**Am J Physiol - Regul Integr Comp Physiol 2007 291(1): R368-R372**

# Regular heartbeat dynamics are associated with cardiac health

Dirk Cysarz[1,2], Silke Lange[3], Peter F. Matthiessen[1], Peter van Leeuwen[3]

[1] Chair of Medical Theory and Complementary Medicine, University of Witten/Herdecke, D-58313 Herdecke, Germany

[2] Integrated Studies of Anthroposophic Medicine, D-58452 Witten, Germany

[3] Department of Biomagnetism, Grönemeyer Institute for Microtherapy, D-44799 Bochum, Germany

Corresponding author:
Dirk Cysarz, PhD
Chair of Medical Theory and Complementary Medicine
University of Witten/Herdecke
Gerhard-Kienle-Weg 4
D-58313 Herdecke, Germany
Tel: +49 2330 62-3637
Fax: +49 2330 62-4062
Email: d.cysarz@rhythmen.de

## Abstract

The human heartbeat series is more variable and, hence, more complex in healthy subjects than in congestive heart failure (CHF) patients. However, little is known about the complexity of the heart rate variations on a beat-to-beat basis. We present an analysis based on symbolic dynamics that focuses on the dynamic features of such beat-to-beat variations on a small time scale. The sequence of acceleration and deceleration of 8 successive heartbeats is represented by a binary sequence consisting of 1s and 0s. The regularity of such binary sequences is quantified using Approximate Entropy. Holter electrocardiograms from 30 healthy subjects, 15 patients with congestive heart failure (CHF) and their surrogate data were analyzed with respect to the regularity of such binary sequences. The results of this approach are compared to spectral analysis and Approximate Entropy of heart rate variability. Counter-intuitively, healthy subjects show a large amount of regular beat-to-beat patterns in addition to a considerable amount of irregular beat-to-beat patterns. CHF patients lack the regular patterns observed in healthy subjects. Instead, they show a predominance of one regular beat-to-beat pattern (alternation of acceleration and deceleration) as well as some irregular beat-to-beat patterns similar to the beat-to-beat patterns observed in the surrogate data. In healthy subjects regular beat-to-beat patterns reflect the physiological adaptation to different activities, i.e. sympathetic modulation, whereas irregular beat-to-beat-patterns may arise from parasympathetic modulation. CHF patients show regular as well as irregular beat-to-beat patterns close to a purely erratic behaviour indicating a largely reduced influence of the autonomic nervous system. In conclusion, the analysis of short beat-to-beat patterns with respect to regularity leads to a considerably increase of information compared to spectral analysis or ApEn of heart rate variations.

## Introduction

On a neural basis dynamic features of the human cardiac activity are modified by two different inputs of the autonomic nervous system: sympathetic activity increases heart rate and parasympathetic activity lowers heart rate. This seems to be a simple antagonism but in healthy subjects these competing branches are influenced by numerous different inputs mediating many kinds of stimuli. Hence, the resulting time series of interbeat intervals is highly non-stationary and complex (Fig. 1a). The analysis of such time series has revealed a reduced heart rate variability (HRV) in patients with cardiac disease such as e.g. congestive heart failure (CHF) (6). Likewise, CHF patients show decreased fractal and chaotic features of heartbeat dynamics (11, 15, 21).

These findings and their implications with respect to complexity are based on the analysis of the heartbeat series containing at least a hundred or more consecutive heartbeats, some methods even require $10^3$ or $10^4$ consecutive heartbeats. Here, we investigate dynamic features of particularly short beat-to-beat sequences in the order 10 consecutive heartbeats by means of symbolic dynamics. At present, two different approaches to derive symbolic dynamics from a time series may be distinguished. One approach uses local mean and standard deviation of the heart rate time series to create a symbolized time series. E.g. a symbolic sequence may be created assigning ‘1’ to a heartbeat if the instantaneous heart rate is near the average heart rate, assigning ‘2’ for heart rates considerably below the average heart rate, and assigning ‘3’ if the heart rate is considerably above the average heart rate (13, 16-18). The analysis of such symbolic sequences has proven useful to improve the detection of cardiac patients at high risk (16) or to characterize dynamic differences of slow and fast ventricular tachycardias (17).

Recently, a similar approach revealed a loss of complexity in cardiac patients with life-threatening arrhythmias before the onset of these arrhythmias (13). The analysis of this kind of symbolic sequences led to the notion that the heart rate variations are more complex in healthy subjects than in e.g. cardiac patients. This notion is compatible with the results from approaches that investigate complexity of physiologic time series but do not use symbolic dynamics, such as methods derived from chaos theory (7, 11, 15, 21).

The other approach to derive symbolic dynamics symbolizes the increase or decrease of the instantaneous heart rate by two different symbols. Hence, the local average heart rate or similar quantities of the time series under investigation are not important for the creation of the symbolic sequences. It has already been shown that in healthy subjects the average dynamics of such short beat-to-beat sequences during night-time sleep is more irregular, i.e. more complex and less predictable, compared to heartbeat dynamics during waking time (8). Specific short symbolic sequences appear during night-time as a result of the modulation of heartbeat variations by respiration (respiratory sinus arrhythmia) and is associated with cardiorespiratory synchronization (3, 4). Furthermore, the emergence of certain symbolic sequences on small time scales seems to be an individual characteristic feature. For instance, both pathological states, CHF and atrial fibrillation show characteristic short dynamic patterns (25).

Recently, a classification of short symbolic sequences based on the acceleration or deceleration of heart rate using musical rhythm principles has been developed (2). However, this classification did not emphasize dynamic features of such symbolic sequences. Here, we focus on dynamic features of such short beat-to-beat series from healthy subjects and patients with CHF and their respective surrogate data. We will show that this kind of analysis reveals a fundamental difference between short-scale heartbeat dynamics in health and disease. A comparison of the results of this analysis with the results obtained from spectral analysis and Approximate Entropy of HRV is used to exemplify the augmentation of information made possible by the new method.

## Methods

*Subjects* – Heartbeat time series from thirty healthy subjects (15 female, average age: 29 ± 8 years) (9) and fifteen patients with severe CHF (NYHA class III-IV; age range 22-71 years; 'BIDMC congestive heart failure database' taken from the Physionet-database; see http://www.physionet.org (12)) were analyzed with respect to heartbeat dynamics on small time scales. Holter ECGs of the healthy subjects were recorded with Oxford FD3 solid-state memory recorders with simultaneous R-peak detection. They were about 24 hours in duration. The maximum sampling rate of 1024 Hz provided a temporal resolution of the times of the R-peaks of 1 ms. The data were subsequently visually examined with the Oxford Excel software. After elimination of artifacts (<0.1% of all R-peaks) the times of the R-peaks and the beat annotations were transferred to data files. Data of the CHF group were recorded with Del Mar Avionics Model 445 Holter recorder. They were digitized with a sampling rate of 250 Hz permitting a temporal resolution of the R-peaks of 4 ms. The recordings were about 20 hours in duration. We relied on the information provided in the Physionet database. The data in the database (times of the R-peaks and classification of the heartbeats) were taken as provided and were neither inspected visually nor corrected manually.

*Construction of symbolic sequences* – The series of interbeat intervals $RR_i$ ($i = 1, \ldots, N$) between successive R-peaks served as the basis for the calculations.
A binary sequence $S_i$ ($i = 2, \ldots, N$) was created using the differences $\Delta RR_i = RR_i - RR_{i-1}$ between successive interbeat intervals (Fig. 1c):

$$S_i = \begin{cases} 0, & \text{if } \Delta RR_i \geq 0, \\ 1, & \text{if } \Delta RR_i < 0. \end{cases}$$

Hence, '0' symbolizes a deceleration and '1' an acceleration of the heart rate. Subsequently, the probability of the appearance of the 17 pattern sets in the symbolic series $S_i$ was calculated (see below).

*Approximate Entropy (ApEn)* – In this paper, we analyze dynamic properties of binary sequences of length 8. For example, the binary sequence 00000000 is obviously more regular than e.g. 01100010. I.e., the succession of 0s and 1s is easy to predict in the first sequence whereas the prediction of the succession of 0s and 1s in the latter sequence is more difficult. Approximate Entropy is an appropriate measure for the quantification of such aspects of binary sequences (8, 19). For normal time series ApEn calculates the logarithmic frequency that sequences of length *m* that are close (within a tolerance *r*) remain close (within the same tolerance) in sequences of length *m+1* (20). ApEn(*m*,*r*) depends on the length *m* and the tolerance *r* and it assigns higher numbers to more irregular sequences. For binary sequences the tolerance r is set to $r < 1$ because this is the only practical setting for a binary metric. Furthermore, to apply ApEn to short binary sequences, the length *m* is set to 1. For further details of the implementation of ApEn for binary sequences see reference (19). As a result, a number reflecting the serial irregularity of the succession of 0s and 1s is assigned to each binary sequence: the higher ApEn, the more irregular (and less predictive of the succession of the 0s and 1s) the binary sequence. Due to redundancies with respect to irregularities of the binary sequences, the $2^8 = 256$ different sequences are assigned only 17 different values of ApEn. Hence, 17 different pattern sets are created by merging the binary sequences with the same value of ApEn in one set (for the sequences belonging to each set, see Online Data Supplements). These 17 pattern sets reflect different dynamic properties ranging from regular to irregular. It has to be noted that the appearance of single ectopic heartbeats or single artifacts is not crucial because they only cause an alternation of one symbol resulting in a minor bias in the frequency of some binary patterns. If ectopic heartbeats appear frequently they are relevant for the assessment of the heartbeat dynamics. Consequently, the contribution of ectopic heartbeats to the frequency of several binary patterns is not a disadvantage but reflects a relevant characteristics of the dynamics.

In addition to the binary approach, ApEn was also calculated for the normal RR interval series of each consecutive segment comprising 1000 RR intervals. The length *m* was set to 2 and the radius r was set to 20% of SDNN.

*Heart rate variability* – As basic time domain parameters the mean RR-interval and the accompanying standard deviation (SDNN) were calculated for each consecutive 5-minute epoch. Furthermore, for these epochs, in the frequency domain the low and high frequency power (LF: 0.04 – 0.15 Hz, HF: 0.15 – 0.4 Hz) and the ratio LF/HF were calculated using the fast Fourier transformation (22). For the CHF patients a filtered RR-tachogram was used to reduce the influence of premature ventricular ectopic beats on these parameters (24).

*Surrogate data* – In addition to the original data, one surrogate data set of each recording was created by shuffling the interbeat intervals $RR_i$ in random order (23). The resulting series of interbeat intervals only shares the distribution of the original interbeat series. All other linear and non-linear characteristics, e.g. any temporal correlations, are destroyed (Fig. 1b). Subsequently, the analysis of the binary sequences in the surrogate data was carried out in the same manner as for the original data.

*Statistics* – As circadian variations of heart rate and HRV are well known (14), the analysis was carried out for the daytime (11:00 to 17:00) and night-time (0:00-6:00) period. Based on the binary sequence $S_i$ of each period the probability of each pattern set (i.e. the probability of the binary patterns belonging to each pattern set) was calculated. The results of the binary analysis are presented as box plots in order to give a detailed picture of the distributions. Appropriate to this non-parametric approach, the distributions of patterns of healthy subjects and CHF patients were compared using the Wilcoxon rank sum test. Differences between the distributions of daytime and night-time were evaluated with Wilcoxon signed rank test. The HRV parameters were log-transformed due to their skewed distribution. The transformed HRV parameters and the ApEn of the normal RR-intervals are presented as mean ± standard deviation. Differences in the distributions of these parameters between healthy subjects and CHF patients were examined using Student's t-test. Furthermore, the differences between daytime and night-time in each group were also assessed using the t-test (for dependent samples). A p-value $<0.05$ was considered statistically significant.

## Results

The HRV parameters and ApEn of the RR-tachogram showed the following results. The mean RR-interval during daytime was 703 ms for the healthy subjects and 662 ms for the CHF patients (see Table 1). During night-time the average RR-interval of the healthy subjects and CHF patients increased significantly compared to daytime. Still, the average RR-interval of healthy subjects was significantly larger compared to CHF patients. SDNN was significantly larger for the healthy subjects but did not show a difference between daytime and night-time. For the spectral parameters of HRV ln LF, ln HF and ln LF/HF were significantly larger for the healthy subjects compared to the CHF patients. A significant difference between daytime and night-time was found for ln HF and ln LF/HF of the healthy subjects HRV and ln LF for the CHF patients HRV. During daytime ApEn was significantly lower for the healthy subjects compared to the CHF patients (1.01 vs 1.29). During night-time ApEn of the healthy subjects increased significantly whereas ApEn of the CHF patients did not change.

The analysis of the binary sequences reveals that during daytime the beat-to-beat heartbeat dynamics is clearly different between healthy subjects and CHF patients (Fig. 2a). Sixteen out of 17 pattern sets show significant differences between the groups ($p<0.01$ for the pattern sets 1-15, $p<0.05$ for pattern set 17, pattern set 16 n.s.). Surprisingly the heartbeat dynamics in healthy subjects shows a substantial amount of very regular dynamic patterns during daytime (particularly pattern sets 2-5). At the same time, the binary patterns belonging to these pattern sets appear very seldom in CHF patients. In contrast, only one very regular pattern set prominently appears in CHF patients (pattern set 1 containing only the patterns 01010101 and 10101010 – i.e. alternation of acceleration and deceleration of the heart rate). Obviously, also

pattern sets 6 and 7 with a medium regularity emerge far more often in CHF patients than in healthy subjects. With respect to pattern sets with higher irregularity during daytime, sets 9, 12, 13 and 17 appear more often in CHF patients whereas pattern sets 8, 10, 11, 14 and 15 appear more often in healthy subjects.

During night-time sleep the heartbeat dynamics changes notably in healthy subjects whereas the heartbeat dynamics of CHF patients remains very similar compared to daytime (Fig. 2b). A number of pattern sets containing the dynamic patterns with higher irregularity (pattern sets 9-17) were more likely to occur during night-time sleep compared to daytime ($p<0.01$, pattern sets 9, 13, 15-17; $p<0.05$, pattern sets 12, 14). As a consequence, as opposed to the dynamic properties during daytime, pattern set 14, 15 and 16 appear more often in healthy subjects compared to CHF patients ($p<0.01$). On the other hand, the likelihood of the pattern sets 2-5, containing the more regular patterns, decreased compared to daytime ($p<0.01$, pattern sets 3-5; $p<0.05$, pattern set 2). Still, the pattern sets 2-5 are more likely to appear in healthy subject than in CHF patients ($p<0.01$) and vice versa for pattern sets 1, 6 and 7 ($p<0.01$). In the medium range of irregularity the pattern sets 8, 10 and 11 are again more likely in healthy subjects ($p<0.01$ pattern sets 10 and 11, $p<0.05$ pattern set 8) and pattern set 9 is more likely on CHF patients ($p<0.05$). We also carried out the analysis for other lengths of binary sequences (7-12 successive heartbeats) and found analogous results for daytime and night-time heartbeat dynamics.

The probability of the pattern sets for the surrogate data is the very similar for healthy subjects and CHF patients (Fig. 2 a and b; hence, only one red asterisk is shown per pattern set). The analysis of the surrogate data reveals that the dynamic features observed in beat-to-beat variations of CHF patients is close to the dynamic features of random behaviour of the heartbeat. Remarkably, the dynamics of the random heartbeat is neither particularly regular nor complex. In contrast to healthy heartbeat dynamics, pattern set 1, i.e. a beat-to-beat alternation of acceleration and deceleration, is the only pattern set that substantially contributes to regularity whereas other regular dynamic patterns (pattern sets 2-5; which include most of the regularity in healthy heartbeat dynamics) are rare. Furthermore, the pattern sets 6-17 show a probability which is obviously typical for random behaviour. Hence, from a dynamic point of view on small time scales, a random heartbeat also shows binary patterns with high irregularity.

## Discussion

The analysis of the irregularity of short beat-to-beat sequences reveals a detailed picture of its dynamic features. On short time scales in the order of some seconds the healthy heartbeat is especially characterized by a large amount of regular dynamics consisting of a succession of beats reflecting heart rate acceleration or deceleration. During daytime such regular dynamics are observable approximately half of the time. Physiologically, the continuous adaptation of the heartbeat to different activities, i.e. the transitions between behavioural states, leads to sequences of acceleration or deceleration lasting several heartbeats. This adaptation is mediated by sympathetic activation or withdrawal (e.g. the transition from sitting to standing causes an increase of sympathetic activity giving rise to an acceleration of the heartbeat). On larger time scales, this continuous adaptation, i.e. the alternation of sympathetic activation and withdrawal, leads to a high variability mainly due to low frequency variations which is reflected by a large value of ln LF. At the same time a prevailing parasympathetic modulation is rather seldom as

indicated by a rather low value of ln HF during daytime. Hence, there is no preference of specific binary patterns with higher irregularity.

During night-time the amount of regular patterns in the healthy beat-to-beat dynamics decreases and the appearance of more complex heartbeat patterns increases. Such complex patterns mainly reflect the ratio between heart rate and respiratory frequency as a result of respiratory sinus arrhythmia (e.g. a ratio of 7:2 is indicated by the pattern 00100110 which belongs to pattern set 17) (4). Hence, the increase of more complex heartbeat patterns is an indicator of an augmented parasympathetic modulation which is also reflected by an increased value of ln HF compared to daytime. On the other hand, physical activity during sleep such as leg movement is accompanied by parasympathetic withdrawal leading to longer sequences of acceleration of the heartbeat, followed by sequences of deceleration when the movement stops. Thus, the corresponding regular binary patterns still occur to a certain extent even during night-time sleep. Consequently, the well-known increase of heart rate variability (especially ln HF) (10) and the well-known increase of complexity (as represented by ApEn of a RR-tachogram) (5) of heart rate during night-time sleep on larger time scales emerges primarily from irregular but also regular heartbeat patterns on small time scales.

The beat-to-beat dynamics of CHF patients hardly show the regular pattern sets observed in healthy subjects. Instead, they show a predominance of regular pattern sets which contain primarily an alternation of acceleration and deceleration of heart rate (pattern set 1, 6 and 7). This alternation reflects the inability of the CHF patients to adapt to different activities. Taking into account that the amplitude of such accelerations and decelerations is rather limited, this alternation obviously leads to a well-known reduction of heart rate variability which is reflected by lower values of ln LF and ln HF compared to healthy subjects (6). However, the predominance of regular pattern sets does not imply a significantly decreased complexity on larger time scales as during daytime ApEn of the RR-tachogram for CHF patients is not different from ApEn for healthy subjects. Hence, very different heartbeat dynamics on small time scales may lead to similar ApEn values on larger time scales. Taking into account that more irregular pattern sets appear in the heart rate dynamics of healthy people during night-time sleep, it seems that the increase of ApEn on longer time scales mainly reflects the increase of the appearance of these pattern sets.

The dynamics of the beat-to-beat patterns of CHF patients approaches random heartbeat dynamics which is characterized by a specific distribution of the different pattern sets. Apart from the predominance of alternation of acceleration and deceleration, this includes binary sequences with high irregularity. This erratic behaviour reflects the absence of influence of the autonomic nervous system and, hence, may contribute as a factor for high-risk of mortality (1).

We only differentiated between daytime and night-time dynamics of the heart rate. Hence, the precise prerequisites of regular or irregular heartbeat dynamics in terms of sympathetic and parasympathetic activity or modulation need to be explored more explicitly, e.g. with the help of pharmacological agents or under specific physiological conditions. We note that the present analysis requires a sampling rate of the electrocardiogram of at least 250 Hz to identify the R-peaks with a sufficient temporal resolution. A low sampling rate in conjunction with a low heart rate variability could lead to a succession of acceleration or deceleration comprising two or three heartbeats. Hence, the assignment of the binary patterns to the pattern sets would be erroneous. Such symbolic sequences would turn out to be an alternation of acceleration and deceleration if

the sampling rate would be sufficiently high. Although symbolic dynamics considerably reduces the amount of information contained in the original time series, the symbolization presented in this paper is advantageous because it does not require stationarity of the time series as a prerequisite for its analysis.

In conclusion, the analysis of different levels of irregularity in short sequences of acceleration or deceleration of the instantaneous heart rate extends and refines the notion of complexity of human heartbeat dynamics. In healthy subjects the continuous adaptation to different activities during daytime, i.e. the sympathetic modulation, leads to regular heartbeat dynamics on small time scales. They mainly contain successions of acceleration or deceleration of heart rate. During night-time sleep irregular heartbeat dynamics on small time scales emerge caused by parasympathetic modulation. Both, regular as well as irregular, contribute to a pronounced heart rate variability as found in healthy subjects. In CHF patients the heartbeat dynamics on small time scales is close to an erratic behaviour. Regular heartbeat patterns containing an alternation of acceleration and deceleration largely contribute to such dynamics, but also heartbeat patterns with high irregularity. They reflect the limited influence of the autonomic nervous system on heartbeat variations. Taken together, it may be worth looking at the amount and the kind of regular beat-to-beat dynamics (pattern sets) to unambiguously distinguish between health and disease.

**Acknowledgements**

This work was supported by grants of the Software AG Stiftung (D.C., P.M.).

**References**

1. **Bauer A, Kantelhardt JW, Barthel P, Schneider R, Makikallio T, Ulm K, Hnatkova K, Schomig A, Huikuri H, Bunde A, Malik M and Schmidt G**. Deceleration capacity of heart rate as a predictor of mortality after myocardial infarction: cohort study. *Lancet* 367: 1674-1681, 2006.
2. **Bettermann H, Amponsah D, Cysarz D and Van Leeuwen P**. Musical rhythms in heart period dynamics - a cross-cultural and interdisciplinary approach to cardiac rhythms. *Am J Physiol* 277: H1762-H1770, 1999.
3. **Bettermann H, Cysarz D and Van Leeuwen P**. Detecting cardiorespiratory synchronization by respiratory pattern analysis of heart period dynamics: the musical rhythm approach. *Int J Bifurcat Chaos* 10: 2349-2360, 2000.
4. **Bettermann H, Cysarz D and Van Leeuwen P**. Comparison of two different approaches in the detection of intermittent cardiorespiratory coordination during night sleep. *BMC Physiol* 2: 18, 2002.
5. **Bettermann H and Van Leeuwen P**. Evidence of phase transitions in heart period dynamics. *Biol Cybern* 78: 63-70, 1998.
6. **Casolo G, Balli E, Taddei T, Amuhasi J and Gori C**. Decreased spontaneous heart rate variability in congestive heart failure. *Am J Cardiol* 64: 1162-1167, 1989.
7. **Costa M, Goldberger AL and Peng CK**. Multiscale entropy analysis of complex physiologic time series. *Phys Rev Lett* 89: 068102, 2002.
8. **Cysarz D, Bettermann H and Van Leeuwen P**. Entropies of short binary sequences in heart period dynamics. *Am J Physiol Heart Circ Physiol* 278: H2163-H2172, 2000.

9. **Cysarz D, Schürholz T, Bettermann H and Kümmell HC**. Evaluation of modulations in heart rate variability caused by a composition of herbal extracts. *Arzneimittelforschung* 50: 420-424, 2000.
10. **Fallen EL and Kamath M**. Circadian rhythms of heart rate variability. In: Heart rate variability, edited by Malik M and Camm AJ. Armonk NY: Futura Publishing, 1995, p. 293-309.
11. **Goldberger AL, Amaral LA, Hausdorff JM, Ivanov PC, Peng CK and Stanley HE**. Fractal dynamics in physiology: alterations with disease and aging. *Proc Natl Acad Sci USA* 99: 2466-2472, 2002.
12. **Goldberger AL, Amaral LAN, Glass L, Hausdorff JM, Ivanov PC, Mark RG, Mietus JE, Moody GB, Peng CK and Stanley HE**. PhysioBank, PhysioToolkit, and PhysioNet: components of a new research resource for complex physiologic signals. *Circulation* 101: E215-E220, 2000.
13. **Guzzetti S, Borroni E, Garbelli PE, Ceriani E, Della Bella P, Montano N, Cogliati C, Somers VK, Malliani A and Porta A**. Symbolic dynamics of heart rate variability. A probe to investigate cardiac autonomic modulation. *Circulation* 112: 465-470, 2005.
14. **Huikuri HV, Kessler KM, Terracall E, Castellanos A, Linnaluoto MK and Myerburg RJ**. Reproducibility and circadian rhythm of heart rate variability in healthy subjects. *Am J Cardiol* 65: 391-393, 1990.
15. **Ivanov PC, Amaral LAN, Goldberger AL, Havlin S, Rosenblum MG, Struzik ZR and Stanley HE**. Multifractality in human heartbeat dynamics. *Nature* 399: 461-465, 1999.
16. **Kurths J, Voss A, Saparin P, Witt A, Kleiner HJ and Wessel N**. Quantitative analysis of heart rate variability. *Chaos* 5: 88-94, 1995.
17. **Meyerfeldt U, Wessel N, Schutt H, Selbig D, Schumann A, Voss A, Kurths J, Ziehmann C, Dietz R and Schirdewan A**. Heart rate variability before the onset of ventricular tachycardia: differences between slow and fast arrhythmias. *Int J Cardiol* 84: 141-151, 2002.
18. **Palazzolo JA, Estafanous FG and Murray PA**. Entropy measures of heart rate variation in conscious dogs. *Am J Physiol* 274: H1099-H1105, 1998.
19. **Pincus S and Singer BH**. Randomness and degrees of irregularity. *Proc Natl Acad Sci USA* 93: 2083-2088, 1996.
20. **Pincus SM**. Approximate entropy as a measure of system complexity. *Proc Natl Acad Sci USA* 88: 2297-2301, 1991.
21. **Poon CS and Merrill CK**. Decrease of cardiac chaos in congestive heart failure. *Nature* 389: 492-495, 1997.
22. **Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology**. Heart rate variability: standards of measurement, physiological interpretation, and clinical use. *Circulation* 93: 1043-1065, 1996.
23. **Theiler J, Eubank S, Longtin A, Galdrikian B and Farmer JD**. Testing nonlinearity in time series: the method of surrogate data. *Physica D* 58: 77-94, 1992.
24. **Wessel N, Voss A, Malberg H, Ziehmann C, Voss HU, Schirdewan A, Meyerfeldt U and Kurths J**. Nonlinear analysis of complex phenomena in cardiological data. *Herzschr Elektrophys* 11: 159-173, 2000.
25. **Yang ACC, Hseu SS, Yien HW, Goldberger AL and Peng CK**. Linguistic analysis of the human heartbeat using frequency and rank order statistics. *Phys Rev Lett* 90: 108103, 2003.

**Supporting Information** listing the binary patterns belonging to each of the 17 pattern sets is available online.

## Figure legends

**Figure 1:**
(A) Non-stationarity of the healthy human interbeat time series. The non-stationarities lead to large fluctuations on large time scales as well as on small time scales (see inset). The fluctuations on small time scales reveal sequences of acceleration and deceleration of the heartbeat often lasting several heartbeats.
(B) Surrogate data for the same data set. Obviously the temporal structure of the original data is completely lost.
(C) Creation of symbolic sequences. Based on the interbeat intervals the acceleration of the heartbeat is symbolized by 1's (negative slope of the line between two successive interbeat intervals) and the deceleration of the heartbeat is symbolized by 0's (positive slope of the line between two successive interbeat intervals).
(D) Symbolic sequences for the surrogate data.

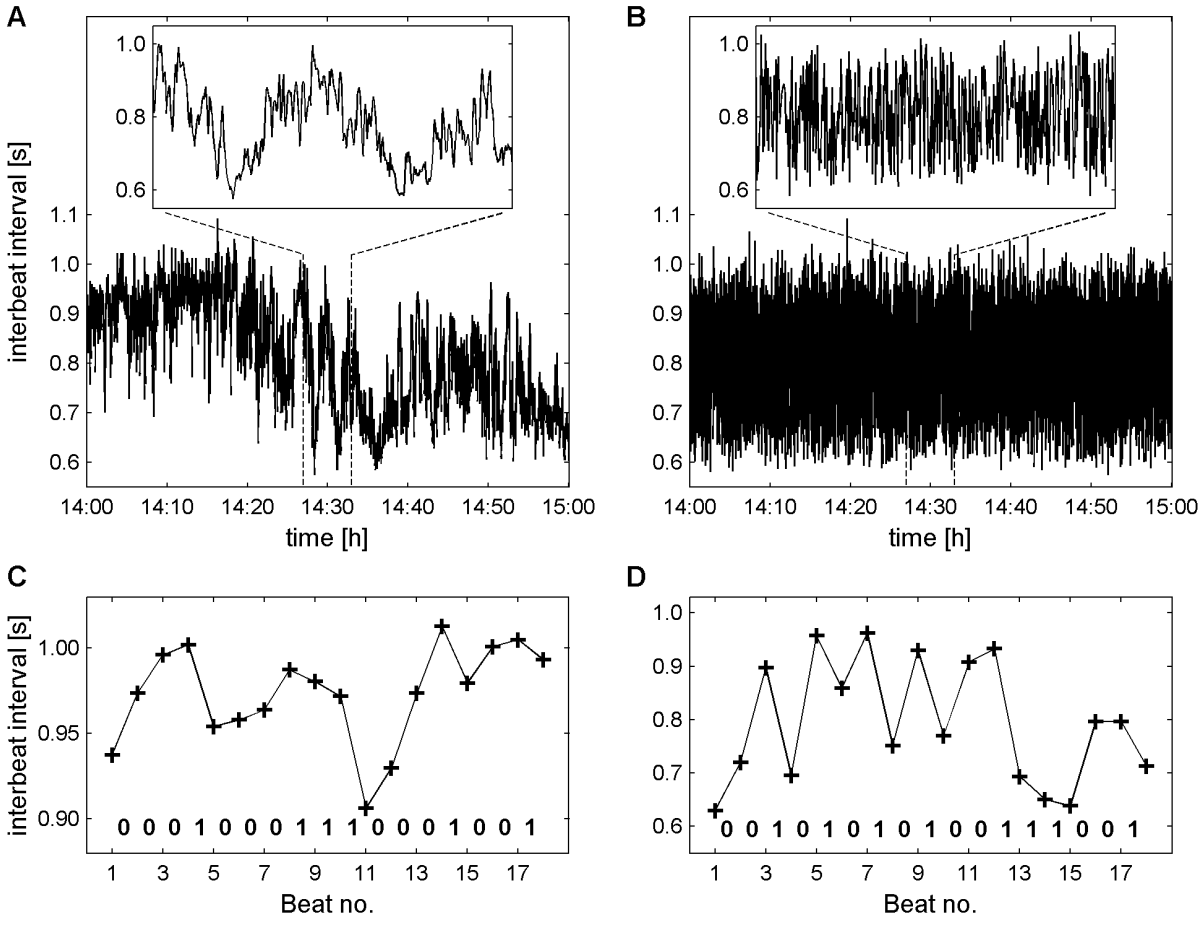

**Figure 2:**
Likelihood of the appearance of the 17 pattern sets in the heartbeat dynamics of healthy subjects (white boxes) and CHF patients (grey boxes) during daytime (A) and night-time (B). The succession of the pattern sets reflects the increase of irregularity of the binary patterns contained in the pattern sets. The red asterisks show the median probability of the 17 pattern sets for the surrogate data (the use of Boxplots was not practical as the distributions are very narrow).