Event and time-scale characteristics of heart-rate dynamics

UnCheol Lee* and Seunghwan Kim†
Asia Pacific Center for Theoretical Physics & Nonlinear Complex Systems Laboratory, Department of Physics, Pohang University of Science and Technology, Pohang, 790-784, Korea

S. H. Yi‡
Department of Computer Aided Science, Inje University, Gimhae 621-749, Korea
(Received 19 December 2004; published 24 June 2005)

The cardiac system shows various scale dynamic activities from secondly to yearly. Therefore multiple time-scale characteristics of heart dynamics have received much attention for understanding and distinguishing healthy and pathological cardiac systems. In this paper we expand the multiple time-scale analysis into event and time scales to investigate scale characteristics in healthy and pathologic cardiac systems. To do this, we define a measure based on symbolic dynamics, which calculates complexity at each time and event scale, called the unit time block entropy (UTBE). This measure allows a reliable comparison of experimental data through matching the number of words and the total measurement time at the same time for all RR interval sequences which are composed of the time durations between consecutive R waves of electrocardiograms. We apply the UTBE to the healthy heart-rate (HR) group and pathological HR groups and find that the RR interval acceleration is more effective than the RR interval in distinguishing each group. And we also find that the normal and pathological HR groups are clearly distinguished in some specific event and time-scale regions.

DOI: 10.1103/PhysRevE.71.061917 PACS number(s): 87.19.Hh, 87.10.+e, 89.75.−k

I. INTRODUCTION

During the last decade, heart dynamics based on nonlinear dynamics theory has been actively investigated [1–3]. However, the direct application of chaos theory encountered difficulties due to intrinsic problems such as limited data, noise contamination, and nonstationarity in physiological data such as the heart rate (HR). Therefore recent research has focused more on irregularity and complexity than chaos and determinism as a language to understand the HR [4]. It is shown that the cardiac system shows various time scales: the yearly scale for an age related change associated with the functional maturation of the cardiac muscle, the monthly scale for a seasonal change associated with temperature fluctuation and the change of hormonal profile, the daily scale for the 24 h change of the autonomic nervous system, the hourly scale for the 1–3 h hormonal change, the minutely scale for the change of circulating blood, and the secondly scale for the activity of the reflex mechanisms involved in cardiovascular control [5]. Thus the highly complex and nonlinear characteristics of the HR may appear due to scale-invariant and multiscale properties of beat-to-beat fluctuations of heart rate variability (HRV). Using these properties, the normal and pathological HRVs have been practically distinguished [6]. This multitime-scale concept could provide an answer on why the healthy HR dynamics, which contains long range correlations, is more complex than that of the pathological HR, which is associated with the random output. To justify this, the multiscale entropy, which quantifies the multitime-scale complexity in the HR, was introduced and applied to the robust classification between the normal HRV group and the pathological HRV groups [7–10].

In order to treat the complex heart rhythms, various techniques based on information theory have been widely applied [11,12]. As a measure of complexity, different definitions of the entropy have been introduced based on symbolic dynamics. Although it is not easy to find the generating partition in real experimental data, which is still an open problem, several studies have suggested that an appropriate symbolization process could provide useful results, in particular, in HRV analysis [13]. The symbolization process loses some amount of detailed information but some of the invariant, robust properties of dynamics survive [14–16]. Cysaz *et al.* showed that the transformation into the binary sequence extracts solely dynamical properties of the RR series which are composed of the time durations between consecutive R waves of the electrocardiogram, and that the symbolization of differences between RR intervals eliminates nonstationarities resulting from a minor bias underlying the RR tachogram [17]. Some complexity measures based on symbolic dynamics, in which four symbols from the RR interval and the RR interval acceleration were chosen, may be used to define the risk for the sudden cardiac death from the HRV [18]. Two parameters from symbolic dynamics for measuring the low variability and regularity in the HRV can be used to discriminate VT-VF patients with implanted cardioverter defibrillators [19]. If a threshold for symbolization is suitably chosen to reflect the whole internal complex structure of the dynamical system, it is possible to consistently quantify the complexity of physiological signals and noisy signals [20].

Most conventional linear and nonlinear measures fix the size of the RR interval due to the algorithmic constraints. However, it may cause a large difference in total measurement time between all HR data sets being compared as in

*Electronic address: uclee@postech.ac.kr
†Electronic address: swan@postech.ac.kr
‡Electronic address: yish@inje.ac.kr

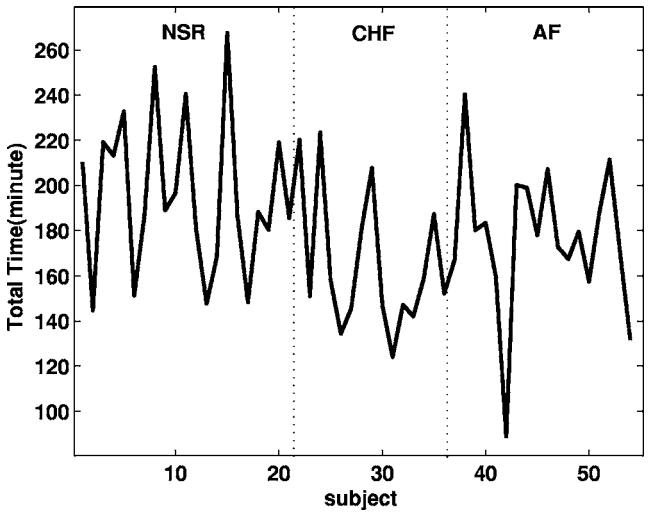

FIG. 1. The variation of measurement time after fixing the number of RR interval sequences in healthy and pathologic groups. The mean and standard deviation of 54 subjects is 180.92±34.825 (min), it shows a large variation. [normal sinus rhythms (NSR), congestive heart failure (CHF), and artrial fibrillation (AF).]

Fig. 1. Particularly, it could influence a nonlinear measure due to the nonstationarity and noise involved in the additional HR periods, which is very difficult to estimate. Conversely, fixing the total measurement time of the RR interval makes it difficult to directly compare nonlinear measures because of the different size of the HR data set. To indirectly handle this fundamental problem of interval data, a few methods such as resampling, appropriate data selection, and correction of the finite sample effect have been introduced.

The resampling method makes the size of the HR data set for comparison to be the same through an even sampling from RR interval sequences interpolated by various fitting methods, after fixing the total measurement time. However, it inevitably produces a number of unexpected artificial data in addition to the original RR sequences, for example, the distortion of the short term correlation of HR data [21]. As in the case of the other methods, if the interval and the duration of HR data deviate more than 20% from those of other HR data sets compared, the HR data is excluded from the analysis. However, this method could result in an artificial homogenous HR data set and it cannot match the size and measurement time at the same time [22]. In particular, when a nonlinear measure such as the approximate entropy (APEN), which depends significantly on the number of data, is used without matching the number of data and the total measurement time at the same time, a reliable comparison between HR groups could not accomplished. In another approach, we may fix the total measurement time and then correct the finite sample effect by estimating the distribution of sampled data, adding a correction term into the entropy estimation. In this case, according to how precisely the distribution of sampled HR data is estimated, which is not an easy task, in practice, the accuracy of entropy estimation is determined [23].

Theoretically, if time interval dynamics of the stationary system with a sufficiently large number of data satisfies one-to-one correspondence with original dynamics, the nonlinear measures such as the Lyapunov exponent and the fractal dimension can reliably approximate those of original dynamics, although data sizes are different [24,25]. But in the case of HR, since it is intrinsically nonstationary and has a limitation of the finite data size, we should take into account matching the size and the total measurement time together before applying any nonlinear measures.

In this paper we expand the multiple time-scale analysis into event and time scales to investigate scale characteristics in healthy and pathologic cardiac systems. We define a measure based on symbolic dynamics, which calculates complexity at each time and event scales, called the unit time block entropy (UTBE). This measure allows a reliable comparison of experimental data through matching the number of words and the total measurement time at the same time for all RR interval sequences. We apply the UTBE to the healthy HR group and the pathological HR groups and find that the RR interval acceleration is more effective than the RR interval in distinguishing each group. By scanning the parameters of the event and time scales we also find that the normal and pathological HR groups are clearly distinguished in some specific event and time-scale regions. We show that the UTBE shows better classification performance than the linear methods and the conventional multiscale entropy. We find that among two types of scale used, the event scale provides us with more important information for the efficient classification of normal and two pathologic HR groups. The practicality of our approach is tested by scanning the event and time-scale and computing the sensitivity and the specificity of the classification. Our method is quite general and can be extended to the symbolic dynamics analysis of other complex time series.

II. SIMPLE BLOCK ENTROPY (SBE) AND UNIT TIME BLOCK ENTROPY (UTBE)

To quantify event and time-scale characteristics of the heart rate, we define an entropy based on symbolic dynamics. First, we define a word sequence from the RR interval sequence. To construct a word, we use two different methods; the block windowing method and the unit time windowing method. In the block windowing method, each word is composed of RR interval values of the same size which are symbolized by the RR interval threshold or the RR acceleration threshold. In unit time windowing method, each word is composed from a unit time window, so the number of symbols involved in each word can be different.

The RR interval sequence is given by $TI=\{x_1,x_2,\ldots,x_i,\ldots,x_n\}$ and the RR interval acceleration sequence by $\Delta TI=\{t_1,t_2,\ldots,t_i,\ldots,t_{n-1}\}$, $t_i=x_{i+1}-x_i$. A word is defined by

$$v_i=\{s_i s_{i+1}\cdots s_{i+j}\cdots s_{i+n}\} \quad \text{(block)}, \tag{1}$$

$$w_i=\{s_i s_{i+1}\cdots s_{i+j}\cdots s_{i+n(i)}\} \quad \text{(unit time)}, \tag{2}$$

where

$$s_{i+j}=\begin{cases}0, & \text{if } |t_{i+j}|\leqslant\tau\\ 1, & \text{if } |t_{i+j}|>\tau.\end{cases} \tag{3}$$

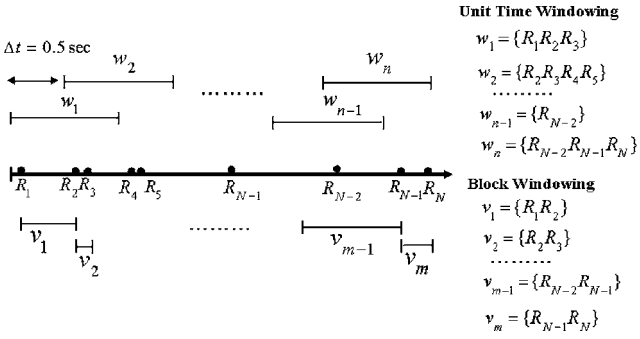

FIG. 2. Two different ways to compose a word sequence from a RR interval sequence. The upper case presents how to compose a word sequence from a RR interval sequence with the unit time windowing method, on the other hand, the lower case presents how to compose a word sequence with the block windowing method. The former focuses on unit time to define a word but the latter focuses on the number of symbols, in this example, the block size is $n=2$, to define a word.

For the case of the unit time windowing method, the number of symbols, $n(i)$, can be different at each unit time-scale U_T, satisfying $\Sigma_{k=i}^{i+n(i)} x_k \leqslant U_T$. A symbol s_{i+j}, which is used to construct a word, is 1 for RR acceleration $|t_{i+j}|$ larger than τ and 0 otherwise. Then U_T is a unit time for constructing a word and τ is a RR interval threshold or a RR acceleration threshold for binary symbolization. Here, the RR acceleration threshold is used for illustration. Thus a certain word w_i defined like this contains both information about the time-scale and the event scale of HRs, so that it defines a state of specific scale events of the cardiac system during a unit time. The event scale varies from 5% to 95% in 20 steps of cumulative rank, which is composed of all RR acceleration values from normal and pathological HR data sets. The time-scale varies from 2 to 20 s in 20 steps, where 2 s is the smallest time to avoid an empty word.

Figure 2 presents different ways to compose a word sequence from a RR interval sequence. In the case of the block windowing method, a word is defined regularly with the block size of $n=2$ and the block is shifted to the next by one step. In the case of the unit time windowing method, a word is defined with unit time U_T and the unit time window is shifted by 0.5 s to define the next word, allowing the window overlap. The window shifting time of 0.5 s is appropriately chosen to take an adequate number of sampled words. When we previously determined the measurement time of all RR interval sequences, the unit time widowing method can match the number of words and the total measurement time of different RR interval sets, while the block windowing method cannot match the number of words of RR interval sets. Therefore through these procedures we will investigate the advantage of the unit time windowing method in the analysis of unevenly sampled RR interval data.

With the above methods for the word construction, we can compose a word sequence from a RR interval sequence. Let $W=\{w_1, w_2, \ldots, w_n\}$ be a finite, nonempty set which we refer to as an alphabet. A string or word over W is simply a finite sequence of elements of W. An alphabet W has the following relation:

$$W^n \subseteq W_n \subseteq W^*, \quad W^0 = W_0 = \Theta \text{ “empty word,”} \tag{4}$$

where W^* is the set of all words over W, including the empty word, Θ, W_n is the set of all words over W of length n or less, and W^n is the set of all words over W of length n. The number of possible words of W_n and W^n are $N(n)=s^1+\cdots+s^i+\cdots+s^n=s^{(n+1)}-s/s-1$ and $N(n)=s^n$, respectively, and s is the s-ary number, which in our case is binary ($s=2$). The number of possible symbols in a word, $n(i)$, varies with the unit time U_T and the smallest RR interval time T_s. Since $n(i)$ depends on T_s, which is sensitive to ectopic beats or short term noisy beats, careful noise reduction methods should be employed during preprocessing.

Based on two methods of composing a word sequence, we calculate two types of the symbolic entropy: The simple block entropy (SBE) quantifies the complexity of a word sequence composed by the block windowing method at a specific event and time-scale region. The unit time block entropy (UTBE) is defined similarly for the unit time windowing method.

The entropy, $H(U_T, \tau)$, is a function of the time-scale U_T and the event scale τ.

$$H(U_T, \tau) = -\sum_{i=1}^{N(U_T)} p_i \log_2 p_i, \tag{5}$$

where $p(i)=N(w_i)/N(W)$ is the estimate of the frequency of a word w_i, $N(w_i)$ the frequency of the word w_i, and $N(W)$ the total number of sampled words. To calculate the exact probability of the word w_i, infinite words should be considered. For $s=2$, the SBE and the UTBE vary from the lower bound with complete regularity, and the upper bound with equally probable words.

We construct an appropriate word ensemble from a RR sequence by taking the unit time-scale up to five steps (about 6 s) for the UTBE. At this time-scale, the largest number of symbols contained in a word from our data set is 11. The number of possible words is $2^{11}=2048$, while the number of sampled words from our RR interval sequence is 10 646 at this unit time-scale, which is sufficient for reliable calculation of the entropy. For the SBE, we take the size of the block up to $n=10$. At this block size, the number of possible words is $2^{10}=1024$. In the following applications, we compare the performance of two different entropies and show that the event scale is more useful for classification of the healthy and two pathological HR groups than the time-scale.

III. APPLICATION TO NORMAL AND PATHOLOGICAL HR

We applied the UTBE to 54 RR interval data from the healthy group [normal sinus rhythms (NSR)=21] and two pathological groups [congestive heart failure (CHF)=15, artrial fibrillation (AF)=18], which are taken from PhysioNet Databank in the MIT-BIH database. Each RR interval sequence has a 10–20 h length, which is taken from the ambulatory ECG recorder and sampled at 128 and 250 samples per second with a 12-bit resolution over a range of ±10 mV. We extracted the RR interval sequence from the ECG record-

ing using the PhysioNet software [26]. After matching the number of RR intervals between 54 subjects with the shortest number(($N=15\,000$) among subjects, the total measurement time is shown in Fig. 1. The measurement time of RR interval sequences is widely varying among the subjects with the mean and standard deviation of 180.92 ± 34.825(min) and the maximal time difference of 178.78(min). For the unit time windowing method, the measurement time is matched to 1 h 28 min, where the number of words varies from $N(W)=10\,652$ at $U_T=2$ s to $N(W)=10\,636$ at $U_T=20$ s, depending on the unit time-scale.

A. Linear properties

Before applying the UTBE to the above data set, we investigate conventional linear properties such as the mean and the standard deviation and the student t-test between the healthy and pathological groups (NSR, CHF, and AF). In Fig. 3(a), linear properties such as the mean, standard deviations, and the log-log distribution of the RR acceleration from the NSR, CHF, and AF groups are presented. The result of the student t-test about the mean and standard deviation distributions, which statistically identifies whether three HR groups have different mean values, shows that three groups are distinguishable by these two linear properties, resulting in significant p-values for the mean and the standard deviations [p-value (for mean/standard deviation): NSR and CHF ($0.005/2\times10^{-4}$), NSR and AF (0.045/0.4), CHF and AF ($0.157/10^{-6}$)]. But although some pairs of HR groups are distinguishable in the mean values of their groups, the classification performance is not so good, in the practical view point, it might not be helpful. So we need more information from HR data groups. In Fig. 3(b), the RR interval acceleration shows a power-law distribution, while the RR interval shows the Gaussian distribution which is not presented in this figure. This suggests that the RR interval acceleration, not the RR interval, has nonlinear characteristics, so that the RR interval acceleration is more relevant as a threshold for the binary symbolization than the RR interval.

B. Simple block entropy

In order to get additional information from nonlinear properties, we investigate the relative scale characteristics between the normal HR group and two pathological HR groups at various event and time scales using the simple block entropy (SBE). Each event scale is determined by the RR acceleration values, which vary in 20 steps from 5% to 95% of the accumulative rank for all RR interval acceleration values from three groups. After the binary symbolization at each event scale and composing a word set with each time-scale, we calculate the entropy of the binary symbolized word set. Though the meaningful time-scale region is up to five steps (about 6 s), its size is expanded up to 20 steps to show that the classification works for a larger block size. For comparing SBE between 54 subjects, the number of RR intervals is determined with the shortest number ($N=15{,}000$) among subjects, so the number of words is the same but the measurement time is different between 54 subjects.

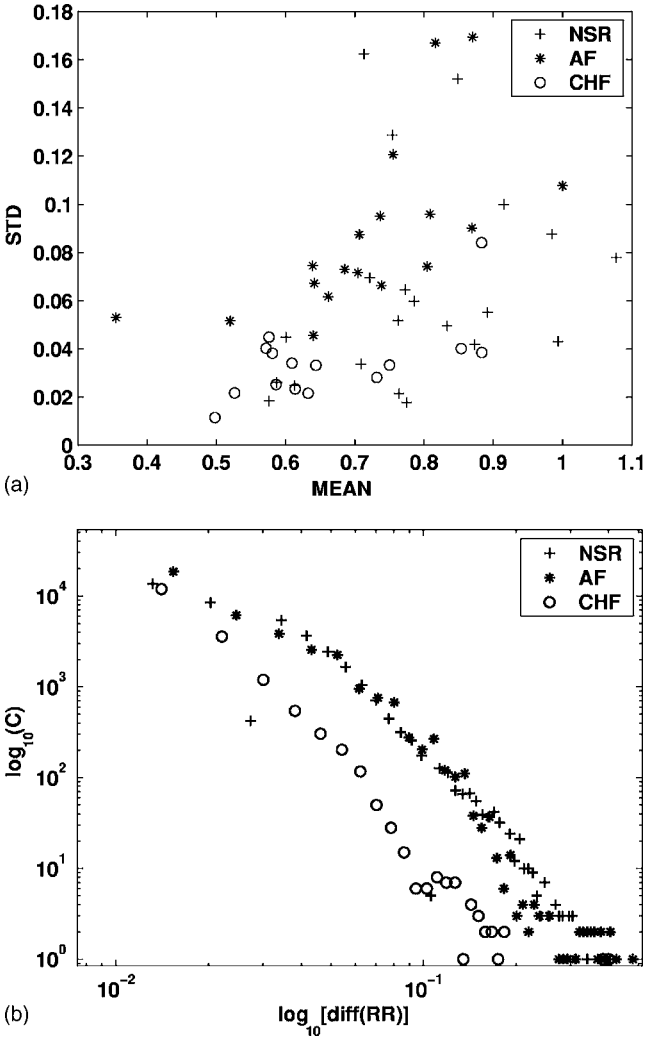

FIG. 3. (a) The mean and standard deviations of NSR, CHF, and AF's RR interval sequences (unit: second). (b) The log-log plot of RR interval acceleration. The log-log distribution of RR acceleration shows power-law distribution, while the log-log distribution of RR interval shows Gaussian distribution [diff(RR): the time duration between two consecutive R waves (second), and C: the count in each bin].

In Figs. 4(a)–4(f), in order to compare SBE distributions among NSR, CHF, and AF groups, all p-values of the student t-test in the (U_T,τ) parameter plane are presented. Since the scale characteristics of three groups are not known *a priori*, we scanned all event and block sizes for optimization of the classification. For the CHF and AF cases in Figs. 4(a) and 4(d), most event sequences composed by 60–95% rank thresholds are significantly distinguished over all time scales for both the RR interval and the RR interval acceleration used as the threshold ($p<0.01$). This suggests that the CHF and AF groups have relatively different characteristic scales in dynamical complexity in the larger RR interval and the larger RR interval acceleration sequences. For the CHF and NSR groups, event sequences composed by most acceleration scales except the 50–65% rank region are distinguished in their complexity ($p<0.01$) [Fig. 4(e)], whereas the difference is not significant for event sequences constructed by the

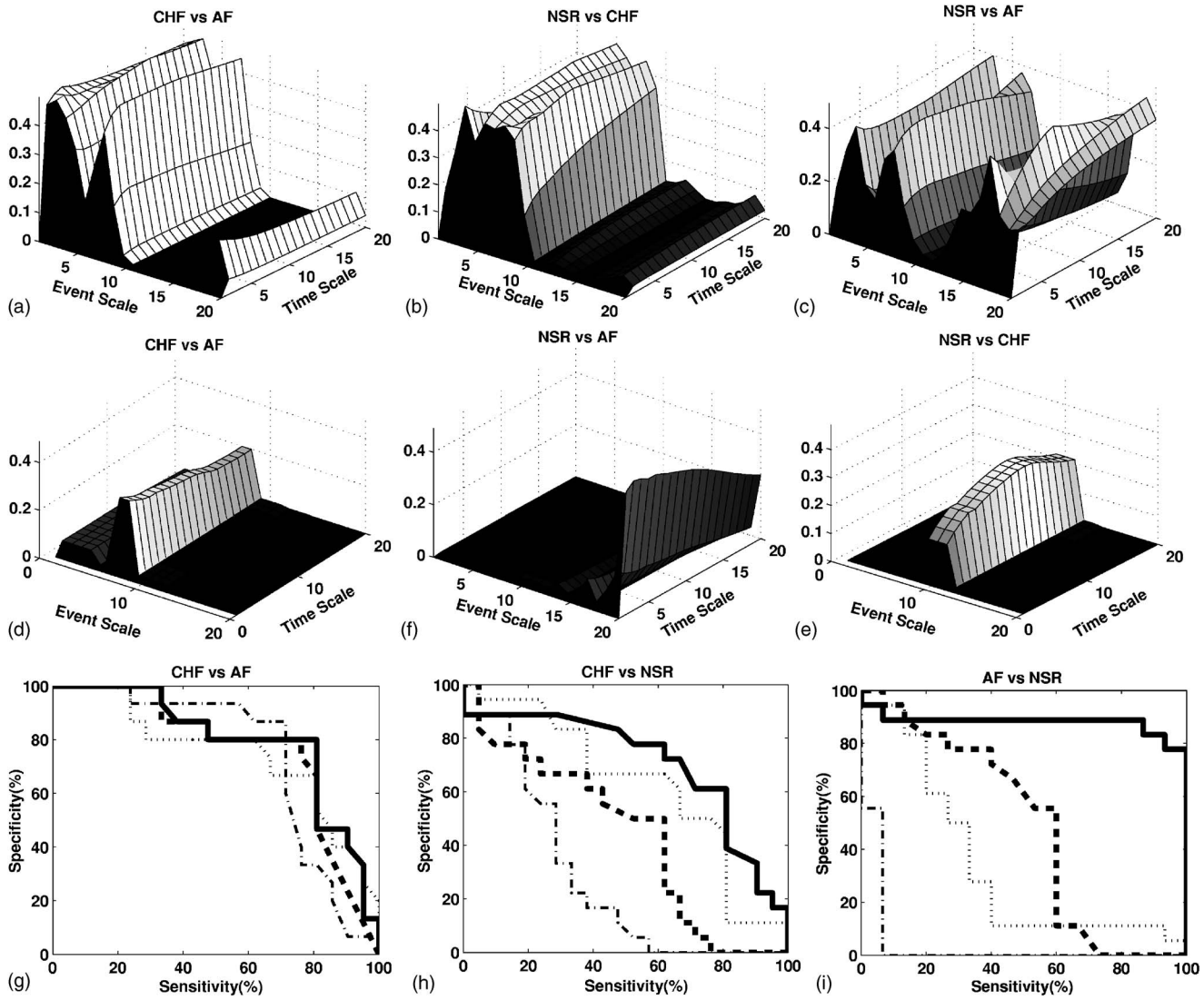

FIG. 4. The student t-test (p-value) and the sensitivity and specificity between NSR, CHF, and AF groups for the SBE using the RR interval and the RR interval acceleration as the symbolization thresholds. (a)–(c) The p-values between three groups at the (U_T, τ) parameter set using the RR interval as a threshold. (CHF and AF, CHF and AF, AF and NSR). (d)–(f) The p-values between three groups at the (U_T, τ) parameter set using the RR interval acceleration as a threshold. (CHF and AF, CHF and AF, AF and NSR), Units [event scale: 20 steps from 5% to 95% of the accumulative ranks for all RR interval or RR acceleration values, time scale: the block size (1–20)]. (g)–(i) The sensitivity and specificity between three groups in two SBEs and two linear properties (mean, standard deviation) (dotted line: mean, dot dashed line: standard deviation, bold solid line: the SBE using the RR interval acceleration, bold dotted line: the SBE using the RR interval). (g) CHF and AF, (h) CHF and NSR, and (i) AF and NSR.

RR interval scale [Fig. 4(b)]. It suggests that the RR accelerations of CHF and NSR groups contain some information on the different internal dynamics of the cardiac system. For the AF and NSR groups, most RR interval scales could not discriminate between these two groups except the narrow region from the 50 to 55% rank scales [Fig. 4(c)], whereas most acceleration scales below the 75% rank scale significantly discriminate between these two groups [Fig. 4(f)].

The information on the characteristic event and time-scale regions of three different groups can be used to determine the optimal parameters for the classification of one group from the others. It should be noted that between two types of scales, the event scale is more effective than the time scale in classifying these groups. If two groups are discriminated at event scale regions, these are also discriminated well over most time scales for one event scale. These results suggest that the RR interval acceleration contains typical information about cardiac dynamics of three groups, whereas the RR interval does not. Based on the fact that slow or fast acceleration of the cardiac system is associated with vagal activity, it may provide some clues to which functional difference of cardiac systems causes such differences in healthy and pathological groups.

Figures 4(g)–4(i) present the sensitivity and specificity between the NSR, CHF, and AF groups with linear properties and two types of the SBE. The sensitivity determines, when a SBE value is given for classifying two groups (NSR, AF) as a threshold, what percentage of the subjects involved in

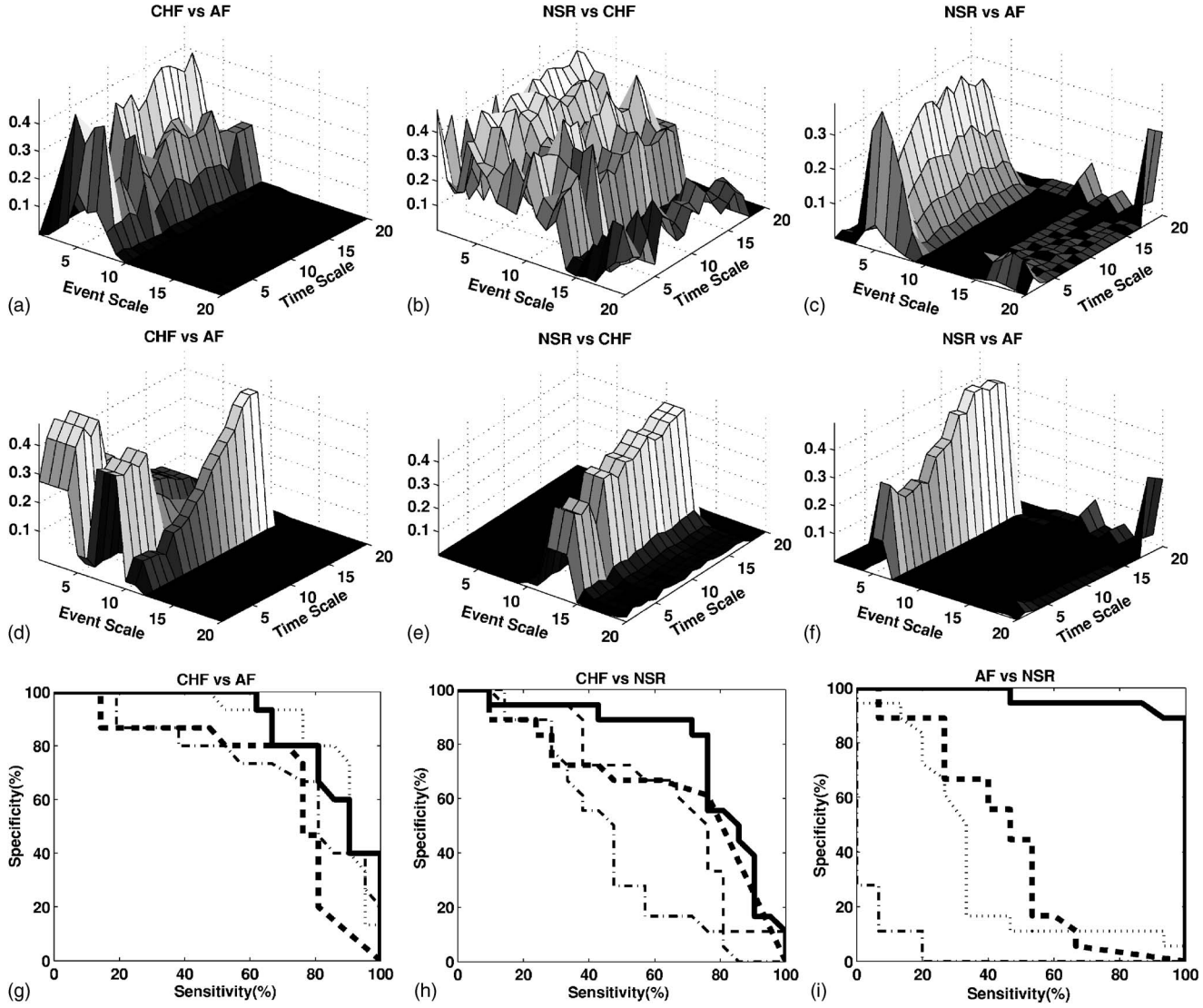

FIG. 5. The student t-test (p-value) and the sensitivity and specificity between NSR, CHF, and AF groups for the UTBE using the RR interval and the RR interval acceleration as the symbolization thresholds. (a)–(c) The p-values between three groups at (U_T, τ) parameter set using the RR interval as a threshold. (CHF and AF, CHF and AF, AF and NSR). (d)–(f) The p-values between three groups at (U_T, τ) parameter set using RR interval acceleration as the threshold. (CHF and AF, CHF, and AF, AF and NSR), Units (event scale: 20 steps from 5% to 95% of the accumulative ranks for all RR interval or RR acceleration values, time scale: 20 steps from 2 to 20 s). (g)–(i) The sensitivity and specificity between three groups in two UTBEs and two linear properties (mean, standard deviation) (dotted line: mean, dot dashed line: standard deviation, bold solid line: the UTBE using the RR interval acceleration, bold dotted line: the UTBE using the RR interval), (g) CHF and AF, (h) CHF and NSR, and (i) AF and NSR.

the NSR group is correctly classified by the given threshold SBE value, while the specificity determines, when a SBE value is given for classifying two groups as a threshold, what percentage of the subjects involved in the other group (AF) is correctly excluded from the NSR group. So if the sensitivity and specificity are all 100%, the two groups are exactly classified by the given threshold. Here, the best sensitivity and specificity are achieved after calculating them at all points of the (U_T, τ) space, varying the threshold from the minimum SBE to the maximum SBE value of the calculated SBE set. Here, when both values which cross the diagonal line in the sensitivity and specificity plane have the highest values comparing with the values at the other (U_T, τ) points, we determine them as the best sensitivity and specificity [27]. In Figs. 4(g)–4(i), the best sensitivity and specificity in the (U_T, τ) plane is presented for the four measures for comparison, respectively. We find that the SBE using the RR interval acceleration as a threshold provides the best performance in classification of CHF and AF, CHF and NSR, and AF and NSR groups. For the case of AF and NSR groups, the SBE using the RR interval acceleration as a threshold significantly distinguishes these groups (sensitivity=91%, specificity=91%), although they cannot be distinguished with linear properties. However, in spite of the good performance by the SBE, we should consider the effects of different measurement time between HR groups being compared. Since the size of the sequence is fixed in advance, the measurement time varies widely as in Fig. 1. From the investi-

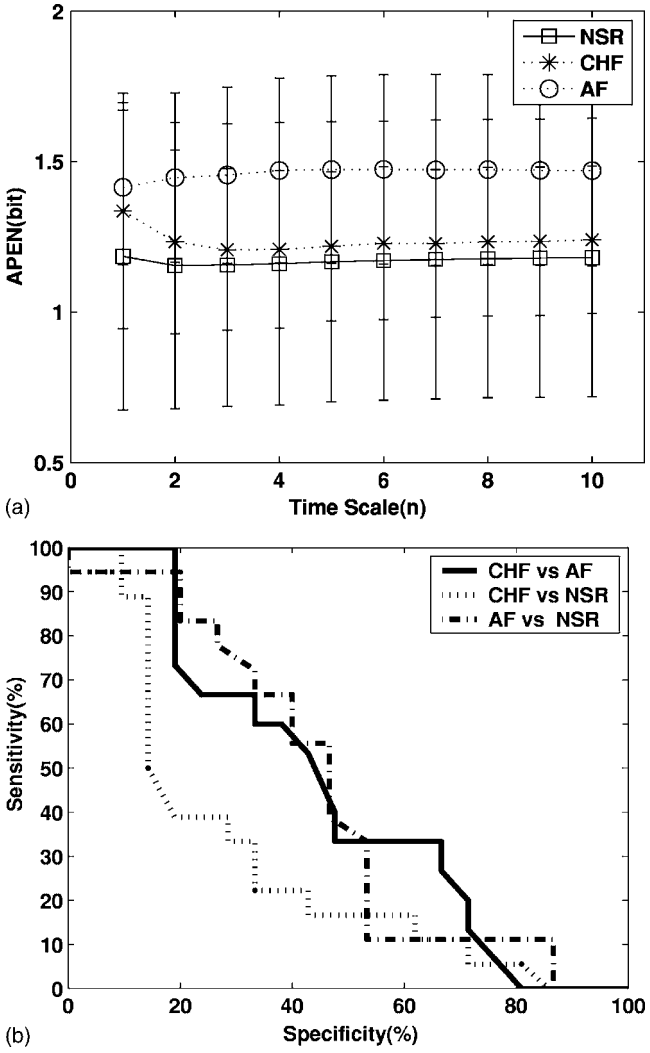

FIG. 6. (a) The mean and the standard deviation of APEN at each scale n [line type: NSR (square), CHF (star), and AF (circle)]. (b) The best sensitivities and specificities selected from the calculation in all scales [line type: CHF vs AF (solid), CHF vs NSR (dot), and AF vs NSR (dash-dot)].

gation of the measurement time of 54 subjects, we find that these groups can be classified roughly only with the measurement time of three groups. In particular, in the investigation of the student t-test, and the sensitivity and specificity, CHF and AF groups are significantly distinguished with the p-value of 0.005, and NSR and AF groups could be classified with the sensitivity of 71% and the specificity of 72%. Since the difference in the measurement time may cause the nonstationarity and the noise effect in classification, it becomes quite difficult to see if the good performance is due to the internal complexity difference of the cardiac system or the nonstationarity involved in the additional time periods of the HR sequence.

C. Unit time block entropy (UTBE)

In order to overcome an ambiguity in comparing SBEs, we applied the unit time entropy (UTBE) to the three HR groups, which estimates the entropy of the activity of the cardiac system at specific event and time scales. Since it matches the measurement time and the number of words in all HR sequences, we can make a reliable and direct comparison between entropy values of all HR groups with respect to the complexity of the cardiac system. Here, the measurement time is taken from the shortest measurement time (88.8 min) among 54 subjects. The number of words is 10 652 at a unit time window (2 s), which changes as the unit time-scale varies and is shorter than that of SBE ($N=15\,000$). All event and time-scale regions are scanned as in the case of the SBE. In Fig. 5 we present the results of the student t-test, and sensitivity and specificity between the NSR, CHF, and AF groups with the UTBE.

The classification performance of the UTBE is found to be comparable to that of the SBE, with only nearly half the size of the RR interval sequence for the SBE. The UTBE method also shows the importance of scale characteristics of the three HR groups. It also shows that the RR acceleration event contains more meaningful information than the RR interval event in classification of healthy and two pathological HR groups. Compared with the SBE, the p-values of the UTBE show more fluctuation, which results from shorter HR sequences. The main difference between two methods is that the large p-value hump on the (U_T,τ) set appears for small event scales in Fig. 5(f). There are some minor differences for the high p-values regions, which can be used to determine the optimal values of parameters for the entropy analysis of the HR data. These results for the UTBE method suggest that the UTBE might be useful for comparing the complexity of the interval data such as HR even with a shorter data length compared with the conventional methods. Moreover, we can reliably explain that the classification performance is due to the difference in complexity of the internal cardiac dynamics, not the system's additional nonstationarity and noise effect due to the different measurement time.

D. Comparision with the conventional method (multiscale entropy)

In this section, we compare the performance of the UTBE with that of multiscale entropy(MSE), which has been widely used in the analysis of HR [7–10]. The MSE calculates the approximate entropy (APEN) or the sample entropy at different scales, which measures the regularity of a given HR data. Here, we calculated the APEN with the same data length ($N=15\,000$). First, in order to calculate the APEN, the RR sequence of length N is divided into segments of length n for which the mean values are calculated. With this coarse-grained sequence at each scale n, the APEN is calculated with the embedding dimension $m=2$, the delay $\tau=1$ [7], and two types of r values are used; one from the original data at $n=1$ $[r=0.15\times\mathcal{D}(n=1)]$ and the other at all n scales $[r(n)=0.15\times\mathcal{D}(n)]$, where $\mathcal{D}$ is the standard deviation. The latter choice of r can remove the effect of variation due to the coarse-graining process [28]. Since the MSEs for both choices of r provide similar results, only the first case is presented here. In Figs. 6(a) and 6(b), we show the performance of the MSE in the classification of three HR groups.

In Fig. 6(a), the best p-values of each pair of groups in the student t-test are $p=0.008$ $(n=10)$ for NSR vs CHF, $p=0.0012$ $(n=4)$ for NSR vs AF, and $p=0.17$ $(n=1)$ for CHF vs AF. Though the mean of each group can be distinguishable at some scales, the deviations are, in general, too large for unambiguous classification. Therefore we investigate the sensitivity and the specificity as in the UTBE. Figure 6(b) presents the best sensitivities and specificities selected from the calculation in all scales. We obtain the best sensitivity and specificity of 50% and 49% at the scale $(n=9)$ for the AF vs NSR case. This classification performance of MSE is worse than that of the UTBE for all classification cases of three HR groups. The UTBE provides a better classification performance than the MSE because it searches the event and time-scale spaces, while the MSE searches only the time-scale. Moreover, it turns out that the event scale contains more effective information for classification than the time-scale as in the previous section. Therefore the UTBE approach is more useful in finding the characteristic difference between healthy and pathologic HR groups, which can be utilized for practical applications.

IV. CONCLUSION

In this work we expanded the multiple time-scale analysis, which has recently received attention in HRV analysis, into event and time scales. By scanning these scales, we found that some event scales contribute most effectively to the classification of healthy and pathological cardiac systems. In particular, we found that NSR, CHF, and AF groups show different scale characteristics in the RR interval acceleration, which is more effective than the RR interval in classifying three groups based on sensitivity and specificity. We also found that for AF and NSR groups, the UTBE and the SBE distinguish them clearly in some event and time-scale regions, while linear properties cannot. The systematic study of various event and time scales of normal and pathological HR has proven to be useful in classifying each group and understanding the RR interval and the RR interval acceleration dynamics of the veiled cardiac systems.

The RR interval data sets used for our study have varying measurement times since the RR interval lengths are fixed in advance due to the algorithmic convenience in most conventional linear and nonlinear measures. Since the cardiac system has several internal rhythms from yearly to secondly and interacts incessantly with external environments, it is not clear whether the difference in complexity is due to the intrinsic difference of two cardiac systems or the additional nonstationarity or noise due to the different measurement time. Because three HR groups can be separated roughly only with the difference of the measurement time, such performance in classification may not be always guaranteed for other HR data sets.

Our method of the unit time block entropy (UTBE) removes this ambiguity, which matches the measurement time and the number of words at the same time in all HR groups for comparison. The performances of the UTBE in measuring the complexity of heart dynamics is found to be nearly the same as that of the SBE, albeit with nearly half the size of RR sequence. The UTBE with the fixed measurement time allows us to determine reliably the dynamical complexity of the cardiac systems. This method may be useful for comparing the other unevenly sampled data set directly, and can be extended to other HR problems, for example, the fetal distress HR for classification of normal and pathological groups [29]. We also show its usefulness in comparison with the multiscale entropy.

ACKNOWLEDGMENT

This work has been supported by the Ministry of Science & Technology through the National Research Laboratory Project.

[1] H. V. Huikuri, T. H. Makikallio, and J. Perkiomaki, J. Electrocardiol. **36**, 95 (2003).
[2] L. Glass, J. Cardiovasc. Electrophysiol. **10**, 1358 (1999).
[3] A. Voss, J. Kurths, H. J. Kleiner, A. Witt, N. Wessel, P. Saparin, K. J. Osterziel, R. Schurath, and R. Dietz, Cardiovasc. Res. **31**, 419 (1996).
[4] P. Van Leeuwen and H. Bettermann, Herzschr. Elektrophys. **11**, 127 (2000).
[5] J. Altimiras, Comp. Biochem. Physiol. A **124**,447 (1999).
[6] S. Havlin, S. V. Buldyrev, A. Bunde, A. L. Goldberger, P. Ch. Ivanov, C.-K. Peng, and H. E. Stanley, Physica A **273**, 46 (1999).
[7] M. Costa, A. L. Goldberger, and C.-K. Peng, Phys. Rev. Lett. **89**, 068102 (2002).
[8] D. R. Chialvo, Nature (London) **419**, 263 (2002).
[9] M. Costa, A. L. Goldberger, and C.-K. Peng, Comput. Cardiol. **29**, 137 (2002).
[10] M. Costa and J. A. Healey, Comput. Cardiol. **30**, 705 (2003).
[11] G. Deco and B. Schurmann, *Information Dynamics* (Springer-Verlag, New York, 2001).
[12] R. Badii and A. Politi, *Complexity* (Cambridge University Press, Cambridge, England, 1997).
[13] J. J. Zebrowski, W. Poplawska, and R. Baranowski, Phys. Rev. E **50**, 4187 (1994).
[14] B.-L. Hao, Physica D **51**, 161 (1991).
[15] J. Plumecoq and M. Lefranc, Physica D **144**, 231 (2000).
[16] M. B. Kennel and M. Buhl, Phys. Rev. Lett. **91**, 084102 (2003).
[17] D. Cysarz, H. Bettermann, and P. Van. Leeuwen, Am. J. Physiol. Heart Circ. Physiol. **278**, H2163 (2000).
[18] J. Kurths, A. Voss, P. Saparin, A. Witt, H. J. Kleiner, and N. Wessel, Chaos **5**, 88 (1995).
[19] N. Wessel, C. Ziehmann, J. Kurths, U. Meyerfeldt, A. Schirdewan, and A. Voss, Phys. Rev. E **61**, 733 (2000).
[20] K. T. Park and S. H. Yi, J. Korean Phys. Soc. **44**, 569 (2004).
[21] M. E. D. Gomes, H. N. Guimaraes, A. L. P. Ribeiro, and L. A.

Aguirre, Comput. Biol. Med. **32**, 481 (2002).
[22] K. K. L. Ho, G. B. Moody, C.-K. Peng, J. E. Mietus, M. G. Larson, D. Levy, and A. L. Goldberger, Circulation **96**, 842 (1997).
[23] H. Herzel, A. O. Schmitt, and W. Ebeling, Chaos, Solitons Fractals **4**, 97 (1994).
[24] T. Sauer, Phys. Rev. Lett. **72**, 3811 (1994).
[25] N. B. Janson, A. N. Pavlov, A. B. Neiman, and V. S. Anishchenko, Phys. Rev. E **58**, R4 (1998).
[26] Databases and softwares are available at http// www.physionet.org/. See A. Goldberger *et al.*, Circulation **101**, E215 (2000).
[27] The sensitivity is a true positive rate which is defined as $A/(A+C)$. The specificity is a true negative rate which is defined as $D/(B+D)$, (A: true positive, B: false positive, C: false negative, and D: true negative). More details are available at http//bmj.bmjjournals.com/ or see T. Greenhalgh, BMJ **315**, 540 (1997).
[28] V. V. Nikulin and T. Brismar, Phys. Rev. Lett. **92**, 089803 (2004).
[29] U. C. Lee and S. Kim, (unpublished).