international public database representing different physiological and pathological states, and we confirmed the problem described above. The aforementioned two approaches to process equal values cannot effectively distinguish the three groups (young, elderly, and congestive heart failure), indicating that they cannot accurately characterize the effects of physiological and pathological conditions on the complexity of cardiovascular modulation.

We improved the method of equality processing used in the original permutation-entropy algorithm. The proposed modified permutation entropy, by using the same symbols to represent equal values, allows for a more accurate characterization of system states. Experimental results on clinically collected data show that the improved entropy can effectively distinguish the three groups. The modified algorithm is more efficient in characterizing the complexity of heart rate variability signals than the original permutation-entropy algorithm.

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APPENDIX: NORMALIZATION OF MODIFIED PERMUTATION ENTROPY

According to Eqs. (6) and (7), the same symbols (tied ranks) must occupy consecutive positions in the symbol sequence, thus one can treat them as one part when considering the arrangement of symbols. In this way, all the possible permutation patterns can be classified into groups according to what kinds of parts they have, i.e., how many "1" 's, how many "2" 's, etc. Provided there are p ($p \leqslant m$) parts (i.e., p different symbols) in a group, the number of patterns belonging to this group is equivalent to the arrangement number of a set of p elements, which is given by $p!$. For example, considering $m = 4$, the group with two "1" 's, one "3," and one "4" (denoted as group $\{11, 3, 4\}$) contains 3! patterns, i.e., [1 1 3 4], [1 1 4 3], [3 1 1 4], [4 1 1 3], [3 4 1 1], and [4 3 1 1].

TABLE V. Permutation patterns with $m = 4$.

Symbol: "1"	Symbol: "2"	Symbol: "3"	Symbol: "4"	Group	Number of patterns in the group
1	2	3	4	{1, 2, 3, 4}	4!
		33	–	{1, 2, 33}	3!
	22	–	4	{1, 22, 4}	3!
		3	–	{1, 22, 3}	3!
	222	–	–	{1, 222}	2!
11	–	3	4	{11, 3, 4}	3!
		33	–	{11, 33}	2!
	2	–	4	{11, 2, 4}	3!
		3	–	{11, 2, 3}	3!
	22	–	–	{11, 22}	2!
111	–	–	4	{111, 4}	2!
		3	–	{111, 3}	2!
	2	–	–	{111, 2}	2!
1111	–	–	–	{1111}	1!
Then the upper bound of k can be calculated as $k_m(4) = 4! + 6 * 3! + 6 * 2! + 1! = 73$					

Thus, to calculate the total number of permutation patterns (i.e., the upper bound of k), one can list all the possible groups by combining symbols from "1" to "m" into parts, and then sum the arrangement number of each group (see Table V). When determining whether the symbol "i" will occur and how many times it will occur in the group, one needs to consider how many positions have been occupied by previously determined symbols and how many positions are left. If the previously determined symbols occupied more positions than $i - 1$, then the number of positions left is less than the number of symbols left, thus the symbol "i" can be omitted. If the occupied positions are equal to $i - 1$ (it cannot be less than $i - 1$), the number of positions left is equal to the number of symbols left. If no tied rank occurs for the remaining symbols, then each symbol occupied one position. If a tied rank occurs, one or more symbols have to be replaced by the smaller symbols according to Eqs. (6) and (7). The symbol "i" cannot be omitted regardless of whether a tied rank occurs or not, since "i" is the smallest symbol left. Taking the same group $\{11, 3, 4\}$ as an example, the symbol "2" is omitted because it is replaced by "1." If there is only one "1" in the group, then "2" must appear at least once because it is the smallest symbol other than "1," and "2" cannot be replaced by other larger symbols, i.e., groups $\{1, 33, 4\}$ or $\{1, 3, 44\}$ are not eligible.

Based on the principles given above, a recursive algorithm is designed to traverse all the possible groups and calculate the number of all the possible permutation patterns with different m. A function is defined with five arguments: the embedding dimension m, the pattern count k, the symbol under consideration i, the number of used symbols c, and the number of occupied positions j, i.e., $k = f(m,k,i,c,j)$. The recursive algorithm of function f can be simply defined as follows:

S1: if $j = m$, let $k = k + c!$ and exit;
S2: if $j > i$, let $k = f(m,k,i,c,j + 1)$;
S3: let $l = 1$;
S4: let $k = f(m,k,i + 1,c + 1,j + l)$;
S5: if $l < m - j$, let $l = l + 1$ and go to S4, otherwise exit.

To get the number of all the possible permutation patterns for embedding dimension m, one can invoke $k = f(m,0,0,0,0)$.

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