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Detecting cardiorespiratory coordination by respiratory pattern analysis of heart period dynamics – the musical rhythm approach

Short title: The musical rhythm approach to cardiorespiratory coordination

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Abstract

The purpose of this study was to demonstrate that cardiorespiratory coordination can be unveiled by analyzing solely heart period data from the electrocardiogram (ECG). The analysis was done (1) on the basis of symbolic musical pattern analysis to detect intermittent cardiorespiratory phase coordination and (2) on the quantitative evaluation of respiratory sinus arrhythmia (RSA) to examine long-term frequency coordination between heartbeat and respiration. The methods were applied to 196 ECGs of 98 healthy subjects. The results showed that at night (1) intermittent phase coordination occurred reproducibly in individual subjects, and (2) long-term frequency ratios statistically approached 4:1 over all subjects to within an accuracy of 0.02, although individual values ranged from 2.5 – 6.0 with a high intraindividual reproducibility ($r = 0.94$, day A vs. day B). Moreover, intermittent phase coordination ratios and long-term frequency ratios corresponded to each other with a remarkably high correlation ($r = 0.95$). In the light of clinical applications, the coordination analysis presented here has an enormous advantage over those techniques depending on respiratory flow measurements, because the pattern technique requires only ECG recordings, and it is thus applicable over a longer period of time under daily life conditions.

1. Introduction

For more than 2000 years musical pulse diagnostics had been a basic and common knowledge for most physicians with its prime in the 16th century [Kümmel, 1977]. Galen (129-199) [Kühn, 1824] or Avicenna (980-1037) [1658] interpreted ratios of diastolic and systolic time intervals harmonically in order to differentiate between regular and irregular behavior. Because exact clocks were lacking, musical notations were also used to communicate the cadence of heartbeat – i.e. pulse rate – to other physicians. The first to consider dynamical aspects of heart rate by means of musical rhythms were S. Hafenreffer (1587-1660) and A. Kircher (1601-1680). In 'Musurgia universalis' [1650] Kircher presented a scheme of 15 composed pulses which, in the notion of modern sciences, could be interpreted as a symbolic rhythm pattern classification scheme of heart period dynamics. It is important to note that, in Kircher's schematic notation of heartbeat, not the absolute but the relative values of musical notes had to be interpreted physiologically. However, since the middle of the 19th century, when sphygmographic techniques became popular, musical pulse diagnostics fell into disuse. In principle, Kircher's 350 years old concept is the same concept we have applied to symbolize heart period sequences presented in this study.

Nowadays, music psychological concepts provide a profound basis for the analysis of physiological time series and, in particular, for approaching cardiac dynamics. Rhythm and time perception is a main topic in this psychophysiological discipline which has been investigated for more than 100 years [Fraisse, 1978, 1982; Handel, 1989; Povel, 1984]. Rhythm perception deals with perceived rhythms in contrast to induced rhythms (e.g. the rhythm of tides, day and night, or the seasons) in which ordering in time is reconstructed on the basis of experiences stored in memory [Fraisse, 1978]. One important finding in this field of rhythm research is the exploration of the psychological present [Fraisse, 1978] which comprises time intervals ranging from 0 - 5 seconds, i.e. the time span which is experienced as the present by human beings. This is approximately the duration of basic rhythm patterns in music and, incidentally, also the time span of heartbeat and respiration.

According to Handel [1989], perceived rhythms can be classified into patterns *of* and *in* time. This classification is important because it comprises the two major methodological aspects for the analysis of rhythmic time signatures from the point of view of rhythm perceptology:

1. the interpretation of rhythms as cyclically recurrent time patterns (i.e. the pattern concept), and,
2. the differentiation between rhythms which are arrangements of durable elements (patterns of time, e.g. percussive strokes and rests) on the one hand, and rhythms which are successions of equidistant time events of different characters (patterns in time, e.g. intensity or pitch) on the other hand.

Obviously, these aspects are fundamental to all scientific fields dealing with rhythm or time series analysis. Fig. 1 shows various time signature notations which illustrate this formal rhythm approach. The figure also demonstrates, how these pattern notations are related to the representation of RR interval series. This concept might be a first step towards a Renaiscance of the musical interpretation of heartbeat rhythms.

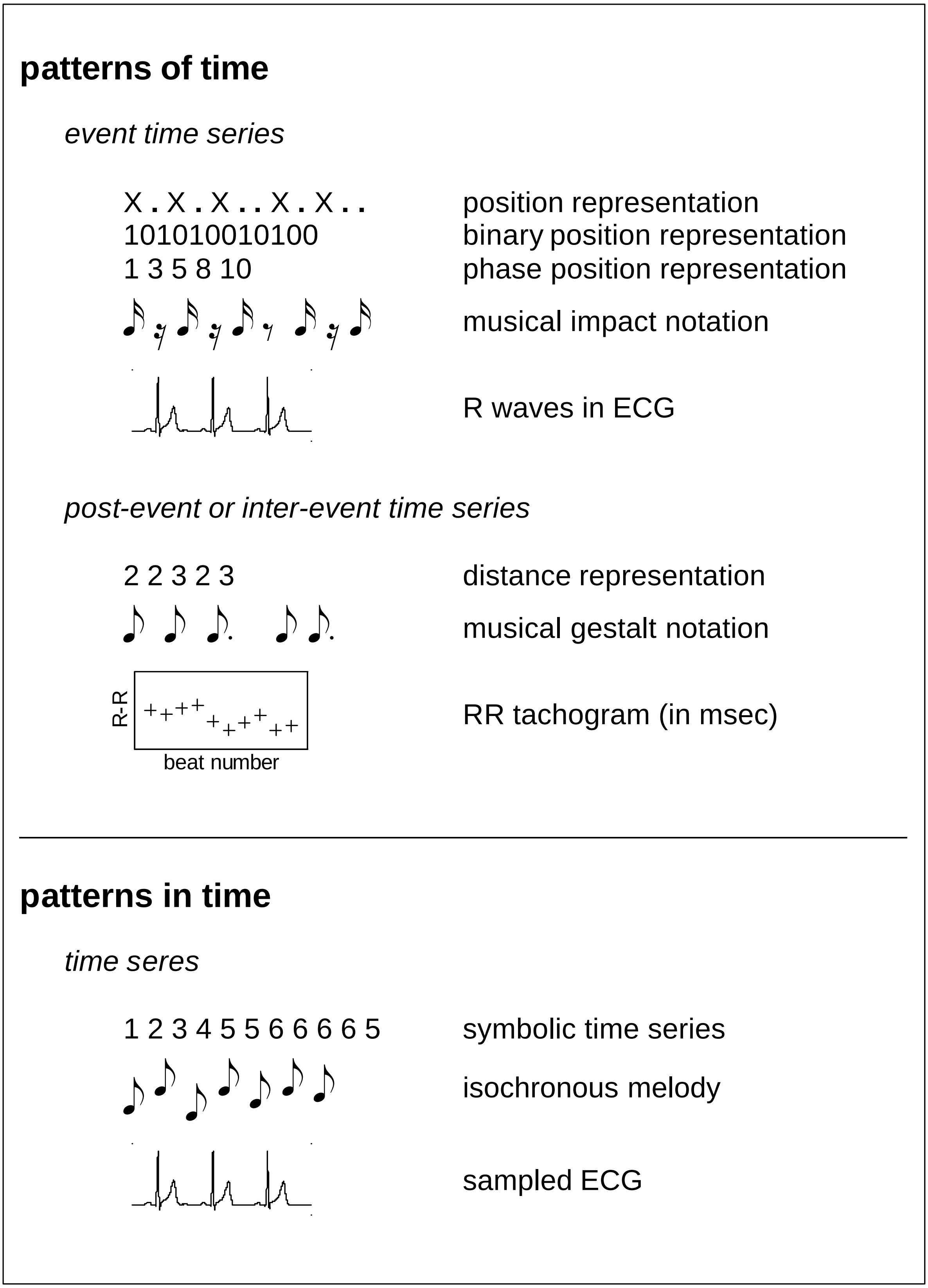


Fig. 1 The pattern concept with different time signature notations

The second step can be done by symbolization or coding of heart period dynamics in a strict musical sense. For this kind of application the heart period tachogram has to be transformed into symbol sequences which can be interpreted as either melodic or rhythmic (percussive) patterns. We decided to apply the latter. Furthermore, the best basis for interpretation of musical rhythm patterns is not to be found in European classical music, but in the music of African origin. For example, African musicology or jazz theory provide profound rhythm schemes or hierarchies to bring the diversity of musical rhythms into an order, and to classify musical rhythms with respect to their perceived complexity. One of these schemes, accounting for the principles of timelines or bell patterns in African music, is the Derler rhythm hierarchy, published by Dauer [1988], which is a strict mathematical approach on the basis of combinatorial theory. The main idea of this classification approach is to merge binary rhythm patterns into musically relevant equivalence classes in order to reduce the huge amount of different binary combinations. Further details of the musicological background of African music are described in detail elsewhere [Bettermann et al., 1999]. Generally, African music seems to be naturally suited to expose the secrets of heartbeat rhythms because of its three compositional principles: polyrhythmic complexity, rhythmic contrast and strict cyclicity [Kubik, 1988, 2000]. All qualities have their equivalent in the multi-dimensional physiological time organism. Moreover, from the point of view of African cultures, music rises directly from the inner dynamic of human beings which is symbolized and brought forth by the human heartbeat. And in this respect, it remains to be further explored if timeline patterns, which play a major part as coordinators in the African musical ensemble, are also to be found in the physiological rhythms of man.

The transformation of heart rate or heart period series into symbolic sequences is not new. Kurths and colleagues [Kurths et al., 1995; Schäfer et al., 1995] have used this instrument with various transformation techniques to facilitate heart period analysis. Each of their symbolization techniques was implemented for a particular approach. The main difference to our approach is that they constructed and analyzed the symbolic sequences solely from the point of view of complexity analysis (e.g. using renormalized entropy). Musical rhythmical aspects were not taken into consideration.

The goal of this paper was to show that cardiorespiratory coordination can be unveiled by applying pure pattern concepts, established e.g. in ethnomusicology or music psychology, and analyzing solely heart period data from the electrocardiogram (ECG). The paper combines the results of two former studies with two different pattern approaches developed in our laboratory. Both methods used are based on the evaluation of the differential heart period dynamics (see also Schäfer et al. [1995]). The first one [Bettermann et al., 1999] is a rigorous application of the above described musical pattern concept to detect 'African' timeline patterns in binary symbolic heart period dynamics (for further details see the methods section). By means of defining pattern equivalence classes it could be shown that most timeline patterns occuring in heart period dynamics can be assigned to phase coordination ratios between the cardiac and respiratory cycles in the sense that, if respiratory sinus arrhythmia (RSA) and intermittent phase coordination are present, certain timelines in heartbeat music must be predominant. The second method was established 15 years ago (later published by Bettermann et al. [1996]) to determine respiratory rate from RSA in heart rate derived from 24-hour electrocardiograms (24h ECG). This method was developed to calculate the frequency ratio of pulse and respiration, a classical parameter in anthroposophic medicine to quantify the 'rhythmic organization' in man (see discussion). This ratio is traditionally referred to as pulse-respiration quotient (*PRQ*) [Moser et al., 1995], and has been used to examine the relative coordination [von Holst, 1939] between heartbeat and respiration. Chronobiology has revealed that, on a large time scale, most rhythms in man tend to coordinate with integer (x:1) frequency ratios [Hilde-

[Hildebrandt, 1987]. These frequency coordinations have also been interpreted musically by using terms from harmonic theory [Hildebrandt, 1997] (e.g. octave (2:1), quinte (3:2), quarte (4:3), ...), not to be confused with the musical rhythm approach we have chosen in our studies. But with respect to cardiorespiratory coordination during night sleep, the harmonic frequency coordination of 4:1 (2 octaves) seems to be obvious, as will be shown in this paper.

Finally the question arises: Why using the term coordination instead of synchronization in this paper? In physical applications synchronization is understood as an entrainment or locking process due to interaction [Rosenblum 1998; Schäfer 1999]. And strictly speaking one has to prove that an observed adjustment of rhythms is not an occasional coincidence but caused by coupling mechanisms. This proof often fails in living systems because of two main reasons: First, periods of synchronization are naturally very short, and consequently testing for deterministic phase relations is not appropriate. Second, the underlying dynamics are unknown which makes it very difficult to decide whether rhythm adjustment is caused by couplings or not. In this context, the term coordination is less restrictive. It is widely used only in a descriptive manner. Introduced by von Holst in the thirties of the last century, (relative) coordination is equivalent with the existence of certain phase relations without claiming that these phase relations are due to true synchronization processes.

2. Methods

The first part of the methods section describes the binary pattern analysis which we have used to detect intermittent phase coordination in heart period dynamics. On the whole, this section is a short excerpt from the methods chapter of Bettermann et al. [1999], to which we refer for further details. The weighted phase coordination ratio (*PCR*, definition see below) has been newly introduced in this paper and is associated with the appearance of so-called phase locking patterns which may (but need not necessarily) result from phase coordination processes.

The second part of this section recapitulates briefly the respiratory rate detection method published by Bettermann et al. [1996], and the computation of the mean frequency ratio (*meanPRQ*).

2.1 Subjects

The baseline ECGs from the Cardiodoron® study [Cysarz et al., 2000] were used as data resource. The study included 100 healthy subjects and was carried out at the Gemeinschaftskrankenhaus Herdecke from January to August 1997. Due to missing data, 2 subjects were excluded from this retrospective analysis. For the remaining 98 subjects (age: 20 to 41 years, mean/SD 28/7 years; 45 men) two successive 24h ECGs (A and B) were available. The sleep times could be determined from the subjects' diaries.

2.2 Construction of symbolic sequences

Oxford FD3 solid state recorders with simultaneous R wave detection were used for the 24h ECG registration. Visual inspection of the automatically detected R waves was performed on an Oxford Excel ECG-Analyzer. The R times of all beats were written to a binary data file which was then exported to a Pentium PC for further analysis.

The times between successive R waves (RR intervals) were calculated in milliseconds, and they form the RR tachogram. Herein artifacts and ectopic beats were marked with the value

9999. Next the differences of all successive RR intervals were calculated. These differences formed the differential RR tachogram which was directly transformed into a binary symbolic sequence as follows (see Fig. 2): (1) RR differences smaller than zero were marked with 1 which corresponds to an acceleration of the heartbeat. (2) RR differences greater than or equal to zero were marked with 0 which corresponds to a deceleration of the heartbeat. (3) Missing values or RR differences which were corrupted by artifacts or ectopic beats were marked with 9.

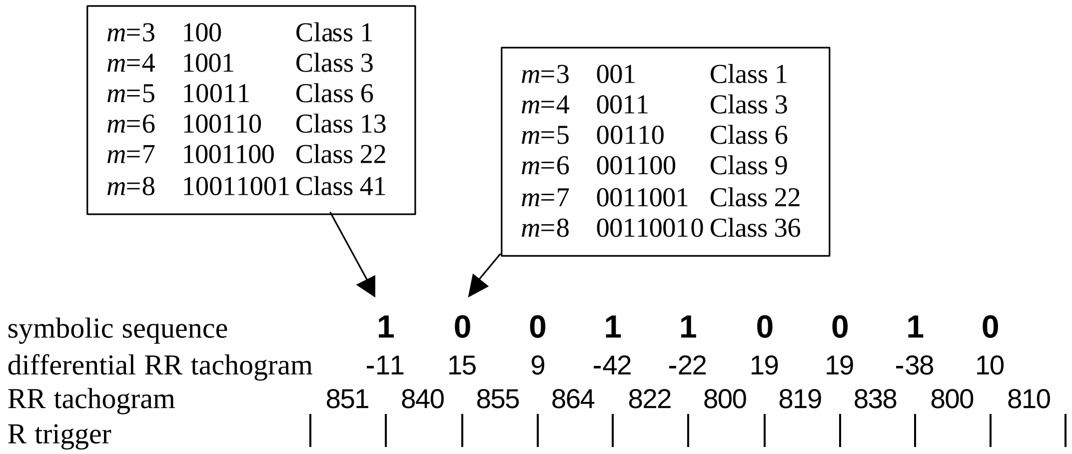


Fig. 2 Example of the construction of a symbolic sequence and determination of the corresponding pattern classes

2.3 Pattern classification

According to the Derler rhythm classification all binary patterns with pattern lengths of $m = 3 \dots 8$ symbols (pulse number) were merged to 42 musically relevant equivalence classes (see Tab. 1). Two redundancy principles were applied: (1) All m patterns, which are identical after rotation, are assigned to one pattern class; e.g. *class*(011) = *class*(110) = *class*(101); m(011) = 3. (2) All complementary pattern classes resulting from the permutation of 1 and 0 were merged to one class.

class	*m*	Pattern	*class*	*m*	Pattern	f_G	f_{max}
1	3	001	-1	3	011	1.22	1.33
2	4	0001	-2	4	0111	0.88	2.00
3	4	0011	-3	0	0011	1.12	4.00
4	2	0101	-4	0	0101	2.12	8.00
5	5	00001	-5	5	01111	0.52	3.20
6	5	00011	-6	5	00111	0.81	3.20

7	5	00101	-7	5	01011	1.86	3.20
8	6	000001	-8	6	011111	0.26	5.33
9	6	000011	-9	6	001111	0.49	5.33
10	6	000101	-10	6	010111	1.28	5.33
11	6	000111	-11	0	000111	0.56	10.67
12	3	001001	-12	3	011011	1.55	10.67
13	6	001011	-13	6	001101	1.68	5.33
14	2	010101	-14	0	010101	3.41	32.00
15	7	0000001	-15	7	0111111	0.11	9.14
16	7	0000011	-16	7	0011111	0.26	9.14
17	7	0000101	-17	7	0101111	0.74	9.14
18	7	0000111	-18	7	0001111	0.32	9.14
19	7	0001001	-19	7	0110111	1.01	9.14
20	7	0001011	-20	7	0011101	1.15	9.14
21	7	0001101	-21	7	0010111	1.14	9.14
22	7	0010011	-22	7	0011011	1.48	9.14
23	7	0010101	-23	7	0101011	2.94	9.14
24	8	00000001	-24	8	01111111	0.04	16.00
25	8	00000011	-25	8	00111111	0.13	16.00
26	8	00000101	-26	8	01011111	0.36	16.00
27	8	00000111	-27	8	00011111	0.17	16.00
28	8	00001001	-28	8	01101111	0.54	16.00
29	8	00001011	-29	8	00111101	0.62	16.00
30	8	00001101	-30	8	00101111	0.65	16.00
31	8	00001111	-31	0	00001111	0.16	32.00
32	4	00010001	-32	4	01110111	0.64	32.00
33	8	00010011	-33	8	00111011	1.02	16.00
34	8	00010101	-34	8	01010111	1.94	16.00
35	8	00010111	-35	8	00011101	0.76	16.00
36	8	00011001	-36	8	00110111	0.96	16.00
37	8	00011011	-37	8	00100111	1.03	16.00
38	8	00100101	-38	8	01011011	2.47	16.00
39	8	00101011	-39	8	00110101	2.58	16.00
40	8	00101101	-40	0	00101101	2.53	32.00
41	4	00110011	-41	0	00110011	1.46	64.00
42	2	01010101	-42	0	01010101	5.60	128.00

μ, No. of patterns in class; f_G, normalized relative frequency for an artificially generated Gaussian-distributed random RR tachogram; $f_{max} = 2^m / \mu(class)$. See text for details.

Tab. 1 Rhythm scheme

In the language of combinatorial theory the redundancy principles correspond to the definition of a cyclic group C_m of ‘shifts in origin’ which act on a set P_m of sequences with period m. The shifts can be compared with the rotation of a necklace which, in our case, is made from m beads of 2 different kinds [Gilbert & Riordan, 1961; Golomb, 1961]. The second principle can be interpreted as the definition of a symmetric group S_2 of permutations which here simply means exchanging 1 and 0. The combination of the two principles results in the symmetry transformation group $C_m \times S_2$ which establishes a decomposition of P_m into equivalence classes or symmetry types of periodic sequences. The number of elements in a specific class is given by the sum of the μ values in each row of Tab. 1. Gilbert and Riordan [1961] derived a formula for the number of symmetry types with respect to the period m. According to the data in Table I of their paper and considering the fact that we ignored patterns consisting only of 1s or 0s, the number of types (equivalence classes) with a period e.g. from $m = 3$ to 12 are: 1, 3, 3, 7, 9, 19, 29, 55, 93, and 179. In total this are 398 pattern classes needed to cover all binary rhythm patterns with pulse numbers from 3 to 12, and 42 pattern classes for pulse numbers from 3 to 8.

2.4 Pattern statistics

Next, the relative frequency of all 42 pattern classes for each one-hour interval from 1:00 to 5:00 during night sleep (the time was corrected according to the subject's diary if necessary) was determined by moving a window with a variable length of $m = 3$ .. 8 symbols in equidistant steps of one heartbeat over the one-hour period, providing 6 patterns with a different pulse number for each heartbeat (see Fig. 2). Every pattern, which can be assigned to a pattern class from 1 to 42, is counted by incrementing the corresponding component of a 42-dimensional vector. To make the frequency values of all pattern classes comparable to each other, for each hour the absolute frequencies *F(class)* are divided by *m(class)* as well as by the total number of all registered patterns *N(m)* with the same pulse number *m*, and are multiplied with 2^m, the number of all possible *m*-dimensional binary combinations:

$$f(class) = \frac{F(class) \cdot 2^m}{N(m) \cdot m(class)} \tag{1}$$

The resulting normalized relative frequency *f(class)* is smaller than 1 if *class* is less frequent and greater than 1 if *class* is more frequent than would be expected in equally distributed random symbol sequences (corresponding to a random walk RR tachogram). The resulting *f* values for a Gaussian-distributed random RR tachogram are shown in the seventh column of Tab. 1, indicating that the normalized relative frequency naturally depends on the underlying distribution of the RR intervals. This results in the paradox that for example, the irregularity of binary heart period patterns, quantified by approximate entropy, is greater for RR tachograms with pronounced 5:1-locked RSA than for improved surrogates, as has been pointed out by Cysarz et al. [2000]. This may also be one reason for the abrupt increase of heart period complexity during night sleep which was interpreted as synergetic phase transition in heart period dynamics [Bettermann & Van Leeuwen, 1998]. The last column of Tab. 1 summarizes the possible maximal values of *f* which would be found if the corresponding patterns appear exclusively, i.e. if $F(class) = N(m)$.

Furthermore, we also calculated the mean step number *s(class)* for which the class of the pattern remains unchanged, when moving the window stepwise over the entire symbol sequence. *s(class)* is termed cyclic pattern stability.

2.5 Phase locking patterns and PCR

Some typical patterns are probably the result of phase coordination processes. These patterns predominantly occur if the phases of the heart period and a heart period modulating harmonic oscillation tend to lock frequently with same locking ratio. Fig. 3 demonstrates this by way of example for a 7:2 phase locking. In the range from 3:1 to 8:1 these patterns will likely correspond to RSA, the strongest heart period modulation which primarily occurs due to interaction in the central nervous system of the cardiac and respiratory systems. Referring to Tab. 1, the following relations hold: 3:1 $\rightarrow$ classes 1,12; 4:1 $\rightarrow$ classes 3,41; 5:1 $\rightarrow$ class 6; 5:2 $\rightarrow$ class 7; 6:1 $\rightarrow$ class 11; 7:1 $\rightarrow$ class 18; 7:2 $\rightarrow$ class 22; 7:3 $\rightarrow$ class 23; 8:1 $\rightarrow$ class 31; 8:3 $\rightarrow$ class 40. These relations should be read as follows: if *x:y* phase locking occurs *and* RSA is present, *then* patterns of class *z* must be predominant. They should not be read the other way round.

Pattern classes were judged as predominant if during a one-hour interval these patterns occur with $f > 2$ and $s > 2$. Then, for each phase locking ratio (*PLR*), all one-hour intervals during night sleep of two successive days were counted, for which a *PLR* phase locking pattern predominance had been detected. Furthermore, for each subject the weighted phase coordination ratio (*PCR*) was calculated:

$$PCR = \frac{\sum_{PLR} n(PLR) \cdot PLR}{\sum_{PLR} n(PLR)} \tag{2}$$

with $n(PLR)$ = {number of one-hour intervals for which a *PLR* pattern predominance was detected}; *PCR* weights the ‘locking ratios’ of the above defined phase locking pattern classes according to the frequency of their hourly predominance; e.g. if $n(4{:}1) = 3$ and $n(7{:}2) = 2$ then $PCR = (3 \cdot 4 + 2 \cdot 3.5)/5 = 3.8$.

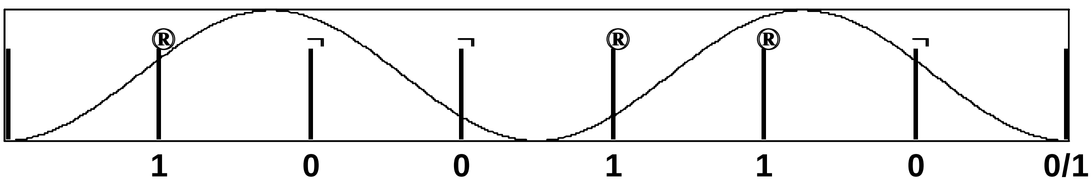


Fig. 3 Illustration of a 7:2 phase locking of heartbeat (the vertical bars mark the R time) and a heart period modulating harmonic oscillation (e.g. respiration); shown are the effect on the heartbeat period and its symbolic dynamic; the two possible binary patterns are complementary and belong to the same pattern class 22

2.6 Respiratory rate detection

Respiratory rate was computed from 24h ECGs on the basis of RSA. This was done in 4 steps. (1) The resampled RR tachograms of all successive one-minute intervals during the day were first band pass filtered in the respiratory band from 6 to 30 min^{-1}. This resulted in the RSA curve which was (2) subsequently normalized by dividing by the 75th-percentile of all local maxima. (3) Respiratory cycles were determined by analyzing the maxima, minima and zero crossings of the normalized RSA curve. Each cycle must have the following shape: zero crossing – maximum – zero crossing – minimum – zero crossing – maximum – zero crossing, with maxima > 0.2. (4) The last step was to calculate the (momentary) respiratory rate as the reciprocal of the corresponding RSA cycle length for each accepted RSA cycle.

It should be noted that the characterization of the RSA shape by sequences of only three different attributes – maximum, minimum, and zero crossing – is based on a mixture of static and differential symbolization, i.e. taking absolute and relative RR values under consideration. However, in the context of our study this analogy has no relevance.

2.7 Frequency coordination and PRQ

The *PRQ* parameter was defined as the ratio of the momentary RSA cycle length and the mean RR interval during the respective RSA cycle. As the results of our previous study [Bettermann et al., 1996] have shown, *meanPRQ* can be reliably interpreted as the mean frequency ratio of pulse and respiration. This ratio can be used to detect long-term frequency coordination between these electro-mechanically coupled systems.

3. Results

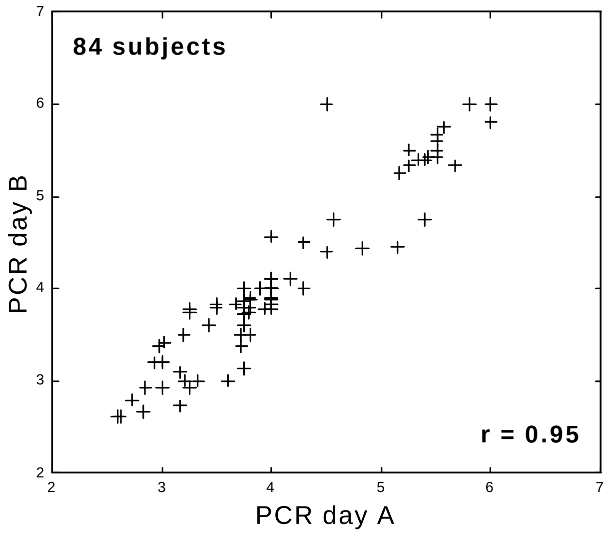
3.1 Phase coordination and PCR

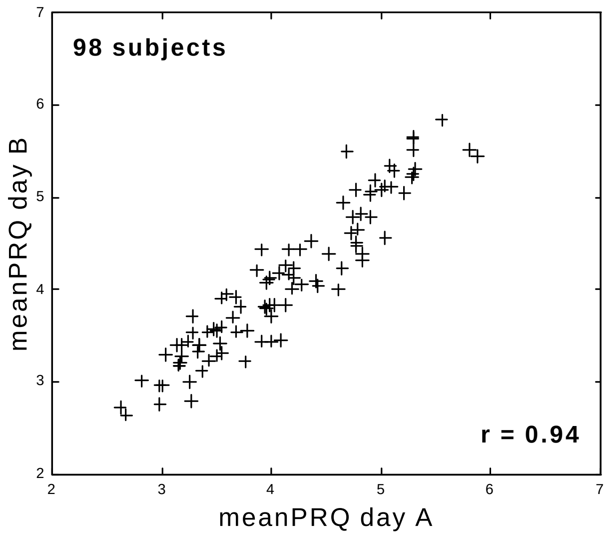
In our previous study [Bettermann et al., 1999] we were able to show that there is an obvious hierarchy in the predominance of phase locking patterns, as shown in Tab. 2. In all, 784 one-hour intervals were analyzed. For 7 subjects no patterns were registered which fulfilled the above predominance conditions, neither in ECG A nor in ECG B. According to Tab. 2, the heart period dynamics of the remaining 91 subjects most frequently yielded the 4:1 phase locking pattern (35%), followed by the 7:2 (19%), 3:1 (17%), 5:1 (15%)[1], 6:1 (12%), and 8:3 (5%). 9:2, 11:2, and 13:2 phase locking ratios were not detectable because of the implemented maximum cycle length of 8 heartbeats in our algorithm. All phase locking patterns were specific to individuals and thus highly reproducible. Furthermore the predominance of phase locking patterns was lost in shuffled data (see second row in Tab. 2).

	2:1	3:1	4:1	5:1	5:2	6:1	7:2	7:3	8:3	other	total analyzed
originals	8	130	275	121	14	96	145	2	37	188	784
surrogates	179	0	0	0	0	0	0	0	0	0	784

Tab. 2 Number of one-hour intervals during night-time with a predominance of phase locking patterns ($f > 2$ and $s > 2$) for the original and for shuffled surrogate data

[1] See restriction under 3.3.





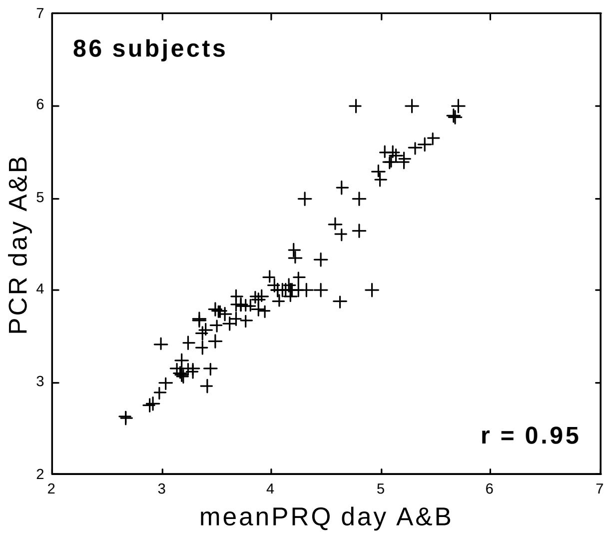


Fig. 4 Correlation diagrams between (1) the weighted phase coordination ratios (*PCR*) during night sleep on day B vs. day A (upper diagram), (2) the mean frequency ratios of heartbeat and respiration (*meanPRQ*) during night sleep on day B vs. day A (middle

diagram), and (3) *meanPRQ* vs. *PCR* over day A and B during night sleep (lower diagram). The first two diagrams display the high intraindividual reproducibility of the coordination parameters, the third diagram demonstrates the close relationship between long-term phase and frequency coordination of heartbeat and respiration in individuals.

The weighted phase coordination ratio *PCR* was > 0 in 84 subjects on both days separately, and in 86 subjects on either day A or day B. *PCR* confirms the intraindividual reproducibility of phase coordination ratios clearly. In the upper diagram of Fig. 4 a high correlation with $r = 0.95$ between *PCR* of day A vs. B for each subject can be observed. That is, if one subject tends to a certain intermittent phase coordination predominance on day A, it is likely that the same predominance will be present on the following day.

3.2 Frequency coordination and meanPRQ

Qualitatively and quantitatively the same results were found for the mean frequency ratio of pulse and respiration (*meanPRQ*). (1) The second diagram of Fig. 4 demonstrates that *meanPRQ*, which could be determined in all 196 ECGs, was highly reproducible intraindividually with $r = 0.95$. (2) The median of *meanPRQ* over all subjects (4.01 on day A and 4.03 on day B) confirms the expected preferred frequency ratio of 4:1 during nighttime for the subjects as a group while ranging from 2.5 to 6 in individual subjects.

3.3 Phase versus frequency coordination

The correlation between *PCR* over two successive days and *meanPRQ* over two days is shown in the third diagram of Fig. 4. Paradoxically, these data also correlate strongly with $r = 0.95$. This finding is not a matter of course, inasmuch as the methodological approaches of *PCR* and *meanPRQ* were totally different: *PCR* is based solely on the detection of intermittent phase coordination which sometimes covers only 5% of the entire time period under consideration. On the contrary, *meanPRQ* is calculated by evaluating all RSA cycles during the whole period of time.

The spurious gaps between approximately *PCR* = 4.5 and 5.2 in the first and third diagram of Fig. 4 are likely due to disregarding 9-pulse, 10-pulse, and 11-pulse pattern classes. 9-pulse and 11-pulse pattern classes would have been needed to register 9:2 and 11:2 phase coordination. Due to the missing 10-pulse pattern classes the 10:2 phase locking patterns were also not counted which resulted in a likely underestimation of the 5:1 phase coordination. All in all, the values 4.5, 5, and 5.5 were not taken accurately into account, when weighting the locking ratios, which resulted in a bias of all *PCR* values > 4.5.

4. Discussion

This study demonstrates that the pattern concept enables the detection and quantification of intermittent phase coordination between heartbeat and respiration, i.e. frequent parallel runs of both rhythms longer than one respiratory cycle. The method is not suited to reveal true physical phase locking or entrainment.

Many patterns in binary heart period dynamics, which describe acceleration and deceleration of instantaneous heart rate, reflect respiratory sinus arrhythmia. Moreover, intermittent phase coordination between heartbeat and respiration[2] evidently causes predominance of certain pattern classes which can be assigned to specific phase locking ratios. These patterns are highly reproducible in individuals, and the frequency distribution of all individually predominant and cyclically stable phase locking patterns (Tab. 2) indicates the preference of 4:1 intermittent cardiorespiratory phase coordination during night sleep in a large group of healthy subjects.

On the whole, identical results were found for the mean frequency ratio of heartbeat and respiration (*meanPRQ*). This parameter was calculated by pattern analysis of respiratory sinus arrhythmia which has been defined as the band pass filtered heart period time series in the respiratory band. The *meanPRQ* is reproducible intraindividually and shows a distinct preference for values around 4:1 during night sleep over all subjects but not in individuals. The correlation between the weighted phase coordination ratio (*PCR*) and *meanPRQ* ($r = 0.95$) is extremely high which supports the validity of each method to determine coordination ratios.

It remains to be proven to what extent the predominance of intermittent phase locking patterns in heartbeat dynamics is due to true electro-mechanical coupling and is also in accordance with findings in the wide field of cardiorespiratory synchronization analysis [e.g. Hoyer et al., 1997, 1998; Raschke, 1987; Rosenblum et al., 1998; Schäfer et al., 1998, 1999; Schiek et al., 1998]. The tremendous advantage of the heartbeat pattern statistics is that it quantifies cardiorespiratory coordination solely on the basis of heart period data from long ECG recordings. This advantage makes the pattern technique easily applicable in clinical practice.

It should first be noted that our results seem to be contradictory to the results of Schäfer et al. [1998, 1999], who pointed out that 'phase locking of respiratory and the cardiac rhythms, and respiratory modulation of heart rate, are two competing aspects of cardiorespiratory interaction'. Referring to the same data, Rosenblum et al. [1998] stated: 'It appears that subjects with epochs of synchronization between the cardiac and respiratory rhythm have no remarkable respiratory modulated heart rate fluctuations, whereas the subjects with the higher RSA exhibit no distinct epochs of cardiorespiratory synchronization.' These findings are in accordance with general observations in chronobiology: enhanced frequency modulation causes loss of phase coordination in many physiological processes [Hildebrandt, 1993]. On the contrary, the circumstantial evidence of phase coordination, presented in this study, could only be found because frequency modulation of heart rate, i.e. RSA, was present. Moreover, analyzing the correlation between the FFT based high frequency power of heart rate variability (HRV), used as a measure of RSA, and the predominance of phase locking related patterns, the opposite was found: e.g. RSA correlated *positively* ($r = 0.48$) with the sum of all numbers of one-hour intervals for which pattern predominance was detected (data not yet published). In other words: the higher RSA the more predominant were phase locking patterns. This conflict cannot be solved in this paper, and it will be a topic of a future study.

Secondly, we may observe that the frequency coordination of heartbeat and respiration has for many years already been seen as the most important parameter to describe hygiogenesis in man. In medicine complemented by the anthroposophic philosophy of R. Steiner (1861-1925), the *PRQ* parameter was introduced around 1920, and has been extensively applied clinically to quantify normalization processes of central human time organization [Heckmann et al.,

[2] It has to be noted that RSA and respiration (respiratory flow) are not identical oscillations. However, in the physiological range a strong 1:1 phase coordination between both cardiorespiratory signals is observed [Schieck et al., 1998], thus coordination between heartbeat and RSA can be directly interpreted as cardiosrespiratory coordination.

1990; Weckenmann et al., 1988]. It has been claimed that *PRQ* should normalize to 4 in healthy subjects during night sleep, although the empirical database was limited. On the one hand this hypothesis can be confirmed: median *PRQ* converges towards four in a large group of healthy persons. But on the other hand our findings have shown that 4.0 does *not* seem to be the 'normal' value in each individual, at least over two consecutive days. The interindividual deviations are large (standard deviation 0.9).

Placing the methods of this study in a wider context, one may view rhythmic organization as an inherent part of all human activity [Handel, 1989], brought forth by musical rhythm which is interpretable as the creative expression of time. Although it seems to be obvious that musical rhythms rise directly from the inner dynamics of man, in most fields of life sciences this close relationship has been disregarded when analyzing physiological rhythmical structures. Rhythm is often reduced to pure periodicity. In the sense of music, rhythms should be regarded as what they are: the cyclic repetition of similar patterns in time or space.

The application of a pure (musical) pattern concept to HRV reaches back to the Middle Ages [Kümmel, 1977]. Despite the long tradition, only few scientists have followed this simple and effective approach in the recent past. Nowadays heartbeat dynamics is preferentially seen as a linear combination of sinus-like rhythms, i.e. sinus functions, and is consequently analyzed by Fourier transform based methods[3]. It has to be shown whether the pattern analysis described here is superior to standard linear and nonlinear HRV techniques in clinical practice.

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[3] One exception is the analysis of fetal cardiotocograms where traditional methods of assessment of HRV are not appropriate. Here, clinical decisions are based on the semi-qualitative analysis of heartbeat patterns.

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