

MEASUREMENT OF THE COMPLEXITY FOR LOW-DIMENSIONAL NON-LINEAR STRUCTURE OF RESPIRATORY NETWORK IN HUMAN

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Abstract: The nonlinear dynamical characteristics of respiratory variables recorded from male subjects during rest were analyzed. Three fundamental techniques were employed: correlation dimension D_2 and the largest Lyapunov exponent LLE calculations as well as the surrogate data analysis. Furthermore, a novel approach named C_0 complexity was introduced, which may improve the understanding of the underlying physiological processes of the autonomic/automatic nervous systems. The results suggest that although the pattern of breathing in the resting human might have properties consistent with that of a chaotic system, the evidence is not conclusive because the LLE values in original data do not differ from the LLE values in the surrogate data. However, the data suggest that the values of C_0 complexity of several respiratory variables are significant. The results also suggest that many aspects of particularly breathing may show a non-random complex nature. Moreover, this method may allow us to quantify changes in the complexity of respiratory variables in response to challenges in a novel manner.

Key Words: Correlation dimension; Largest Lyapunov exponent; Surrogate data analysis; C_0 complexity; Respiration

1 Introduction

The pattern of breathing contains rhythmic components that are generated and reflexly modulated within the respiratory neural networks of the brain stem in a nonlinear manner. The networks of these units with oscillatory behavior interact in a complex way to produce respiratory rhythms, which are either further organized by a pattern generator or might be self-organizing^[1]. As the result, the complex time courses of the respiratory system may be induced by the interactions among the units in the processes, however, the underlying sub-processes include well-determined behavior. Nonlinear dynamics

have been shown to be important in describing a large number of complex physiological systems. Therefore, it is presumed that these complex time courses can be characterized more adequately by nonlinear dynamical analysis rather than by linear time series analyses^[2-4].

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Most investigations of the dynamical behavior of biological systems have employed fractal dimension and /or the largest Lyapunov exponent measurements to distinguish whether or not the underlying system's behavior is deterministic. There were several previous reports related to the study of breath pattern using chaotic dynamics. Donaldson^[5] assessed the respiratory behavior in humans using the largest Lyapunov exponent analysis. He studied resting adults and concluded that resting respiration was chaotic. However, this approach could not distinguish a nonlinear dynamical system from linearly filtered noise. Pilgram et al^[6] employed correlation integral and correlation dimension techniques and analyzed the respiratory time series of infants during rapid-eye-movement (REM) sleep. Their conclusion was that breathing during REM sleep was deterministic. Furthermore, Small et al^[7] utilized a new technique for calculating correlation dimension of breath-by-breath data to measure the respiratory patterns of infants during quiet sleep. They concluded that their data were consistent with respiration being chaotic. In reaching the conclusions, the authors in both investigations employed the surrogate data techniques for calculating the correlation dimension. Sammon et al.^[8-10] analyzed respiratory data of rats in their series studies. From the results they suggested that the respiratory system behaved as an oscillator with a single degree of freedom in anesthetized vagotomized rats. What the respiratory behavior became more complex with the vagus intact indicated the underlying system possibly exhibited low-order chaos.

However, whether a process is chaotic or not is subject to potential errors in computation of indexes of chaos. Indeed, several authors have cautioned about the conclusion that chaos exists simply from satisfying a single criterion of chaos^[11,12]. Undeniably, the correlation dimension and the Lyapunov exponent, as sophisticated mathematical techniques, have been developed as powerful adjuncts to the graphical analysis of

phase space. However, there may be several limitations of these measurements. For example, a large number of data points are required to ensure numerical convergence; the algorithms are very sensitive to the effects of noise; a stationary time series is also theoretically required for using these algorithms. All of the limitations might cause enormous erroneous conclusions. Obviously, human breath-by-breath data sets will be noisy because of multiple factors, including voluntary control, interacting to control respiration, and they usually will be short because it is difficult to constrain human volunteers within specific conditions for long periods of time to obtain representative data^[13].

In this study, three different approaches were employed to explore whether or not the pattern of breathing is deterministic. Firstly, the correlation dimension of the breath-by-breath data was calculated, which was a measure of the complexity of the process being investigated and characterized the distribution of points in the phase space. Secondly, the largest Lyapunov exponent was estimated, which was a measure of the predictability of the process and quantified the exponential divergence of initially close state-space trajectories. Thirdly, surrogate data were generated from the original time series and analyzed using the same approaches applied in the original data. The surrogate data analysis has proven to be a valuable test of nonlinear deterministic systems versus uncorrelated noise^[11]. The results suggested that, particularly, the pattern of breathing in the resting human might have properties consistent with that of a chaotic system. However, the evidence is not conclusive because the values for Lyapunov exponents of the raw data do not differ from the values for Lyapunov exponent of the surrogate data. The issue has arisen as to how to describe the underlying system of breath-by-breath time series when sufficient evidence could not be obtained by chaotic approach. Can one measure the characteristics of the system behaviour using

different approach of the nonlinear dynamics, such as complexity analysis and how does one measure it?

The present study aimed to assess patterns of fluctuations of the breath-by-breath data using nonlinear dynamics. For this purpose, we introduce a recently developed complexity approach named C_0 complexity, which may improve the understanding of the underlying physiological processes of the autonomic/automatic nervous systems. The complexity analysis has been successfully applied in the investigation of information transmission in human cerebral cortex^[14-16], EEG studies in epilepsy patients^[17], heart rate variability sequence analysis^[18] and inspiratory airflow pattern induced by visuomotor reaction time task^[2]. Furthermore, a novel measurement of complexity named C_0 complexity has been proposed for overcoming the deficiency in doing complexity calculation. As we know, when calculating complexity a series needs coarse graining which usually results in losses of lot of significant details. Complexity C_0 may avoid such a deficiency by defining C_0 as a ratio of the areas of the random component with time axis and the whole complex series with time axis^[19].

2 Method

2.1 Data collection and preparation

Seven healthy male volunteers who were free of cardiopulmonary disease were studied. Recordings of tidal volume (V_t), inspiratory (T_{ins}) and expiratory (T_{exp}) durations, breath frequency (Bf), ventilation (V_e), breath-by-breath O_2 uptake (VO_2), CO_2 output (VCO_2) and respiratory exchange ratio (RQ) were made over one hour in resting state. Data were sampled at a rate of 200 Hz using a mass spectrometer (QP9000 AIRSPEC, Biggin Hill, UK). Data from the first 5 min of each run were discarded. Data are $\bar{x} \pm SEM$ and T -tests statistically were used to show significance from zero ($P < 0.05$).

A procedure described by Hathorn^[20] was used to obtain equal space data. The value of each breath measurement was taken as a constant and a continuous time histogram of all variables was constructed. The amplitude of the histogram was then determined at 0.4 s (2.5 Hz) intervals to produce an equal spaced time series.

To eliminate some of high frequency components introduced by representing the breath data as discrete step following changes, the time series were passed through a Hanning filter using the following function:

$x(k) = x(k-1) \times 0.25 + x(k) \times 0.5 + x(k+1) \times 0.25$, where $x(k)$ was a data point.

2.2 Correlation dimension

Grassberger and Procaccia^[21] developed an algorithm to yield the correlation dimension D_2 , which was defined as a dimension with non-integer values. In determining this measure, pairwise distances are calculated by selecting spheres centered at randomly chosen reference points on the attractor. The numbers of neighbors falling within a sphere of radius r are counted by successively higher values of r . Experimentally, the slope of a plot of the number of points inside a sphere of radius r (i.e. $C(r)$ plotted against the radius r ; both in logarithmic scales) yields the correlation dimension D_2 ^[22].

2.3 The largest Lyapunov exponent

This is a fundamental measure of the dynamic nature of a system that completely described the characteristics of the trajectories in phase space^[23]. Lyapunov exponents may be negative, zero or positive. If the exponent is negative, the trajectories converge over time and the system is not chaotic. If the exponent is positive, then the trajectories diverge; that is, insignificant differences in the initial conditions become significant over time. In this situation, the evolution of the trajectory is sensitive to initial conditions and, by definition, chaotic under the condition of no noise contaminations for original signals. In the present study, the largest Lyapunov exponent was estimated via the fix-time

evolution program of Wolf and colleagues^[23].

2.4 Surrogate data analysis

Theiler et al^[11] developed an approach by which surrogate data were generated from the original data. It allows testing of the null hypothesis that the pattern of variation is a result of linearly autocorrelated gaussian noise. Fast Fourier transform (FFT) was employed to transform the original data into frequency domain. The amplitude components of the FFT analysis were retained, and the phase relationships were randomized prior to using an inverse FFT to generate the surrogate data.

2.5 C_0 complexity

In order to define C_0 , we assume that complex time series (CTS) could be divided into two parts: regular and random components. If the regular component of CTS can be obtained, then the random part of CTS will be the difference between the whole CTS and its regular component. Therefore, the C_0 is defined as a ratio of the areas of the random component and CTS with their time axis. If $C_0=1$ then CTS is completely random. If $C_0=0$, then CTS is completely regular. In this study, the frequency characteristics of CTS were used to determine the regular component. All variables had C_0 which was significantly greater than zero; that is they all showed complexity to different degrees.

2.6 Statistics

All the data are expressed as the $\bar{x} \pm SEM$. Data were analyzed using the t -test and significant differences between the raw data and the surrogate data are presented when $P < 0.05$.

3 Results

Figure 1A shows original traces of tidal volume calculated in breath-by-breath data in one male subject with a 200 Hz original sampling frequency over 55 min. Figure 1B gives the two-dimensional return maps generated from the tidal volume time series during resting state in the subject. The two co-ordinates of each point were calculated as $x(t)$ and $x(t+\tau)$, where τ is time lag and was 1 breath data point. Figure 2 presents the saturation curves of the correlation dimension (Fig. 2A) and the largest Lyapunov exponent (Fig. 2B) computed from the tidal volume for both original breathing signals and their surrogate data in the group of seven subjects. The correlation dimension values remain relatively stable over the range of embedding dimension from 8~12 for both original and surrogate data. It can be seen that the curve of original data was significantly ($P < 0.05$) lower at all points compared with those obtained from their surrogate data. However, in

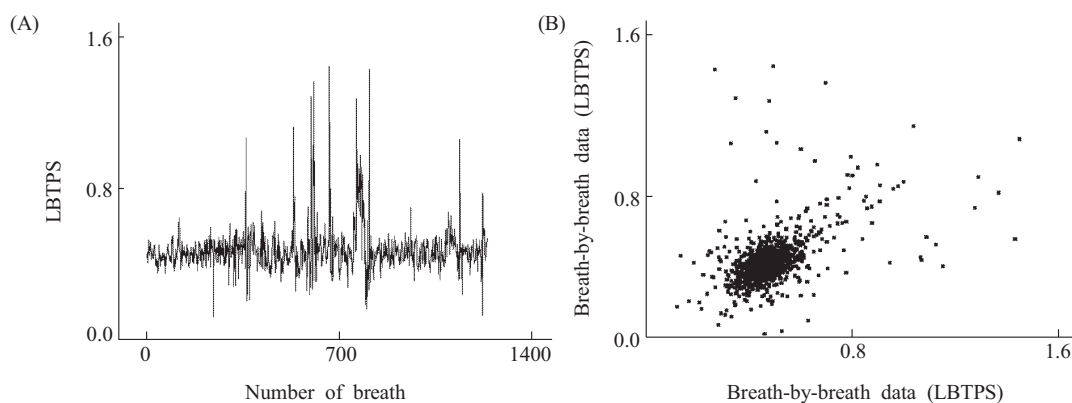


Fig.1 (A) The traces of tidal volume calculated for each breath in one male subject over 55 min; (B) Two-dimensional phase space portraits (return map) using the breath-by-breath data, $x(t)$, of tidal volume. The two co-ordinates of each point were calculated as $x(t)$ and $x(t+\tau)$, where τ is time delay and equals 1 for the variable

Figure 2B, the two curves generated from original and surrogate data were much closer together and were not significantly different from each other.

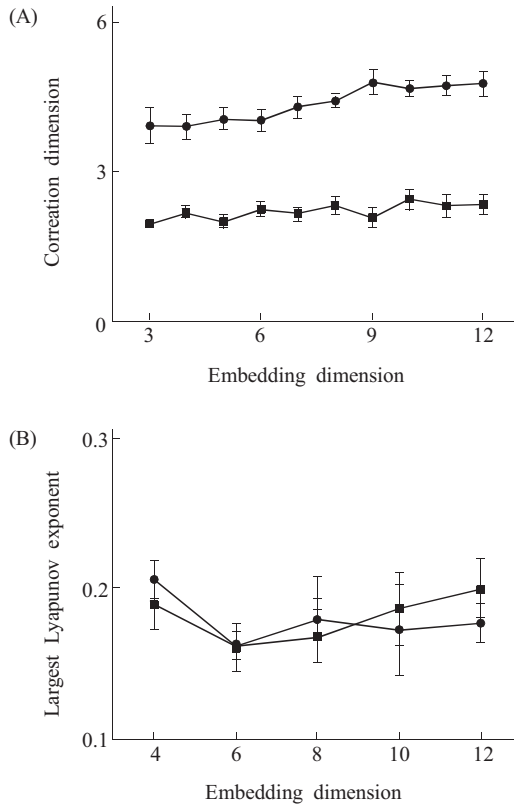


Fig.2 Averaged group values obtained from the time series of tidal volume in seven male subjects. (A) Correlation dimension D_2 ; (B) The largest Lyapunov exponent LLE . ■: Real data; ●: Surrogate data

Table 1 gives the group values of the correlation dimension and the largest Lyapunov exponent of eight respiratory variables for both raw and surrogate data. The values of D_2 for almost all of variables in their original form are around 2.1 to 2.7, except for respiratory exchange ratio RQ . On the contrary, the values of their surrogate data are ranged from 4.6 to 6.5, which are significantly different from that of the raw signals ($P < 0.05$). There is also significant difference between D_2 of original RQ and that of its surrogate data (1.4 ± 0.10 vs. 3.8 ± 0.20 , $P < 0.05$). For most of respiratory variables, except for RQ , the values of the largest Lyapunov exponent of original data are positive ranged from 0.19 to 2.8, which are more or less similar to that of the surrogate data. The value of the raw RQ data was negative (-0.02 ± 0.02).

Figure 3A presents the original traces of respiratory exchange ratio RQ calculated for breath-by-breath data from one male subject (as same as Figure 1) over 55 min. Figure 3B shows the traces of RQ after resampling at 2.5 Hz. The regular part of CTS for RQ can be found in Figure 3C in which the frequency characteristics of the CTS were used to determine its regular component. We used both fast Fourier transform (FFT) and inverse-FFT implemented in Matlab

Table 1 Largest Lyapunov exponents (LE_r & LE_s : real and surrogate data, bits/s) and correlation dimension (D_{2r} & D_{2s} : real and surrogate data) in seven male subjects

	LE_r	LE_s	D_{2r}	D_{2s}
V_t	0.19 ± 0.04	0.18 ± 0.03	2.3 ± 0.10	$4.7 \pm 0.30^*$
T_i	0.21 ± 0.05	0.14 ± 0.02	2.7 ± 0.10	$5.2 \pm 0.30^*$
T_e	0.23 ± 0.02	0.16 ± 0.03	2.5 ± 0.10	$6.5 \pm 0.70^*$
B_f	0.18 ± 0.03	0.15 ± 0.02	2.4 ± 0.10	$6.4 \pm 0.30^*$
V_e	0.21 ± 0.03	0.19 ± 0.02	2.1 ± 0.20	$4.6 \pm 0.20^*$
VO_2	0.28 ± 0.07	0.23 ± 0.04	2.3 ± 0.10	$4.9 \pm 0.40^*$
VCO_2	0.25 ± 0.02	0.22 ± 0.03	2.3 ± 0.10	$5.9 \pm 0.40^*$
RQ	-0.02 ± 0.02	0.09 ± 0.03	1.4 ± 0.10	$3.8 \pm 0.20^*$

Values are $\bar{x} \pm SEM$. *, significant difference, raw data vs. surrogate data ($P < 0.05$)

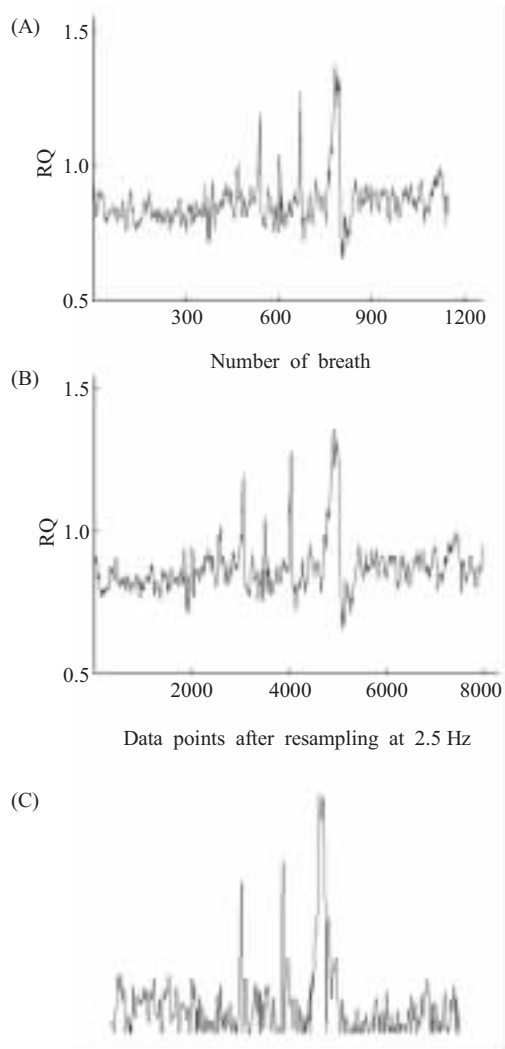


Fig.3 (A) Original traces of RQ (respiratory exchange ratio) obtained from for one male subject; (B) The traces of RQ after resampling at 2.5 Hz; (C) Traces of the regular part of the complex time series (CTS)

(v5.2, The Math Works, Inc., 1998) to achieve this procedure. Complexity C_0 measurements of the time series of the eight respiratory variables, which includes breath-by-breath O_2 uptake (VO_2) and CO_2 output (VCO_2), respiratory exchange rate (RQ), inspiratory and expiratory duration (T_I & T_E), breath frequency (BF), tidal volume (V_t) and ventilation equivalent (V_e), are presented in Figure 4. All variables have C_0 , which are significantly greater than zero; that is, they all show complexity of different degrees. However, the C_0 value for RQ is less than 0.05, that is, it is more regular, rather than random signals. On the other

hand, several respiratory variables present a much more random nature, with a C_0 of >0.2 .

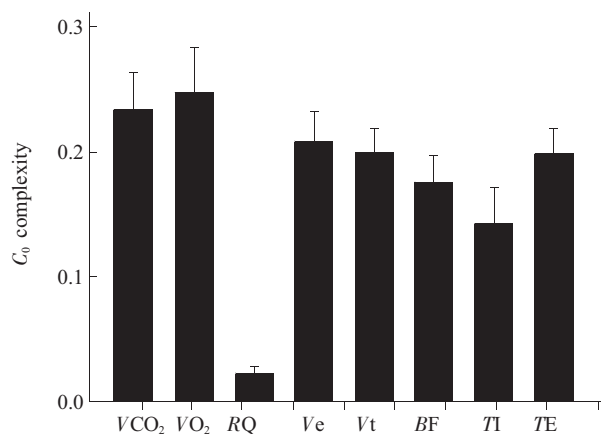


Fig.4 Complexity (C_0) of 8 respiratory variables including breath-by-breath O_2 uptake (VO_2) and CO_2 output (VCO_2), respiratory exchange rate (RQ), inspiratory and expiratory duration (T_I & T_E), breathe frequency (BF), tidal volume (V_t) and ventilation equivalent (V_e). All data are $\bar{x} \pm SEM$ and significant from zero ($P < 0.05$)

4 Discussion

Recently, there have been many claims of evidence of chaos in a wide range of physical and physiological systems. Because of the implication that a chaotic system is deterministic, presentation of evidence for chaos could mean that the system under study can be described by relative simple mathematical relationships. But there have been many presentations of incorrect application of the methods of nonlinear mathematics. In almost every case, the weak link in the argument was the supposition that a single test providing evidence of chaos was adequate. The method of surrogate data analysis has provided the opportunity to evaluate a relationship by testing the null hypothesis that chaos is present in the randomly generated data. Theiler et al^[11] evaluated the Lyapunov exponent algorithm of Wolf et al^[23]. They found that the algorithm did not yield realistic values with surrogate data. Therefore, it should not be surprising that there were more positive Lyapunov exponent with surrogate data in the results (Table 1). The

implication is that the ventilatory and gas exchange variables might have been chaotic, but there is no evidence based on the analysis performed.

The findings of the present study would suggest that the pattern of breathing in the resting human might have properties consistent with that of a chaotic system (i.e. lower D_2 in real data compared to surrogate data and positive Lyapunov exponents for each of the respiratory variables). However, the evidence is not conclusive because the algorithm of Wolf et al for determining Lyapunov exponent failed to provide a reliable estimation of the exponents for the surrogate data (Table 1 and Figure 2). Furthermore, noise contaminations always increase the dimensional complexity of the real data, and almost any experimental data will exhibit noninteger correlation dimension^[7]. Therefore, caution needs to be applied as it has been pointed out several times that concluding the presence of chaos simply on the basis of results from one test can be misleading^[11,12]. No matter how the pattern of breath-by-breath sequence in resting human occasionally appears to have properties consistent with deterministic system, the evidence is not strong. It is no doubt that there are some limitations of attempting to study patterns of breathing in human. In contrast to the rat model studied by Sammon and his co-workers^[8-10], human subjects have the ability to voluntarily over-ride the respiratory controller. Further, even though we attempted to strictly control the environment, the possibility of external cues influencing the pattern of breathing cannot be eliminated^[13].

In the early fifties von Neumann raised the concept of complexity and its importance. Kolmogorov^[24] wrote the real description of definition of complexity, i.e. the algorithmic complexity. Kaspar and Schuster^[25] gave the procedures for computing complexity. Xu and his co-workers^[15] defined two complementary complexity measures, which were C_1 complexity and C_2 complexity, base on Kolmogorov

complexity algorithm. To avoid coarse graining during C_1 and C_2 complexity calculation, they^[26] proposed a new measurement of complexity, C_0 complexity, which was defined as a ratio of the areas of the random component with time axis and the whole complex series with time axis. This novel approach has been successfully applied in studying EEG mutual information^[26] and analyzing inspiratory airflow curve responding to the influence of a simple visuomotor reaction time task^[2]. As an alternative way to measure breath-by-breath sequences in human subjects we, in this study, have presented the approach of the complexity measurement, C_0 complexity measurement. Although such measures are not suited to provide direct evidence of deterministic chaos comparison with the estimation of correlation dimension and Lyapunov spectra for respiratory time series, they might allow the classification of respiratory dynamics and the identification of changes in respiratory complexity^[2].

Our results suggest that the C_0 complexity of the respiratory variables is significant. This method may allow us to quantify changes in the complexity of respiratory variables in response to challenges in a novel manner. The results also suggest that many aspects of particularly breathing may show a non-random complex nature. Moreover, the measurement of the C_0 complexity, by which the nonlinear behavior of respiratory variables could be interpreted with regards to terms such stochastic and regular deterministic, may provide significant information about respiratory processes. However, the mechanism responsible for this complexity is unknown, such as whether it represents chaotic "system" noise or serves a deterministic function in central nerve system (CNS) driven respiratory control.

In conclusion, this report has addressed the limitations of previous studies that have examined whether respiratory is chaotic. Unlike in most previous studies, we used surrogate data method, not only in measurement of the largest Lyapunov

exponent but also correlation dimension, to check whether the apparently chaotic behaviour was due to linearly filtered noise. The results suggest that although the pattern of breathing in the resting human might have properties consistent with that of a chaotic system, the evidence is not conclusive because the *LLE* values in original data do not differ from the *LLE* values in the surrogate data. However, the data suggest that the C_0 complexity of several respiratory variables is significant. Moreover, this method may allow us to quantify changes in the complexity of respiratory variables in response to challenges in a novel manner.

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低维非线性呼吸系统的复杂性计算

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摘要: 首先应用混沌计算方法: 关联维数 D_2 和最大李亚普努夫指数 LLE , 以及替代数据分析法, 分析了男性受试者在平静状态下记录的呼吸系统时间序列的混沌特征。同时, 在呼吸变量的非线性分析中首次引进了被称为 C_0 复杂度的新技术。它的应用将有助于更好地理解自主神经系统中潜在的生理过程。 LLE 计算的替代数据分析结果显示, 没有明确的证据可以证实受试者在平静状态下的呼吸时序的模式是混沌的。然而, C_0 复杂度的计算结果却表明大部分呼吸系统的时间序列表现为某种程度的复杂性, 这为呼吸模态的非随机变化的属性提供了部分的实验和计算证据。更进一步, C_0 复杂度有可能以一种新的、确定的方式给出呼吸系统在激励状态下的量化改变。

关键词: 关联维数; 最大李亚普努夫指数; 替代数据分析; C_0 复杂度; 呼吸
中图分类号: Q412

第三届全国神经信息学研讨会征文通知

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