Time irreversibility and its application in epileptic brain electrical activities

Wenpo Yao
School of Telecommunications and Information Engineering, Nanjing University of Posts and Telecommunications, Nanjing 210003, China

Wenli Yao
School of Mines, China University of Mining and Technology, Xuzhou 221116, China and Department of Mining and Metallurgical Engineering, Western Australian School Mines, Curtin University, Kalgoorlie, WA, Australia

Jiafei Dai
Nanjing General Hospital of Nanjing Military Command, Nanjing 210002, China

Jun Wang
School of Geography and Biological Information, Nanjing University of Posts and Telecommunications, Nanjing 210023, China

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Time irreversibility (temporal asymmetry) is one of fundamental properties that characterize the nonlinearity of complex dynamical processes, and our brain is a typical complex dynamical system manifested with nonlinearity. Two subtraction-based parameters, \( Y_s \) and \( \chi^2 \), are employed to measure the probabilistic differences of permutations instead of raw vectors for the simplified quantification of time irreversibility, which is validated by chaotic and reversible processes and the surrogate data. We show that it is equivalent to quantify time irreversibility by measuring probabilistic difference between the forward and its backward processes and between the symmetric permutations. And we detect time irreversibility of two groups of epileptic EEGs, from the Nanjing General Hospital (NJGH) and from the public Bonn epileptic database. In our contribution, the manifestation of nonlinearity of whether healthy or diseased brain electrical activities is highlighted, and the highest time irreversibility of epileptic EEG during seizures is demonstrated. NJGH epileptic EEGs during seizure-free intervals have lower time irreversibility than the control data while those of the Bonn data sets have higher nonlinearity than the healthy brain electrical activities. For the inconsistent results, we conduct multi-scale analysis and elucidate from the circadian rhythms in epileptic nonlinearity, however, more targeted researches are needed to verify our assumptions or to determine if there are other reasons leading to the inconsistency.

I. INTRODUCTION

The human brain, a collection of huge number of neurons and glial cells and endowed with overdeveloped cerebral cortex [1], is complex system featured with nonlinearity and nonequilibrium. Nonlinear approaches, like low dimension chaos for quantifying the complexity, unpredictability or randomness of underlying nonlinear dynamical systems [2–4], interactive couplings or synchronization for understanding the connective association [5–7], networked science [8–10] for elucidating the structural neuronal activities, are proposed to characterize the highly complex brain activities [11] and having shown promising nonlinear features detection. Among these methods, time irreversibility, one of fundamental properties of nonlinear processes, has been paid much attention for characterizing complex dynamical systems.

Time reversibility describes the invariant statistical properties of processes under the reversal time scale [12]. A time series is said to be irreversible if its probabilistic properties depend on the time direction. Time irreversibility, also in term of temporal asymmetry, could be quantified from two perspectives, namely probabilistic difference between the forward and its backward processes and the probabilistic differences between the symmetric joint distributions of a process [13]. Mathematically speaking, to measure the probabilistic differences between joint distributions is not trivial, and several alternative simplified approaches are proposed to quantify time irreversibility. P. Guzik [14] and A. Porta et al. [15, 16] measure the temporal asymmetry based on the probabilistic difference between ups and downs in time series. M. Costa et al. [17, 18] provide a computational method to quantify time asymmetry by measuring the difference between the average energy for activation and relaxation. L. Lacasa et al. [19] measure the probabilistic difference between in and out degrees of horizontal visibility graph for time irreversibility. W. Yao et al. [3] simplify the quantification of time irreversibility by measuring the probabilistic difference between symmetric permutations instead of the vectors in raw time series. C. Daw et al. [20] propose a symbolic approach, "false flipped symbols", that is computationally efficient and insensitive to noise without the need of surrogate data. Among these simplified analytical measures, approaches based on symbolic dynamics [3, 21, 22] that transform raw time series into symbol series and calculate probability distribution of symbolic sequences (words) have been gaining popularity for their simplicity, robustness,
fast, insensitivity to noise, etc.

Epilepsy is an all-age affected neurological disorder characterized by recurrent epileptic seizures 24, 25, and conceptual and operational definitions 26 are proposed to characterize the chronic unpredictable disease and for clinical use. Epileptic seizures develop abruptly and last a few seconds, and the seizures’ clinical onset, synchronous neuronal firing in the cerebral cortex, could be recorded by intracranial or surface EEG 27, 28. Several nonlinear approaches have been applied to characterize the epileptic brain activities during seizures or seizure-free intervals 2, 4, 23.

In our contribution, we use the probabilities of permutations rather than the raw vectors to simplify the quantification of the time irreversibility, and considering the forbidden permutation, we employ two subtraction-based parameters, $Y_s$ 3 and $\chi^2$ 21 22, to measure the probabilistic differences for time irreversibility. The two parameters are verified by three chaotic series, logistic, Henon and Lorenz series, reversible Gaussian process and their surrogate data. And we conduct comprehensive research on the nonlinearity of time irreversibility of epileptic EEGs from Nanjing General Hospital(NJGH) and from the Bonn epileptic database.

II. MEASUREMENTS FOR THE NONLINEARITY OF TIME IRREVERSIBILITY

A. Basic definitions of time reversibility

Time reversibility is to describe the invariant probabilistic properties of a process with respect to time reversal. Here are two statistical definitions for time reversibility.

Definition I. In the definition of G. Weiss 12, a stationary process $X(t)$ is time reversible if $\{X(t_1), X(t_2), \ldots, X(t_m)\}$ and $\{X(-t_1), X(-t_2), \ldots, X(-t_m)\}$ have the same joint probability distributions for every $t$ and $m$.

Definition II. Another definition of F. Kelly 29 suggests that if $X(t)$ is reversible, $\{X(t_1), X(t_2), \ldots, X(t_m)\}$ and $\{X(-t_1 + n), X(-t_2 + n), \ldots, X(-t_m + n)\}$ have the same joint probability distribution for every $n$ and $m$, under which $\{X(t_1), X(t_2), \ldots, X(t_m)\}$ and have same probability distribution with its symmetric vector $\{X(t_1), \ldots, X(t_2), X(t_1)\}$ if $n = t_1 + t_m$.

From the above definitions, if $X(t)$ is time reversible, its $m$-dimensional vectors have same joint probabilities with the time-reversal forms, $p(x_1, x_2, \ldots, x_t) = p(x_{-1}, x_{-2}, \ldots, x_{-t})$, and with the symmetric vectors, $p(x_1, x_2, \ldots, x_t) = p(x_t, \ldots, x_2, x_1)$, suggesting that it is equivalent to quantify time irreversibility using the probabilistic differences between the forward and reverse distributions or between the symmetric distributions. In a visual perspective, illustrated in Fig. 1 for the vector $(x_1, x_2, \ldots, x_t)$ in time series $X(t)$, its symmetric vector $(x_1, \ldots, x_2, x_1)$ and corresponding vector $(x_{-1}, x_{-2}, \ldots, x_{-t})$ in the reversible time series $X(-t)$ are in fact same.

![Exemplary illustration of the vector and its symmetric form](image)

**FIG. 1.** Exemplary illustration of the vector and its symmetric form and the corresponding one in reverse time series. In the forward time series $X(t)$, to reverse the $(x_1, x_2, x_3, x_4)$, in subplot a), is to construct its symmetric vector $(x_4, x_3, x_2, x_1)$, in subplot b), which is the same with its corresponding vector $(x_{-1}, x_{-2}, x_{-3}, x_{-4})$, in subplot c), in the reverse $X(-t)$.

Therefore, the terms of time irreversibility and temporal asymmetry are equivalent to describe the nonlinear irreversible behavior.

As for the condition of stationarity imposed to stochastic process in the definitions, we should note that the stationarity is in fact a separate concept to the general definitions of time irreversibility. There exists nonstationary process that is time reversible 12, and there are examples of stationary processes which are not time reversible 12. The two concepts, stationarity and time irreversibility, therefore, do not imply each others.

B. Simplified alternative: order patterns

The quantification of time irreversibility (directionality), involving measuring the probabilistic differences in joint distributions of processes, is not trivial. To simplify the quantification of time irreversibility, W. Yao et al. 30 measured the probabilistic difference of permutation instead of the raw vectors, inspired by the mathematical similarity of the calculation of joint probability and the embedding phase space. The permutation-based method, coming naturally from and inheriting causal structures of the time series, is introduced by C. Bandt and B. Pompe 30 in permutation entropy and has been gaining popularity in several areas 31.

Let us briefly introduce the permutation method. We first construct $m$-dimensional delay vectors as Eq. 1 for dimension $m$ and time delay $\tau$.

$$X_m^t(i) = \{x(i), x(i + \tau), \ldots, x(i + (m - 1)\tau)\} \quad (1)$$

And then we organize the elements according to their relative values in ascending order $x(j_1) \leq x(j_2) \leq \cdots \leq x(j_m)$, involving measuring the probabilistic differences between the forward and reverse distributions or between the symmetric distributions.

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indexes of the original values, its symmetric pattern is \( \pi \). The order pattern, \( \pi = \{ j_1, j_2, \cdots, j_i \} \), is the vector of indexes of the original values, its symmetric pattern is \( \pi_s = p(j_i, \cdots, j_2, j_1) \) and the corresponding permutation in reverse time series is \( \pi_{-i} = \{ j_{i-1}, j_{i-2}, \cdots, j_1 \} \). Fig. 2 illustrates the ordinal patterns when \( m \) are 2 and 3. Assuming the continuous distribution of \( X(t) \), equal states are very rare, so that we neglect the equal values and rank them according to the order of their appearances.

\[
\begin{align*}
\text{m=2} & \quad \text{m=3} \\
12 & \quad 123 \quad 132 \quad 213 \\
21 & \quad 321 \quad 231 \quad 312
\end{align*}
\]

FIG. 2. Ordinal patterns when \( m \) are 2 and 3. Taking equal values out of consideration, there are 2 (2!) ordinal patterns, up and down, when \( m \) is 2, and 6 (3!) permutations when \( m \) is 3.

The quantification of time irreversibility or temporal asymmetry could be simplified by measuring the probabilistic difference between the symmetric \( p(\pi_i) \) and \( p(\pi_s) \) or between \( p(\pi_i) \) and \( p(\pi_{-i}) \).

C. Forbidden permutation

Regarding the symbolic encoding scheme based on permutation, there are at most \( m! \) order patterns for dimension \( m \), however, all permutations are not realizable. In symbolic time series analysis, the symbols or words that have no occurrence are called forbidden symbols or forbidden words [32]. The forbidden symbols or words contain important information about the systems, and have close connection with structural or dynamical information about the processes. D. Alessandro and Politi [32] introduced a novel indicator for complexity based on the growth rate of irreducible forbidden words, and contributed to a more precise computation of the topological entropy. The existence of forbidden permutation is proved to have close connections with nonlinearity of model-based processes and real-world data [3]. The decay rate of forbidden order patterns is reported to be related to correlation structures of stochastic process, which might serve as a tool for discrimination between deterministic and stochastic series [3]. Using properties of the missing permutations to detect nonlinearity in time series has been verified to be effective by both model and real-world series [34]. By tracing forbidden patterns and their outgrowths, J.M. Amigo et al. [35] proposed a non-statistical test to discriminate chaotic from random processes, and they find that there are true forbidden patterns that are robust against noise disintegrate with noise dependable rates and false ones that decay with data length in deterministic and random dynamical systems [32]. The properties of forbidden ordinal patterns have been given in-depth study and attention due to its close connections to dynamical complexity and structural information [37].

Given the existence of forbidden permutations, there might be order patterns that do not simultaneously exist in the forward and backward series or do not have symmetric forms, case like this implies there is significant difference between their probabilities. To measure the time irreversibility, the probabilistic difference between corresponding permutations that contain forbidden permutation should be quantifiable. The outcome of parameters based on division such difference, however, is zero or infinity. Therefore, the division-based parameters like Kullback-Leibler or Chernoff distance are not suitable while measures based on subtraction will be more reliable to measure the probabilistic difference [3].

D. Subtraction-based parameters for probabilistic difference

While the parameters based on division are not proper to quantify the probabilistic difference for time irreversibility, the subtraction-based measurements should be appropriate alternatives. We apply a subtraction-based parameter, \( Y_s \) in Eq. 2 where \( p(\pi_i) \geq p(\pi_j) \), to measure the ordinal patterns probabilistic difference.

\[
Y_s = \sum p(\pi_i)\frac{p(\pi_i) - p(\pi_j)}{p(\pi_i) + p(\pi_j)}
\]  

(2)

Another parameter based on subtraction is the chi-square statistics \( \chi^2 \) [20, 22] in Eq. 3 that has similar characteristic with the \( Y_s \).

\[
\chi^2 = \sum \frac{[p(\pi_i) - p(\pi_j)]^2}{p(\pi_i) + p(\pi_j)}
\]  

(3)

The two subtraction-based parameters satisfy following basic features. First, when \( p(\pi_i) \) is equal to \( p(\pi_j) \), the difference is 0; second, when absolute differences between different pairs of \( p(\pi_i) \) and \( p(\pi_j) \) are the same, there is an additional parameter to adjust the difference like \( \kappa \times [p(\pi_i) - p(\pi_j)] \), and \( \kappa = \frac{p(\pi_i)}{p(\pi_i) + p(\pi_j)} + \frac{p(\pi_j)}{p(\pi_i) + p(\pi_j)} \) in \( Y_s \) and \( \chi^2 \); third, if \( p(\pi_j) \) is zero, the results should be accountable that \( Y_s \) and \( \chi^2 \) share the result of \( p(\pi_i) \).

To measure the rates of single permutation that does not have symmetric form or do not have the corresponding permutation in reverse series, we employ the parameter \( R_a \) in Eq. 4 where \( N(\pi_u) \) is the amount of single order patterns and \( N(\pi) \) is the number of existing permutations.

\[
R_a = \left[ N(\pi_u)/N(\pi) \right] \times 100\%
\]  

(4)
In this section, we generate chaotic and reversible series and their surrogate data to validate $Y_s$ and $\chi^2$ of probabilistic differences for time irreversibility.

Logistic equation [38], mathematically written as $x_{t+1} = r \cdot x_t (1 - x_t)$, even though simple and deterministic, can exhibit complex, chaotic behaviour. The bivariate Henon map [39], given by the coupled equations $x_{t+1} = 1 - \alpha \cdot x_t^2 + y_t$, $y_{t+1} = \beta \cdot x_t$, presents a two-dimensional invertible iterated map with quadratic nonlinearity. And the three-variable Lorenz system [40], generated by the three coupled nonlinear differential equations with respect to time, $dx/dt = \sigma (y - x)$, $dy/dt = x(r - z) - y$ and $dz/dt = xy - bz$, is a simplified model to originally represent forced dissipative hydrodynamic flow. The logistic ($r=4$, $x_1=0.01$), Henon ($\alpha=1.4$, $\beta=0.3$, and $x_1=0.01$, $y_1=0.01$) and Lorenz ($x_1=0$, $y_1=0$ and $z_1=1 \times 10^{-10}$, $\sigma=10$, $b=8/3$ and $r=\frac{\sigma(\sigma+b+3)}{\sigma-b-3}=24.74$ whose slightly super-critical alternative is chosen as $r=28$) equations are used to generate chaotic series, and linear reversible Gaussian white noise is constructed.

To verify the simplified measures for time irreversibility, we also use surrogate technology to generate linear surrogate data for each series and detect the nonlinearity by determining whether some statistic aspects of the original and surrogate data are significantly different [41, 42]. The improved amplitude adjusted Fourier transform (iAAFT) [43] is employed to construct linear data sets that have same autocorrelations, power spectrum and distribution to the data in our contribution.

$Y_s$ and $\chi^2$ of the probabilistic differences between symmetric permutations and between the forward and backward sequences, and the rates of single permutation $R_m$, of the three chaotic series and Gaussian process are shown in Fig. 3. When data length is bigger than $7m!$, the three parameters come to their converges. In our test, to have reliable nonlinearity detections, we set $m=7$ and data length to $10 \times 7! = 50400$.

Through the Fig. 3 we show that it is equivalent to quantify time irreversibility by measuring probabilistic difference between the forward and its backward processes and between the symmetric permutation. The $Y_s$ and $\chi^2$ for forward-backward probabilistic differences come to 1 for the logistic and Henon series when $m$ becomes 5 and bigger, and the $Y_s$ and $\chi^2$ for symmetric divergences, although slightly different, are more than 90%, and they have same swift upward changes when $m$ become from 3 to 4. The $Y_s$ and $\chi^2$ of the Lorenz and Gaussian processes have almost same results in the forward-backward and symmetric probabilistic differences, and the rates of single order patterns of the two processes are also identical. The four processes also have similar time irreversibility of the surrogate data sets either for the forward-backward or for the symmetric divergences.

$Y_s$ and $\chi^2$ of the three chaotic series are all much higher than the 97.5th percentile of time irreversibility of the surrogate data. Of the reversible Gaussian process, $Y_s$ and $\chi^2$ are both between the the 2.5th and 97.5th percentile of its surrogate data sets. According to the surrogate theory [41, 42], the null hypothesis that the chaotic series are linear is rejected while that the Gaussian process is linear should be accepted, validating the effectiveness of $Y_s$ and $\chi^2$ for quantification of time irreversibility.

III. TIME IRREVERSIBILITY IN MODEL PROCESSES

FIG. 3. $Y_s$ and $\chi^2$ of chaotic series, reversible process and the surrogate data. a), b), c) and d) are about the probabilistic difference between symmetric permutations, and e), f), g) and h) are about the probabilistic difference of permutations in forward and backward sequences. 97.5th and 2.5th percentile of $Y_s$ and $\chi^2$ of surrogate are denoted 'Ys-97.5%S', 'Ys-2.5%S', 'Y^2-97.5%S' and 'Y^2-2.5%S'.
Due to the structural and dynamical differences, the rates of forbidden order patterns and time irreversibility of the three chaotic series are different, however, the $Y_u$ and $\chi^2$ have consistent changes with $R_u$, particularly for the logistic and Henon chaotic series, suggesting the close connections of the rates of single permutation with time irreversibility. Logistic process has the fastest increase when $m$ increases from 3 to 4, and $R_u$ becomes bigger than 90% when $m$ is 5. When $m$ is 7 or bigger, there is almost none of co-exist symmetric permutations that the $R_u$ comes to bigger than 98% for the logistic and Henon series, and for the forward and backward symbolic sequences, when $m$ is 5 or bigger, $R_u$, $Y_u$ and $\chi^2$ of logistic series are all 1. $R_u$ of the Lorenz series has the slowest growth but still indicates that more than a half orders are single when $m$ is 7.

The chaotic and Gaussian processes have different nonlinearities due to their structural and dynamical differences while they share the conclusion that it is effective to characterize time irreversibility by using the subtraction-based parameters, $Y_u$ and $\chi^2$, to measure the probabilistic differences between symmetric order patterns or between the forward and backward permutation sequences.

IV. TIME IRREVERSIBILITY IN EPILEPTIC BRAIN ELECTRICAL ACTIVITIES

We use $Y_u$ and $\chi^2$ of the probabilistic difference between symmetric permutations to quantify time irreversibility of two groups of epileptic EEGs from Bonn database [4] and NJGH in this section.

A. Time irreversibility in brain electrical activities

Of the public Bonn epileptic data, there are 5 sets (denoted A-E) of EEG, of which sets A (eyes open) and B (eyes closed) are recorded from healthy volunteers by surface electrodes following the standard electrode positions in Fig. 4 sets D (seizure-free) and E (seizure) are collected from within the epileptogenic zone and set C (seizure-free) is obtained from the hippocampal formation of the opposite hemisphere through intracranial electrodes [4]. Each data set contains 100 single-channel EEG recordings of 173.61 sampling rate in duration of 23.6s.

Two groups of volunteers, 22 epilepsy patients (aged 4 to 51, mean 30±13.1 years) and 22 control subjects (aged 15 to 49, mean 26.95±8.91 years), are enrolled from Nanjing General Hospital of Nanjing Military Command (NJGH) [3]. Brain electric activities are recorded at sampling frequency of 512 Hz in duration of 1 minute according to the 10-20 system illustrated in Fig. 4. All of the volunteers are in idle resting states, and the epileptic are all in seizure-free intervals.

The rates of single order patterns of Bonn and NJGH EEGs are listed in Table I and illustrated in Fig. 5. Considering the data length of the two groups of EEG data sets, we set up bound of Bonn to $m=5$ and NJGH to $m=7$. When $m=2$ and 3, all of the permutations of the two groups of EEGs have symmetric forms that $R_u=0$.

| $m$ | $R_u$ (mean±std) of the Bonn epileptic EEGs. |
|-----|----------------------------------|
| 1   | 0.04±0.43 0.00±0.00 5.84±3.89 2.71±1.88 |
| 2   | 0.78±1.80 0.08±0.61 11.55±5.56 5.63±4.16 |
| 3   | 0.00±0.00 0.00±0.00 3.55±3.26 3.84±2.83 |
| 4   | 0.00±0.00 0.00±0.00 4.85±3.41 4.95±3.00 |
| 5   | 3.28±4.91 1.06±3.12 17.88±6.85 11.96±6.13 |

Consequently, the results of the Bonn and NJGH EEGs are shown in Fig. 5 and 6. The NJGH EEGs and Bonn during-seizure EEG (set E) have higher $Y_u$ and $\chi^2$ than the 97.5th percentile of the surrogate data and other 4 Bonn data sets have smaller
manifestation of time irreversibility lies in that the brain is subject to internal physiological factors and external environmental influence. Physiological significance of the nonlinearity of brain electrical activities are typical nonlinear processes, and the inherent feature of nonlinearity that might be affected by different physiological or pathological conditions will not change.

The seizure activities (set E) among the five Bonn data sets have the highest temporal asymmetry, displayed by Fig. 6, and the nonlinearity of set E are significantly different from those of other 4 sets. The discrimination between seizure EEG and healthy data sets, A-E ($Y_s$, $p<1 \times 10^{-15}$; $\chi^2$, $p<1 \times 10^{-9}$) and B-E ($Y_s$, $p<1 \times 10^{-14}$; $\chi^2$, $p<1 \times 10^{-9}$), and that between seizure and seizure-free EEG, C-E ($Y_s$, $p<1 \times 10^{-12}$; $\chi^2$, $p<1 \times 10^{-7}$) and D-E ($Y_s$, $p<1 \times 10^{-11}$; $\chi^2$, $p<1 \times 10^{-7}$), are all acceptable statistically. And the results show that $Y_s$ has more preferable nonlinearity detection than $\chi^2$ statistically. Pathological features about the epilepsy should account for the highest nonlinearity of the seizure EEG. The recurrent seizures is the hallmark of epilepsy and it is the sudden development of synchronous neuronal firing [27]. During seizures, severely abnormal brain activities and dynamical disorders recorded by invasive or non-invasive EEG have abnormally high nonlinearity. Our findings verify the significantly higher nonlinearity of the brain activities during seizures than that of the healthy control subjects and the seizure-free patients.

As for the seizure-free EEGs in the two groups, the results are inconsistent that the NJGH seizure-free epileptic patients have significant lower time irreversibility of EEG than the healthy volunteers ($Y_s$, $p<0.003$; $\chi^2$, $p<0.01$) while those of Bonn have evidently higher time irreversibility than the two healthy groups ($Y_s$, $p<0.002$; $\chi^2$, $p<0.003$). As for the NJGH EEG, nonlinear features characterized by other methods in previous researches [3, 44] indicate that the seizure-free epileptic EEG have lower nonlinear dynamics or complexity than the control EEG, which is further verified in our contribution. The reduced nonlinearity of the epilepsy may indicate the long-term damage to nonlinear behaviors led by the brain disease. However, the higher nonlinearity of Bonn epileptic seizure-free EEGs in our analysis is also in line with the original literature and some following reports. In the original introduction of the Bonn EEGs [4], nonlinear prediction error and correlation dimension of the seizure-free sets are inbetween the healthy (the lowest) and the seizure (the strongest) sets. The nonlinearity characterized by other measures, such as the missing or-dinal patterns [34] or networked irreversibility [45], also have the same conclusions. Reasons that might account for the inconsistence, like the multi scale theory, epileptic circadian rhythms or data collection, are analyzed in the following subsection.

B. Nonlinearity of epileptic EEGs during seizure-free intervals

As for the inconsistent conclusions of nonlinearity series-free epileptic EEGs, physical reason that may ac-
count for the contradictory findings might be the multiscale theory \[18, 46\]. The increase of temporal asymmetry of Bonn EEGs with epilepsy in seizure free interval might lie in that the inherent multiple time scale in the healthy brain electric activities is neglected by single-scale measures. We conduct multiscale time irreversibility of \(Y_s\) for the Bonn EEGs, in Fig. 8 and the NJGH EEGs, in Fig. 9.

As for the Bonn EEGs, the seizure data set E has the highest nonlinearity while changes dramatically to close to other data sets. The seizure-free sets of C and D and the healthy A and B have no evident changes in their relationships and the discrimination are unacceptable (\(p > 0.5\)) with the increase scale factors. Of the NJGH epileptic EEGs, when \(m = 2\), the healthy have lower time irreversibility than the epileptic under some scale factors while the discriminations are not acceptable (\(p > 0.05\)). The healthy and epileptic EEGs’ \(Y_s\) increase with scale factor when \(m = 3\) and 4, however, the discriminations between them deteriorate with scale factor (\(p > 0.5\)). Through the adjustment of scale factor, we do not have reliable conclusions about the inconsistent nonlinearity of seizure-free EEGs. Therefore, the multi-scale theory should not be the determinant reason accounting for the inconsistent time irreversibility of seizure-free EEGs of the two groups of brain electrical activities.

From the physiological or pathological perspective, the manifestation of cyclic rhythm \[17\] in human epilepsy may have an impact on the nonlinearity detection of seizure-free EEGs. The rates of the seizures oscillate in the cycles of days, months, and years, and seizure cycles are subject to various factors including stress levels, sleep quality, and other innate biological drivers and unknown reasons \[48, 49\]. After patients’ seizure onset, partial seizures may also remain localized and cause abnormal brain nonlinear activities \[27\]. The time between the seizure-free brain recordings to the seizures play important role in the brain nonlinear dynamical features detection. The intervals of the NJGH epileptic patients from brain recordings to the nearest seizures are around 20 to 30 days. The lower time irreversibility of the NJGH epileptic EEGs might suggest the long-term negative effects of the neural disorder on the brain nonlinearity. The exact time between the seizure data E and the seizure-free sets C and D are not available. Considering the circadian and circaseptan rhythms in human epilepsy, the patients in different stages of epilepsy might have totally different brain behaviors, leading that the two kinds of seizure-free EEGs could contain different nonlinear characteristics although both are collected in seizure-free intervals. From the highest nonlinear activities during seizures to the lower nonlinearity than the healthy, the nonlinear dynamics of the brain behaviors maybe also in line with circadian rhythms, and the brain activities during different epileptic stages, although all in seizure-free

FIG. 8. Multi-scale \(Y_s\) of Bonn EEG. Due to the limit of data length, we set dimension to 2 and 3.

FIG. 9. Multi-scale \(Y_s\) of NJGH EEGs.
intervals, should show totally different nonlinear features.

There are differences in EEG collection between the two groups of epileptic EEGs, and the difference may also be responsible for the inconsistent findings. Epileptic EEG of the Bonn data are recorded by the invasive intracranial electrodes from the epileptogenic (set D) and hippocampal formation of the opposite hemisphere (set C) while the NJGH EEG and the healthy Bonn EEGs (sets A and B) are collected by surface scalp electrodes from the whole brain regions. And the sampling frequency of the NJGH (512 Hz) and Bonn (173.61 Hz) EEGs are also different.

We show that the multiscale theory is not the reason leading to the contradictory nonlinearity of seizure-free epileptic EEG, however, our assumption of circadian rhythms of nonlinearity requires further targeted studies, and there might be other possible reasons like data collection that contribute to the mixed results remaining to be discovered.

V. DISCUSSIONS

In symbolic time series analysis, the forbidden words or permutations play important role in nonlinear dynamics analysis, especially the time irreversibility. Forbidden words or permutations have been paid much attention, however in time irreversibility, some scholars neglect them. When we consider vectors with short length, the might be no existence of forbidden permutation. For example, when \( m=2 \), there are only two order patterns, up and down, that are generally exist in dynamical systems. When \( m=3 \), the nonlinear Lorenz series have all of the 6 (3!) order patterns that each permutation its their symmetric form and coexist in the forward and backward series. If we take more values into consideration, the forbidden permutation have significant effects on nonlinearity detections, like the logistic and Henon chaotic processes that almost have no symmetric permutation or same forward-backward order patterns when \( m>5 \). Therefore, the classical measures for probabilistic difference based on division in fact are not suitable for quantifying time irreversibility, and the subtraction-based measures like \( Y_s \) and chi-square statistics \( \chi^2 \) should be more rational choices.

The forbidden permutation not only impacts the simplified quantification of time irreversibility, it also contains important structural or dynamical information about dynamical processes \( [S,[5,67] \), which is further verified by our time irreversibility detection of the chaotic series and epileptic EEGs. Of the three chaotic series, temporal asymmetries have similar changes to the rate of single permutation that the step increase of \( R_u \) in logistic and Henon series and the seemingly linear growth in Lorenz series with \( m \) are shared by \( Y_s \) and \( \chi^2 \). \( R_u \) of the Gaussian process are all 0 for the forward-backward and the symmetric permutations, which are associated with the reversible feature. The bigger \( R_u \) are also in line with the higher time irreversibility of NJGH healthy EEG. As for Bonn EEG, the highest rates of single permutation are also consistent with the highest time irreversibility although the seizure-free sets of C and D have lower rates of single order patterns than the healthy sets of A and B. In simplified time irreversibility analysis, particularly the symbolic approaches, forbidden sequences or words that might have significant impacts on nonlinear dynamics analysis should be taken into serious consideration.

VI. CONCLUSIONS

We employ the subtraction-based parameters, \( Y_s \) and \( \chi^2 \), to measure probabilistic difference of symmetric permutations for time irreversibility of epileptic EEGs. In nonlinear model processes and real-world physiological data, there are existence of forbidden permutation suggested by the rates of single order patterns, and \( R_u \) has consistent results with the \( Y_s \) and \( \chi^2 \), indicating its close association to the nonlinearity of time irreversibility. The manifestation of nonlinearity of whether diseased or healthy brain electrical activities is verified, and the high time irreversibility of the EEG during seizures characterized by abnormal neuronal firing is highlighted. Our findings provide valuable information for elucidation of epileptic brain endogenous mechanisms.

As for the inconsistent findings about the nonlinearity of seizure-free epileptic EEGs, we show that the multiscale theory is not the reason. We try to elucidate the inconvenience from physiological or pathological perspective of epileptic cyclic rhythms, and we assume that the human epilepsy is characterized with circadian rhythms in the nonlinearity of brain activities. However we would like to emphasize that our proposed interpretations should be verified by more representative number of epilepsy patients and more targeted experimental methods.

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