



タイトル Title	Comparison of cardio-locomotor synchronization during running and cycling
著者 Author(s)	Nomura, Kunihiko / Takei, Yoshiaki / Yanagida, Yasuyoshi
掲載誌・巻号・ページ Citation	European Journal of Applied Physiology,89(3-4):221-229
刊行日 Issue date	2003-05
資源タイプ Resource Type	Journal Article / 学術雑誌論文
版区分 Resource Version	author
権利 Rights	
DOI	10.1007/s00421-002-0784-0
JaLDOI	
URL	http://www.lib.kobe-u.ac.jp/handle_kernel/90000081

Comparison of cardio-locomotor synchronization during running and cycling

Kunihiko NOMURA¹, Yoshiaki TAKEI², Yasuyoshi YANAGIDA²

¹; Graduate School of Human Science, Kobe University, 3–11, Tsurukabuto, Nada-ku,
Kobe-shi, Hyogo 657–8501, Japan

²; Faculty of Human Development, Kobe University, 3–11, Tsurukabuto, Nada-ku,
Kobe-shi, Hyogo 657–8501, Japan.

Manuscript Length: 19 text pages, 3 figures, and 2 tables

Address correspondence to:

Yoshiaki Takei

Associate Professor

Faculty of Human Development, Kobe University

3–11, Tsurukabuto, Nada-ku,

Kobe-shi, Hyogo, 657–8501 JAPAN

Phone: +81–78–803–7815

Fax: +81–78–803–7815

E-mail: takei@kobe-u.ac.jp

ABSTRACT

By comparing the characteristics of cardiac-locomotor synchronization (CLS) in running and cycling individuals, we tested whether the characteristics of CLS occurring during rhythmic exercise adhere to the central origin hypothesis, which postulates a direct interaction between cardiovascular centers in the brain and the pattern generator in the spinal cord. Ten healthy subjects performed both exercises at the same intensity ($150 \text{ beats}\cdot\text{min}^{-1}$) and cadence ($150 \text{ steps}\cdot\text{min}^{-1}$ during running and 75 rpm during cycling), while electrocardiograms and electromyograms from the right vastus lateralis muscle were monitored continuously. An examination of the occurrence of heart beats with respect to the locomotor phase revealed that, in running subjects, CLS exists for relatively prolonged periods at specific phases, whereas, in cycling subjects, it occurs intermittently and is not phase-specific (Max duration of CLS: 113.6 ± 66.5 and 58.0 ± 29.3 ($P < 0.05$), respectively). Determining the probability of CLS by chance as a function of its duration, we also found that, during running, CLS likely results from entrainment, whereas, during cycling, it results from chance, occurring when the cardiac rhythm approached the locomotor rhythm. As our result, it was indicated that the duration of muscle contraction during cycling (317.0 ± 18.1 msec) was significantly longer than during running (205.6 ± 20.2 msec). These results indicated that the difference in the CLS characteristics between running and cycling might be influenced by differences in peripheral inputs between exercise modes.

Keywords. entrainment; coupling; synchronization; running; cycling

INTRODUCTION

The concept of “entrainment” or “synchronization” (Pavlidis 1973), wherein a nonlinear oscillator is entrain to an external oscillator when the frequency of external oscillator approaches that of the system, may be the basis of a general mechanism for heart rate regulation during the increase in heart rate but the decrease in heart beat fluctuations to the contrary. Such synchronization has been reported between the rhythms of biological oscillators that exhibit nonlinear behavior, in particular those that have relatively short periods, e.g., cardiac and locomotor synchronization (CLS) (Kirby et al. 1989b, Niizeki et al. 1993, Nomura et al. 2001), locomotor and respiratory synchronization (LRS) (Bechbache and Duffin 1977, Bernasconi and Kohl 1993, Paterson et al. 1986) and cardiac and respiratory synchronization (CRS) (Kenner et al. 1976, Seidel and Herzel 1998, Schäfer et al. 1998). During exercise, the increase in heart rate, which is important for blood circulation, result from the increase in the cardiac sympathetic nervous activity and the withdrawal of the cardiac vagal nervous activity. The transmission of an efferent signal via the sympathetic nervous system is, however, too slow to regulate cardiac rhythm on beat-by-beat basis (Berger et al. 1989).

Previous studies have shown that CLS occurs during walking, running and cycling (Kirby et al. 1989b, Niizeki et al. 1993, Udo et al. 1990). For example, Kirby et al. (1989b) found that the frequency ratio of cardiac and locomotor rhythms, which were determined by means of brief (10-steps during walking and running, 4 sec during cycling) samples, become integer within 1.0 % of each other with a spontaneous cadence during all three activities. Furthermore, some investigators have analyzed the dynamics of heart beats with respect to locomotor phase, namely the phase domain approach (Udo et al. 1990, Niizeki et al. 1993, Nomura et al. 2001). Udo et al. (1990) showed that R waves repetitively occur at a specific phase within each step cycle during running, and Niizeki et al. (1993) showed phase locking between the cardiac and locomotor rhythms during both walking and running. These studies did not, however, address the question of whether CLS occurred as a matter of coincidence or whether there was a linkage between the two rhythms.

Kirby et al. (1991, 1992) tested whether the observed CLS during rhythmic exercise occurred sta-

tistically significant using a cross-over test in which they compared cardiac rhythm of each subject to locomotor rhythm of another age- and gender-matched subject. Since they did not analyze CLS with beat-by-beat and/or step-by-step analysis, the accidental possibility of CLS during skipping, hopping and finger tapping might not be rejected. Using beat-by-beat analysis of CLS and rejection of the null hypothesis that CLS reflects a chance intersection between two independent rhythms, we recently demonstrated that, during running, the phase relationship between cardiac and locomotor rhythms is likely a consequence of entrainment of one rhythm by another (Nomura et al. 2001). To characterize the relationship between cardiac and locomotor rhythms independently in that experiment, we generated surrogate data by means of a random shuffle of the gait cycle time series. In that case, if CLS occurred by chance, the surrogate data would have the same characteristics as the original in a phase domain. After surrogation, however, the phase relationship between the two rhythms was not indicative of CLS; in other words, the null hypothesis was rejected. Whether, during cycling, CLS occurring results from entrainment or by chance is still unknown, however.

It has been proposed that the activity of neural circuits originating in the periphery (e.g., muscle afferents) (Niizeki et al. 1993) or in the central nervous system (Kawahara et al. 1993, Kirby et al. 1990) is the physiological process underlying CLS. Based on analysis of phase response curves, Niizeki et al. (1999) proposed that CLS has a peripheral origin and described the phase dependence of heart rate responses on the temporal relationship between muscle contraction with and cardiac phase. They suggested, based on the concept of Pavlidis (1973), that because the relationship between the timing of muscle contractions and normalized heart beat intervals had a positive slope for the first one-fourth of the cardiac cycle and a negative slope for the latter, muscle contractions occurring during the middle phase of the cardiac cycle might cause stable CLS. They further suggested that the physiological mechanism would involve a phase dependent effect of afferent signaling from active muscle to the cardiovascular centers (CVC) in the brain via group III fibers.

On the other hand, Kawahara et al. (1993, 1994) proposed that modulated heart beat rhythm by locomotor rhythm is originated in the central nervous system and described the existence of a distinct peak in coherence between heart rate variability and lateral gastrocnemius nerve discharge

that corresponded to the mean stepping frequency in paralyzed, vagotomized, decerebrate cats during mesencephalic locomotor region elicited fictive locomotion. The concept of a central origin is that there are interactions between the CVC in the brain and the central pattern generator (CPG) in the spinal cord, which generates locomotor patterns (Grillner 1975).

Because running and cycling generate the same locomotor rhythm, if centrally originating CLS exists in humans, it should have the same characteristics, including rejection of the null hypothesis mentioned above, during rhythmic exercises with the same work rate and locomotor rhythm, even though the exercise mode may differ (e.g., running and cycling). The aim of the present study was to determine whether or not the same characteristics of CLS observed during different mode of rhythmic exercise. To that end, we compared the phase relationship between cardiac and locomotor rhythms during cycling and running, which can be performed at the same heart rate level and locomotor rhythm, but represent different modes of exercise. We used the surrogate data technique (Nomura et al. 2001) and the phase domain approach to decide whether it resulted from entrainment or by chance, and used an index based on conditional probability (Stefanovska et al. 2000) to assess the strength of the CLS.

METHODS

Subjects.

Ten healthy men [mean age 22.9 (range 20–25)] with no history of cardiopulmonary disease participated in the study. Each subject signed informed consent after being provided with a verbal explanation of the intent and procedures of the experiments. This study was approved by Human Subjects Committee of our department in Kobe University.

Protocols.

A 5-min warm-up period was followed by at least 15 min of rest during which subjects were instrumented for data collection. Thereafter, each subject participated in a 20-min session in which he ran on a treadmill (Treadmill NT-12, Nishikawa) at 150 steps·min⁻¹ or cycled on a cycle ergometer (STB-1400, Nihonkoden) at 75 rpm with controlled by metronome at 2.5 Hz throughout a session. Subjects performed the two exercises randomly on non-consecutive days. Before the measurement period, a variety treadmill speeds or work rates were used in an attempt to explore the exercise intensity that produce the HR of 120 beats·min⁻¹ while they practiced running or cycling in time to the metronome at 2.5 Hz. For the first 5-min of the measurement periods, the subjects worked at a rate that produced a heart rate (HR) of 120 beats·min⁻¹. During the next 5–10 min, the treadmill speed or cycling work rate was gradually increased until a target HR (THR) of 150 beats·min⁻¹ was achieved, which was then maintained for a minimum of 5 min. The level of HR on which a subject can continue exercising for 20 minutes does not reach high level such as a maximum HR. Furthermore, a locomotor cadence during running is obviously different with each subjects. When the pitch is controlled, the range of controllable pitch for a long period of running can be restricted within a narrow range. Thus, we set the level of HR at 150 beats·min⁻¹ and the pitch at 2.5 Hz corresponding to 150 steps·min⁻¹ in order to solve both problems (i.e. pitch control and HR level). During that period, the treadmill speed ranged from 100–200 m·min⁻¹ (0 % grade), and the cycling work rate was ranged from 100–180 W.

Data collection.

Beat-to-beat RR interval (RRI) was measured continuously from a surface electrocardiogram (ECG) by using standard bipolar leads (CM_5). To distinguish the R waves of the QRS complex, the ECG signal was amplified, filtered (10–300 Hz) (AB-621G, Nihonkoden) and digitized using a 16-bit analog-to-digital converter (DR-Ma2, TEAC) sampling at 1,000 Hz. To avoid movement artifact, we set filtering frequency band as ten to 300 Hz. The data were stored on a MS-DOS-formatted magnetic optical disk for the later analysis. A customized computer (PC9821Xc13, NEC) program detected the occurrence of the QRS spikes in ECG at a sampling frequency of 1,000 Hz.

To estimate gait cycle (GC), we defined as the interval between the onsets of one muscle contraction and next muscle contraction. GC was measured continuously from a surface electromyogram (EMG) from right vastus lateralis muscle by using bipolar leads. Surface electrodes were placed along the longitudinal axis of the muscle ; the electrodes place was a little to the knee, the electrodes were placed at approximately 10 cm superior to the head of fibula to avoid EMG baseline agitation by motion of a leg, the interelectrode distance was about 30 mm, and the earth electrode was placed on the upper thigh. As with the ECG signal, the EMG signal was amplified, filtered (50–1,000 Hz), digitized using the analog-to-digital converter and stored on a magnetic optical disk and processed off-line. To obtain an integrated EMG, the signal was full-wave rectified and smoothed. Because EMG of vastus lateralis muscle discharges mostly at initial contact of the foot with the treadmill surface, the onset of muscle contraction was defined as the time at which the integrated EMG increased above a preset trigger level using the customized computer program.

Data analyses.

The phase difference between cardiac and locomotor rhythms will need to be studied with beat-by-beat and/or step-by-step analysis over prolonged periods (Kirby et al. 1989b). Consequently, after removing a small number of abnormal RRIs and GCs, the occurrence of CLS was monitored using a phase synchrogram (Rosenblum et al. 1998, Schäfer et al. 1999). Each successive QRS spike and muscle contraction onset was marked as equivalent to one oscillatory cycle, corresponding to which a

2π increment was added. Within this one oscillatory cycle, the instantaneous phase is

$$\phi(t) = 2\pi \frac{t - t_k}{t_{k+1} - t_k} + 2\pi k, \quad t_k \leq t < t_{k+1},$$

where $\phi(t)$ is the instantaneous phase at t , and t_k is time of the k th marker event. In this definition, the phase is a monotonically increasing piecewise-linear function of time defined on a real line. The onset of muscle contractions were taken for the marker events of the locomotor oscillator. The generalized relative phase ($\Psi_{\text{RR-GC}}$) of the GC for the occurrence of an R wave with respect to one GC was calculated as follows.

$$\Psi_{\text{RR-GC}} = \frac{1}{2\pi} (\phi_{\text{GC}}(t_k) \bmod 2\pi),$$

where t_k is the time of k th occurrence of an R wave, and ϕ_{GC} is the instantaneous phase of GC. The time trace of $\Psi_{\text{RR-GC}}$ was visualized by plotting generalized relative phase vs. time (Fig. 1).

[Insert Figure 1 here about]

As mentioned above, our THR was $150 \text{ beats} \cdot \text{min}^{-1}$, and the locomotor rhythms, which were controlled at 2.5 Hz , were $150 \text{ steps} \cdot \text{min}^{-1}$ when running and 75 rpm when cycling. In addition, because we used EMG from only the right vastus lateralis muscle to estimate locomotor rhythms, the estimated rhythm was $1.25 \pm \zeta \text{ Hz}$ (ζ is variability of locomotor rhythm). As a result, the $2 : 1$ phase synchronization observed in the phase synchrogram corresponds to $1 : 1$ entrainment of cardiac rhythm to locomotor rhythm as reported by Kirby et al. (1989b, 1992, 1989a, 1993).

We used an index based on conditional probability to characterize synchronization strength (Stefanovska et al. 2000, Tass et al. 1998). To investigate the strength of the $n : m$ phase synchronization between two oscillators, we regarded cardiac rhythm as a faster oscillator, $\phi_{\text{RR}}(t_k)$, and locomotor rhythm as a slower one, $\phi_{\text{GC}}(t_k)$. The interval of the faster oscillator ϕ_{RR} , $[0, 2\pi n]$ was divided into N bins. The values of $\phi_{\text{RR}}(t_j)$ belong to l th bin, and in the case of $t_k - t_p/2 \leq t_j < t_k + t_p/2$, for each j the distribution is quantified as $r_l(t_k) = \frac{1}{M_l(t_k)} \sum_{i=1}^{M_l(t_k)} e^{i\phi_{\text{GC}}(t_j)}$. According to the Euler's formula,

$$r_l(t_k)^2 = \left(\frac{1}{M_l(t_k)} \sum_{i=1}^{M_l(t_k)} \cos \phi_{\text{GC}}(t_j) \right)^2 + \left(\frac{1}{M_l(t_k)} \sum_{i=1}^{M_l(t_k)} \sin \phi_{\text{GC}}(t_j) \right)^2$$

where $M_l(t_k)$ is the number of points in the bin at the k th instant. t_p is a sliding window period in which $t_p = 30$ s in this study. Where the phases were completely locked or completely unlocked we obtain $|r_l(t_k)| = 1$ or $|r_l(t_k)| = 0$, respectively.

Although an actual R wave occurs only at $\phi_{RR} \bmod 2\pi = 0$, to improve reliability, we also calculated $|r_l(t_k)|$ over all bins and averaged them as follows:

$$\lambda_{n,m}(t_k) = \frac{1}{N} \sum_{l=1}^N |r_l(t_k)|.$$

Since the purpose of our experiment was to measure the strength of the 2 : 1 phase synchronization between cardiac and locomotor rhythms when HR approached $150 \text{ beats}\cdot\text{min}^{-1}$ while running at $150 \text{ steps}\cdot\text{min}^{-1}$ and cycling at 75 rpm, we calculated $\lambda_{2,1}(\lambda_{2:1(\text{CLS})})$.

In this study, we defined CLS as being present when $\lambda_{2:1(\text{CLS})}$ exceeds 0.8, because when $\lambda_{2:1(\text{CLS})}$ continuously exceed 0.8, the phase relationship between cardiac and locomotor rhythms seemed to be a horizontal alignment. To quantify the characteristics of CLS, we first estimated the duration of CLS and the strength of CLS. The duration was defined as a period of continuous $\lambda_{2:1(\text{CLS})} > 0.8$ throughout the 10–20 min measurement period. The strength was defined as mean $\lambda_{2:1(\text{CLS})}$ in the period when $\lambda_{2:1(\text{CLS})}$ exceeds 0.8 for the 10–20 min measurement period.

We used the surrogate data technique (Nomura et al. 2001) to determine whether the observed CLS occurred by chance or whether the two rhythms were linked. If two oscillators are independent, the phase relationship between them should be the same in surrogate data having the same statistical characteristics as the original data (Palus and Hoyer 1998). In this case, because the GC time series was stable throughout the measurement period, it was transformed to surrogate data, which was achieved by random shuffle, yielding a surrogate in which the mean, variation and histogram were the same as the original data.

Statistics.

To evaluate heart rate level, mean gait cycle and mean duration of muscle contraction, average of RRI, GC and duration of muscle contractions during the 10–20 min measurement period were calculated for all subjects. Also, to compare variation of the locomotor rhythm during cycling and running, the

standard deviation (SD) of GC time series (SD_{GC}) under both exercise modes was calculated. For the CLS characteristics, CLS duration and mean $\lambda_{2:1(CLS)}$ under both exercise modes with the original and surrogate data were calculated. Data obtained for the characteristics of CLS during running and cycling tests and with the original and the surrogate data were compared using paired t tests. Values of $P < 0.05$ were considered significant.

RESULTS

There were no significant differences in the mean value of RRI and GC between running and cycling subjects (Table 1), indicating that the intensity and locomotor rhythms were the same for both exercises.

[Insert Table 1 here about]

Moreover, there was no significant difference between SD_{GC} for the two exercise modes, indicating no significant effect of exercise mode on the variability of locomotor rhythms. The mean values of RRI of both exercise modes during the 10–20 min measurement period correspond to about $151 \text{ beats}\cdot\text{min}^{-1}$. There was no significant difference between exercise modes. Although THR was $150 \text{ beats}\cdot\text{min}^{-1}$, mean HR during the 10–20 min measurement period was slightly above THR because there were subjects whose HR gradually increase near the end of measurement period. However, the mean value of durations of the contractions of the right vastus lateralis muscle were significantly longer when cycling than when running ($P < 0.05$).

Fig. 2 shows representative RRI (Fig. 2A and A') and GC (Fig. 2B and B') time series, and the trace of Ψ_{RR-GC} (Fig. 2C and C') recorded from one subject while he was running (Fig. 2A, B and C) and cycling (Fig. 2 A', B' and C').

[Insert Figure 2 here about]

While the subject was running, three horizontal plateaus in Ψ_{RR-GC} were observed after 9–15, 16–18, and 19–20 min of exercise, indicating the occurrence of CLS, which was about 0.4 and 0.9 of GC (Fig. 2C). GC was not specifically changed during CLS, but remained stable throughout the experimental period (Fig. 2B); likewise, heart rate variability remained steady during these periods (Fig. 2A).

On the other hand, as a consequence of differences in the phase relationship, Ψ_{RR-GC} , CLS occurred only intermittently during cycling and was not specific for any particular phase (Fig. 2C'). As the GC time series again remained steady throughout the experimental period (Fig. 2B'), we deduced that, in this case, CLS occurred when the cardiac and locomotor rhythms intersected during transitions of RRI (Fig. 2A').

We next used the surrogate data technique (Nomura et al. 2001) to determine whether the observed CLS resulted from entrainment of the cardiac rhythm by the locomotor rhythm, or whether it occurred when the cardiac and locomotor rhythms approached one another by chance. We found that, during running, the trace of the original Ψ_{RR-GC} showed prolonged periods of CLS (Fig. 3A), whereas the surrogate data showed no horizontal plateaus in Ψ_{RR-GC} together with repetitive phase drifts (Fig. 3B).

[Insert Figure 3 here about]

During cycling, by contrast, there was little difference between the original and surrogate data, and the trace of the original and surrogate Ψ_{RR-GC} showed repetitive phase drifts (Fig. 4A and B).

[Insert Figure 4 here about]

In addition, as a result of changes in the strength of the CLS, $\lambda_{2:1}(\text{CLS})$ was significantly smaller after surrogation (Fig. 3C; solid line: original data; dashed line: surrogate data), particularly during the period spanning min 12 to 14 of the exercise. For the 10–20 min measurement period, the maximum CLS duration for the original and surrogate data were 294.5 sec and 127.7 sec in the subjects, respectively. During cycling, by contrast, there were no specific differences in the maximum CLS duration for the 10–20 min of original and surrogate data were 28.6 sec and 28.2 sec, respectively.

For the distribution of Ψ_{RR-GC} in the 10–20 min measurement period during running, the histogram of the original Ψ_{RR-GC} showed two peaks at 0.3~0.4 and 0.8~0.9 (Fig. 3A the right side). In contrast with the original data, the peaks in histogram of Ψ_{RR-GC} of the surrogate data showed lower (Fig. 3B the right side). As a result, the distribution of Ψ_{RR-GC} in the 10–20 min measurement period during cycling, there were no specific differences in the histograms of Ψ_{RR-GC} of the original and surrogate data: both histograms showed no any peaks.

When the CLS criterion, which has been conducted by Kirby et al. (1992), was adopted here, the difference between the original and surrogate Ψ_{RR-GC} trace during running observed by our method became indefinite (Fig. 5).

[Insert Figure 5 here about]

Also, the frequency ration between heart rate and gait rate, which were determined by 5 s data samples, showed no difference in CLS between the original and surrogate data during running and cycling.

Finally, Table 2 shows that both the maximum durations of the CLS periods and the total CLS time were significantly ($P<0.05$) longer during running than during cycling.

[Insert Table 2 here about]

Furthermore, the mean values of $\lambda_{2:1(\text{CLS})}$ in the measurement periods was significantly reduced by surrogation of the data obtained during running ($P<0.05$), but there were no significant differences between the original and surrogate data obtained during cycling. Although there was no specific variation in the mean $\lambda_{2:1(\text{CLS})}$ among subjects because the value was calculated in the period when $\lambda_{2:1(\text{CLS})}$ are more than 0.8 for the 10–20 min measurement period, there was a little variation in duration of CLS among subjects.

DISCUSSION

In the present study, we demonstrated that, during running, relatively long periods of phase synchronization between cardiac and locomotor rhythms occurred at specific phases using the phase synchronogram, and that the strength of the phase synchronization is diminished significantly after surrogation of the original data using the surrogate data technique (Nomura et al. 2001) (Fig. 3). During cycling, by contrast, only comparatively brief, intermittent periods of phase synchronization occurred at no specific phase, and the strength of phase synchronization was changed little by surrogation (Fig. 4). This result that the phase difference between cardiac and locomotor rhythms did not hold a specific phases is in agreement with the findings of Kirby et al. (1989a). It is highly likely that CLS occurring during running results from entrainment of the cardiac rhythm by the locomotor rhythm. During cycling, by contrast, the phase relationship seems to be due solely to CLS occurring when the cardiac rhythm approaches the locomotor rhythm by chance.

Methodological considerations

The rationale for using the phase synchronogram to investigate the phase relationship between cardiac and locomotor rhythms was manifested by Niizeki et al. (1993) and Udo et al. (1990), and was illustrated by the results of Kirby et al. (1989a). Niizeki et al. (1996) have shown that, during walking, the phase synchronization between cardiac and locomotor rhythms occurred at the specific phases corresponding to 0.1~0.3 and 0.6~0.8 per interval of the left heel strikes. Our previous study (Nomura et al. 2001) has shown that, during running, the phase synchronization occurred at specific phases corresponding to 0.2~0.4 and 0.7~0.9 per gait cycle. As shown in the previous studies and the current study (Fig. 3A), during walking and running, the phase synchronization between cardiac and locomotor rhythms at specific phases indicates that the timing of the muscle contractions corresponded to the end systolic to early diastolic phase of the cardiac cycle. By contrast, the results of Kirby et al. (1989a), which during cycling the phase difference between cardiac and locomotor rhythms gradually lengthened and shortened, is in consistent to our results (Fig. 4A). Consideration about the phase difference between cardiac and locomotor rhythms was not completed in the frequency ration of heart rate and gait rate,

which is mean value of brief (5 sec) samples.

The present study demonstrated that using the surrogate data technique (Nomura et al. 2001), during running, the accidental provability of CLS was rejected but, during cycling, was not rejected. Not all synchronization phenomena represent entrainment in that synchronization between two rhythms may occur by chance when one oscillator rhythm is close to that of the other. To solve this problem, Kirby et al. (Kirby et al. 1992, Kirby et al. 1991) used “cross-over test”, which the cardiac data from one subject is compared to the locomotor rate data from another. And then, they suggested that CLS during hopping and skipping (Kirby et al. 1992) and finger tapping (Kirby et al. 1991) were not statistically significant. Because they defined CLS as being when cardiac and locomotor rate were within 1 % of the closest integer ratio, phase differences between cardiac and locomotor rhythms was not taken into consideration. As our results, the frequency ration between heart rate and gait rate, which were determined by means of 5 sec data samples, showed no obvious differences in the integer ration within 1.0 % each other between the original and surrogate data during running and cycling (Fig. 5). These results indicate that beat-by-beat and/or step-by-step analysis to relationship between cardiac and locomotor rhythms is needed to test whether CLS represents an entrainment or if it is accidental.

Although the past studies evaluated the degree of CLS, which was duration (Niizeki et al. 1993) or incidence (Kirby et al. 1989b, Kirby et al. 1992) of CLS, qualitatively, the current study demonstrated the duration and strength over 10–20 min of measurement period quantitatively using the $\lambda_{2:1(\text{CLS})}$ index. In addition, using of the surrogate data technique and the $\lambda_{2:1(\text{CLS})}$ index, we determined the probability of accidental CLS as a function of its duration. The $\lambda_{2:1(\text{CLS})}$ index detects phase synchronization at not only specific phases but also any phases, however. Therefore, in addition to use the $\lambda_{2:1(\text{CLS})}$ index, evaluation of distribution of $\Psi_{\text{RR-GC}}$ is also required when the phase difference is important.

CLS originating directly from active muscles

In the relationship between CLS occurring and vertical acceleration of the body, Kirby et al. (1992) evaluated CLS during skipping and hopping in human. They suggested that the vertical movements

of visceral is unimportant to the CLS. As for a difference of exercise mode like running and cycling, not only the existence of vertical acceleration of the body but the muscle contraction behavior, e.g. concentric or eccentric, differs. As our result, it was indicated that, during cycling, the duration of muscle contraction was longer than during running (Table 1). Although differences in the characteristics of CLS between running (Fig. 3) and cycling (Fig. 4) cannot be explained only from the results of the current study, one possibility is the difference in the duration of muscle contraction.

According to the concept of peripheral origin, CLS occurs because the afferent signal from active muscles during voluntary contraction is phase dependent within the cardiac cycle. According to the study conducted by Niizeki and Miyamoto (1999), it has been speculated that the phase dependency of the afferent signal from muscle to the CVC via group III fibers would modulate cardiac parasympathetic nervous (CPN) activity. In that regard, Niizeki et al. (1999, 1998) assessed the effects of the timing of muscle contraction within the cardiac cycle on heart beat by estimating the phase response curve for muscle contractions within several cardiac phases. The phase response curve showed that muscle contractions occurring early phase in the cardiac cycle i.e., during systole provoke a shortening of RRI, while muscle contractions occurring in the middle or later phase of the cycle i.e., during diastole provoke a lengthening of RRI. Consequently, the slope of the phase response curve ($-2 \sim 0$) in the mid to latter phase of the cardiac cycle is negative and therefore consistent with the condition of stable phase synchronization described in the theoretical analysis by Pavlidis (1973). Consistent with those findings, we observed that CLS during running occurs at 0.4 and 0.9 of GC (Fig. 3A), indicating that the timing of the muscle contractions corresponded to the end systolic to early diastolic phase of the cardiac cycle.

On the other hand, Niizeki et al. (1999) also reported that the phase response curve from some subjects did not exhibit the aforementioned characteristics. They speculated that if the duration of muscle contraction was comparable to heart beat interval, despite the fact that subjects were asked to contract impulsively their muscles as rapidly as possible, the phase-dependent heart beat response to the muscle contraction occurring within the cardiac cycle is considered to be smoothed or averaged over the duration of the muscle contraction. This might also explain, why, during cycling in the present

study, CLS was intermittent and occurred at no specific phase; in that case, RRI was approximate 400 msec and duration of muscle contraction was approximate 320 msec corresponded to 80 % of the cardiac cycle.

If as suggested above CLS is the product of the phase-dependent signaling via group III muscle afferents to the CVC, and that information in turn plays a role in inhibiting CPN activity (Niizeki and Miyamoto 1999), this inhibitory effect on CPN activity would likely induce a phase-dependent efferent signal and would be synchronized to the heart beat. Evidence support such a scenario include the observations that: 1) stimulation of group III afferent fibers drives the CVC (McMahon and McWilliam 1992, Rowell and O'Leary 1990); 2) with the muscle contracting every two heart beats, the frequency is too high to transmit an efferent signal via the sympathetic nervous system (Berger et al. 1989); 3) cardiac responses to sympathetic stimulation are phase-independent (Spear and Moore 1973); and 4) CPN activity is phase-dependent within cardiac cycle (Levy et al. 1972, Yang et al. 1984). Recently, Nakamura et al. (1997) found that respiratory sinus arrhythmias (RSA) were decreased with muscle contraction during inspiration and increased with muscle contractions during expiration. By way of explanation, they suggested that afferent information from contracting muscle might inhibit the CPN activity, which is consistent with concept of Niizeki et al. (1999).

CLS of indirect peripheral origin

One alternative explanation for the difference of CLS characteristics could be locomotor-induced changes in thoracic and abdominal pressures vary the rate of venous return (VR) and/or ventricular ejection (VE), and thereby influence cardiac rhythm (Simmons et al. 1997). Simmons et al. (1997) observed the intermittent CLS in trotting dogs, and suggested that the variation in cardiac period and the resulting intermittent CLS are a function of locomotor and ventilatory influence on VR and/or VE. They emphasized that the systole of the cardiac cycles began early in support phase of locomotion during the intermittent CLS. In running mammals, the thoracic is subjected to repeated impact loading as the limbs strike the ground (Bramble and Carrier 1983). However, there would be little impact loading in cycling humans. Although, locomotor-induced changes in thoracic and abdominal pressures may

vary the rate of VR and/or VE in quadrupedal species (Simmons et al. 1997) and running humans, locomotor-induced changes are expected to be less pronounced in cycling humans.

Another alternative possibility is that respiratory rhythms exert an effect on cardiac rhythm. If so, CRS would likely be indicative of CLS when LRS occurs during rhythmic exercise. This indirect peripheral origin hypothesis may explain the difference in the characteristics of CLS seen with running and cycling because, like CLS, LRS occurs intermittently during cycling but for more prolonged periods during running (Paterson et al. 1986, Bernasconi and Kohl 1993). In addition, CRS occurs while individuals are at rest (Kenner et al. 1976, Schäfer et al. 1998, Seidel and Herzel 1998, Galletly and Larsen 1990). Niizeki et al. (1993) reported that both CLS and LRS occur during walking, when respiratory and locomotor rhythms are spontaneous; however, LRS was abolished when subjects voluntarily synchronized locomotor rhythm to cardiac rhythm. They speculated that to exhibit CLS, LRS might need to be abolished, but emphasized that this was mere speculation. Since effects of respiratory rhythm on CLS cannot be determined from the results of the current study, further study would be needed to test these effects.

CLS of central origin

The cardiac rhythm is modulated by the centrally generated locomotor rhythm. For example, Kawahara et al. (1993, 1994) reported that heart beat fluctuations are modulated by the frequency of locomotor rhythm, which is indicated by integrated efferent discharges (time constant 0.1 s) in the hind-limb muscle nerve during fictive locomotion in decerebrate cats whose hindlimb muscle nerves were dissected peripherally to eliminate afferent discharge from the muscles. However, although they found a coherence peak in heart beat fluctuations at a frequency corresponding to the mean stepping frequency, they did not evaluate the phase relationship between cardiac and locomotor rhythms. Their findings nonetheless suggest that the modulated heart beats rhythm by locomotor rhythm originates centrally, and is the product of a direct interaction between the CVC and the CPG, though it is not clear whether or not CLS occurred. If CLS is originated by the neural circuits in central nervous system, the characteristics of CLS observed during different exercise modes, which have the same locomotor rhythm and the same

intensity, may resemble each other.

To address that question, we compared CLS during cycling and running using a protocol in which the two exercise modes had the same locomotor rhythm and the same intensity. In addition, we used the surrogate data technique to assess whether the observed CLS resulted from entrainment of cardiac to locomotor rhythms or from chance. As our results, the characteristics of the observed CLS during running and cycling were different (Fig. 3, 4 and Table 2). It is, thus, suggested that the concept of central origin might not be able to explain the CLS that occurs in rhythmically exercising humans. The locomotor CPG, however, might behave differently depending on the exercise mode. In this study, there was difference of the duration of muscle contraction between running and cycling.

In conclusion, the present study showed differences between running and cycling in the characteristics of CLS. These differences may be used to explain the observed difference in the duration of muscle contraction between two modes of locomotion. For running, the phase dependent afferent signals from the muscle might influence on CVC and inhibit CPN activity when a relative short duration of muscle contraction occurs within one cardiac cycle. By contrast, for cycling, because a duration of muscle contraction is long enough within one cardiac cycle, the phase dependent effect of afferent signals from the muscle might be smoothed or averaged. Further study are needed to investigate a phase dependent heart beat response by muscle contractions during running.

ACKNOWLEDGMENTS

We are grateful to Professor Y. Yamamoto (Graduate School of Education, The University of Tokyo, Tokyo, Japan) for his useful suggestions, and to Professors M. Yamaguchi and H. Ando (Faculty of Health Science, Kobe University School of Medicine, Kobe, Japan) for their valuable discussions.

Correspondence and requests for materials should be addressed to Y. Takei (e-mail: takei@kobe-u.ac.jp)

REFERENCES

- Bechbache RR, Duffin J (1977), The entrainment of breathing frequency by exercise rhythm, *J. Physiol. (Lond)* **272**: 553–561.
- Berger RD, Saul JP, Cohen RJ (1989), Transfer function analysis autonomic regulation I. Canine atrial rate response, *Am. J. Physiol.* **256**: H142–H152.
- Bernasconi P, Kohl J (1993), Analysis of co-ordination between breathing and exercise rhythms in man, *J. Physiol. (Lond)* **471**: 693–706.
- Bramble DM, Carrier DR (1983), Running and breathing in mammals, *Science* **219**: 252–256.
- Donville JE, Kirby RL, Doherty TJ, Gupta SK, Eastwood BJ, MacLeod DA (1993), Effect of cardiac-locomotor coupling on the metabolic efficiency of pedalling, *Can. J. Appl. Physiol.* **18**: 379–391.
- Galletly DC, Larsen PD (1990), The determination of cardioventilatory coupling from heart rate and ventilatory time series, *Res. Exp. Med-Berl.* **199**: 95–99.
- Grillner S (1975), Locomotion in vertebrates: central mechanisms and reflex interaction, *Physiol. Rev.* **55**: 247–304.
- Kawahara K, Yamauchi Y, Niizeki K, Yoshioka T (1994), Interactions between respiratory, cardiac and stepping rhythms in decerebrated cats: functional hierarchical structures of biological oscillators, *Methods. Inf. Med.* **33**: 129–132.
- Kawahara K, Yoshioka T, Yamauchi Y, Niizeki K (1993), Heart beat fluctuation during fictive locomotion in decerebrate cats: locomotor-cardiac coupling of central origin, *Neurosci. Lett.* **150**: 200–202.
- Kenner T, Pessenhofer H, Schwabberger G (1976), Method for the analysis of the entrainment between heart rate and ventilation rate, *Pflügers. Arch.* **363**: 263–265.

- Kirby RL, Atkinson SM, Donville JE, Urdang MF, Stanley DA, Gupta SK, MacLeod DA (1992), Failure of accentuated vertical body movements to induce cardiac-locomotor coupling, *J. Appl. Physiol.* **72**: 1368–1374.
- Kirby RL, Carr SE, MacLeod DA (1990), Cardiac-locomotor coupling while finger tapping, *Percept. Mot. Skills* **71**: 1099–1104.
- Kirby RL, Gupta SK, Carr SE, MacLeod DA (1991), Cardiac-locomotor coupling while finger tapping: Part II. A cross-over control study, *Percept. Mot. Skills* **73**: 831–834.
- Kirby RL, MacLeod DA, Marble AE (1989a), Coupling between cardiac and locomotor rhythms: the phase lag between heart beats and pedal thrusts, *Angiology* **40**: 620–625.
- Kirby RL, Nugent ST, Marlow RW, MacLeod DA, Marble AE (1989b), Coupling of cardiac and locomotor rhythms, *J. Appl. Physiol.* **66**: 323–329.
- Levy MN, Iano T, Zieske H (1972), Effects of repetitive bursts of vagal activity on heart rate, *Circ. Res.* **30**: 186–195.
- McMahon SE, McWilliam PN (1992), Changes in R-R interval at the start of muscle contraction in the decerebrate cat, *J. Physiol.(Lond)* **447**: 549–562.
- Nakamura Y, Hayashi N, Muraoka I (1997), Temporal effect of muscle contraction on respiratory sinus arrhythmia, *Methods. Inf. Med.* **36**: 268–270.
- Niizeki K, Kawahara K, Miyamoto Y (1993), Interaction among cardiac, respiratory, and locomotor rhythms during cardiocomotor synchronization, *J. Appl. Physiol.* **75**: 1815–1821.
- Niizeki K, Kawahara K, Miyamoto Y (1996), Cardiac, respiratory, and locomotor coordination during walking in humans, *Folia. Primatol. Basel.* **66**: 226–239.
- Niizeki K, Miyamoto Y (1998), Cardiocomotor interactions during dynamic handgrip and knee extension exercises. phase-locked synchronization and its physiological implications, *Adv. Exp. Med. Biol.* **450**: 199–206.

- Niizeki K, Miyamoto Y (1999), Phase-dependent heartbeat modulation by muscle contractions during dynamic handgrip in humans, *Am. J. Physiol.* **276**: H1331–H1338.
- Nomura K, Takei Y, Yanagida Y (2001), Analysing entrainment of cardiac and locomotor rhythms in humans using the surrogate data technique, *Eur. J. Appl. Physiol.* **84**: 373–378.
- Palus M, Hoyer D (1998), Detecting nonlinearity and phase synchronization with surrogate data, *IEEE. Eng. Med. Biol. Mag.* **17**: 40–45.
- Paterson DJ, Wood GA, Morton AR, Henstridge JD (1986), The entrainment of ventilation frequency to exercise rhythm, *Eur. J. Appl. Physiol.* **55**: 530–537.
- Pavlidis T (1973), *Biological Oscillators: Their Mathematical Analysis*, Academic Press, New York.
- Rosenblum MG, Kurths J, Pikovsky A, Schafer C, Tass P, Abel HH (1998), Synchronization in noisy systems and cardiorespiratory interaction, *IEEE. Eng. Med. Biol. Mag.* **17**: 46–53.
- Rowell LB, O’Leary DS (1990), Reflex control of the circulation during exercise: chemoreflex and mechanoreflexes, *J. Appl. Physiol.* **69**: 407–418.
- Schäfer C, Rosenblum MG, Abel H, Kurths J (1999), Synchronization in the human cardiorespiratory system, *Phys. Rev. E* **60**: 857–870.
- Schäfer C, Rosenblum MG, Kurths J, Abel HH (1998), Heartbeat synchronized with ventilation, *Nature*. **392**: 239–240.
- Seidel H, Herzel H (1998), Analyzing entrainment of heartbeat and respiration with surrogates, *IEEE. Eng. Med. Biol. Mag.* **17**: 54–57.
- Simmons AD, Carrier DR, Farmer CG, Gregersen CS (1997), Lack of locomotor-cardiac coupling in trotting dogs, *Am. J. Physiol.* **273**: R1352–R1360.
- Spear JF, Moore EN (1973), Influence of brief vagal and stellate nerve stimulation on pacemaker activity and conduction within the atrioventricular conduction system of the dog, *Circ. Res.* **32**: 27–41.

- Stefanovska A, Haken H, McClintock PVE, Bajrović MHF, Ribarič S (2000), Reversible transitions between synchronization states of the cardiorespiratory system, *Phys. Rev. Lett.* **85**: 4831–4834.
- Tass P, Rosenblum MG, Weule J, Kurths J, Pikovsky A, Volkmann J, Schnitzler A, Freund HJ (1998), Detection of n:m phase locking from noisy data: Application to magnetoencephalography, *Phys. Rev. Lett.* **81**: 3291–3294.
- Udo M, Yoshida T, Nakazumi T, Kinugawa K, Watanabe A (1990), Occurrence of entrainment of heart beat into endurance running pitch and its significance in energy consumption, *in* M. Kaneko, ed., ‘Fitness for the Aged, Disabled, and Industrial Worker’, Vol. 20 of *Int. Ser. Sport. Sci.*, Human Kinetics Books, Champaign, Ill., pp. 79–83.
- Yang T, Jacobstein MD, Levy MN (1984), Synchronization of automatic cells in S-A node during vagal stimulation in dogs, *Am. J. Physiol.* **246**: H585–H591.

Table 1

RR interval, gait cycle and muscle contraction duration during running and cycling.

	Run	Bicycle
RRI [msec]	396.6±2.5	395.0±3.0
GC		
mean [msec]	799.9±1.1	800.2±3.0
SD _{GC} [msec]	18.1±2.2	17.7±4.8
Duration of muscle contraction [msec]	205.6± 20.2	317.0±18.1*
Treadmill speed [m·min ⁻¹]	137.3±48.4	–
Work Rate [W]	–	131.8±27.9

Values are group means±SD. RRI, RR interval; GC, gait cycle; SD_{GC}, standard deviation of GC time series. *Significant difference from Run, $P < 0.05$.

Table 2

Max duration and total duration of cardio-locomotor synchronization (CLS) and degree of CLS during running and cycling.

	Run	Bicycle
Max duration of CLS [sec]	113.6±66.5	58.0±29.3*
Total duration of CLS [sec]	368.5±113.3	137.2±73.0*
mean $\lambda_{2:1}(\text{CLS})$		
<i>org.</i>	0.93±0.02	0.90±0.02*
<i>sur.</i>	0.92±0.04§	0.91±0.05

Values are group means±SD. *org.*, the original data; *sur.*, the surrogate data. *Significant difference from Run, $P < 0.05$. §Significant difference from the original data, $P < 0.05$.

FIGURE LEGENDS

Fig. 1 The derivation of cardio-locomotor synchrogram from the phase of locomotor and times of heart beats (R peaks in the ECG).

Fig. 2 Representative phase relationship between cardiac and locomotor rhythms in one subject. Shown are the time series of RR interval (RRI) (A, A'), gait cycle (GC) (B, B') and the trace of the generalized relative phase difference between cardiac and locomotor rhythms (Ψ_{RR-GC}) (C, C') during running (A, B, C) and cycling (A', B', C'). Note that whereas periods of CLS are relatively prolonged and occur in certain phases during running, only brief periods of CLS occurred intermittently and in no specific phase during cycling.

Fig. 3 Comparison of original and surrogate running data. Shown are the trace (left side) and the distribution (right side) of Ψ_{RR-GC} during 10–20 min measurement period from a representative subject (data in Fig. 1 is from the same subject): (A) original data; (B) surrogate data; (C) time courses of $\lambda_{2:1(CLS)}$ for the original (solid line) and surrogate (dashed line) data. Note that after surrogation CLS was disrupted, and $\lambda_{2:1(CLS)}$ was diminished, especially after 12–14.5 min of exercise.

Fig. 4 Comparison of original and surrogate cycling data. Data from the same subject are presented as in Fig. 2. Note that surrogation had little effect on the data in this case.

Fig. 5 CLS criterion of frequency ratio of cardiac and locomotor rhythms. CLS was defined as being present when the frequency ratio of heart rate (HR) and gait rate (GR), which were determined by means of 5 s data samples, become integer within 1.0 % of each other. Shown are the time course of the frequency ratio between HR and GR for 5 s data samples every 5 s: (A) running; (B) cycling for the original (solid line and ●) and surrogate (dashed line and ○) data. Note that after surrogation had little effect on the data in both exercise modes.

Fig. 1

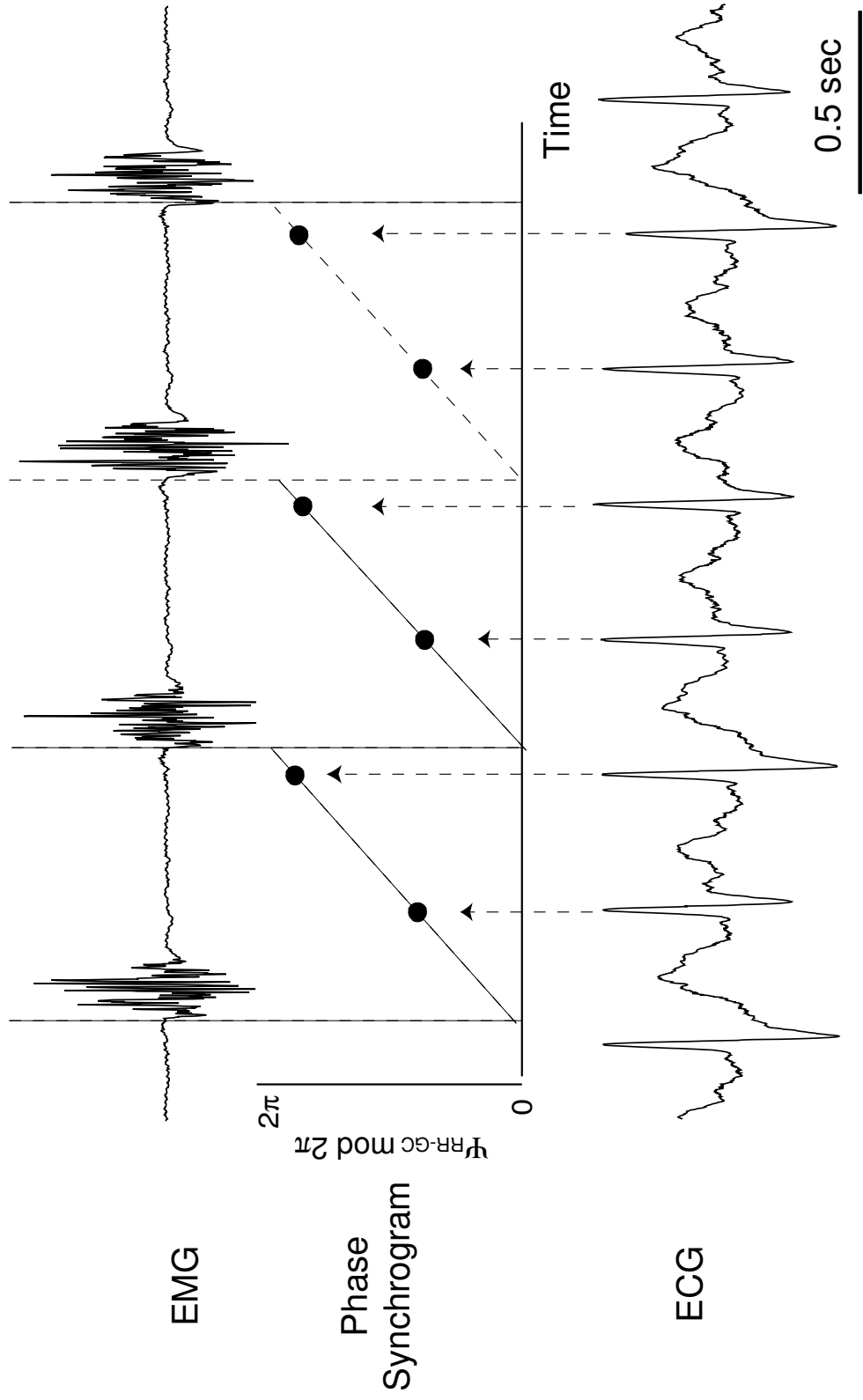


Fig. 2

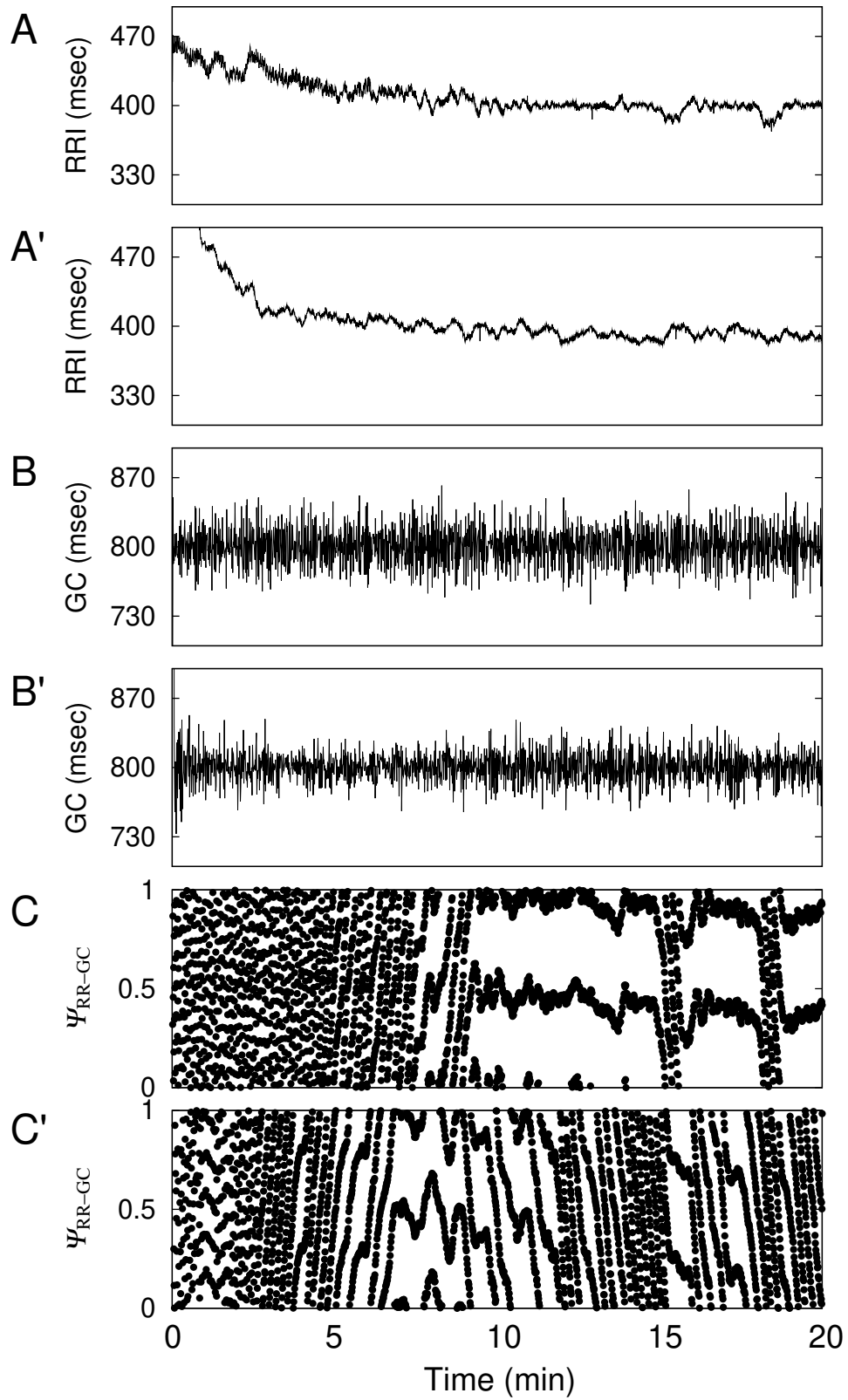


Fig. 3

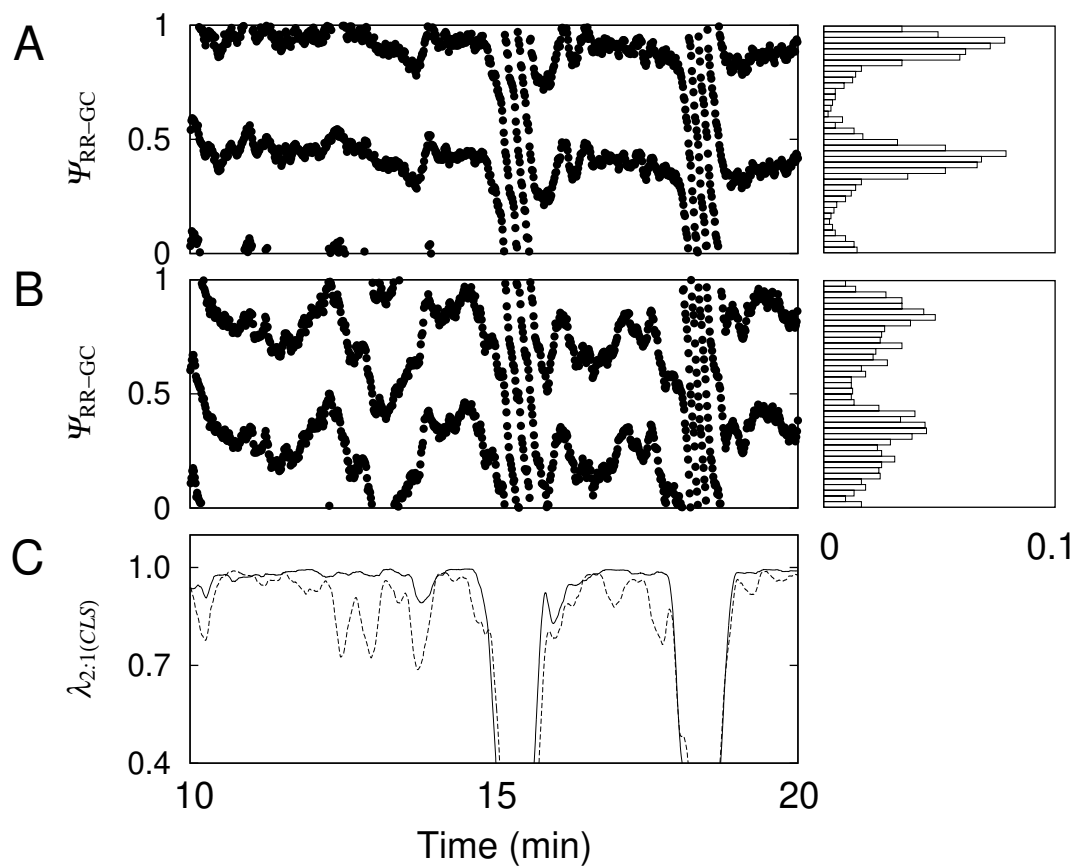


Fig. 4

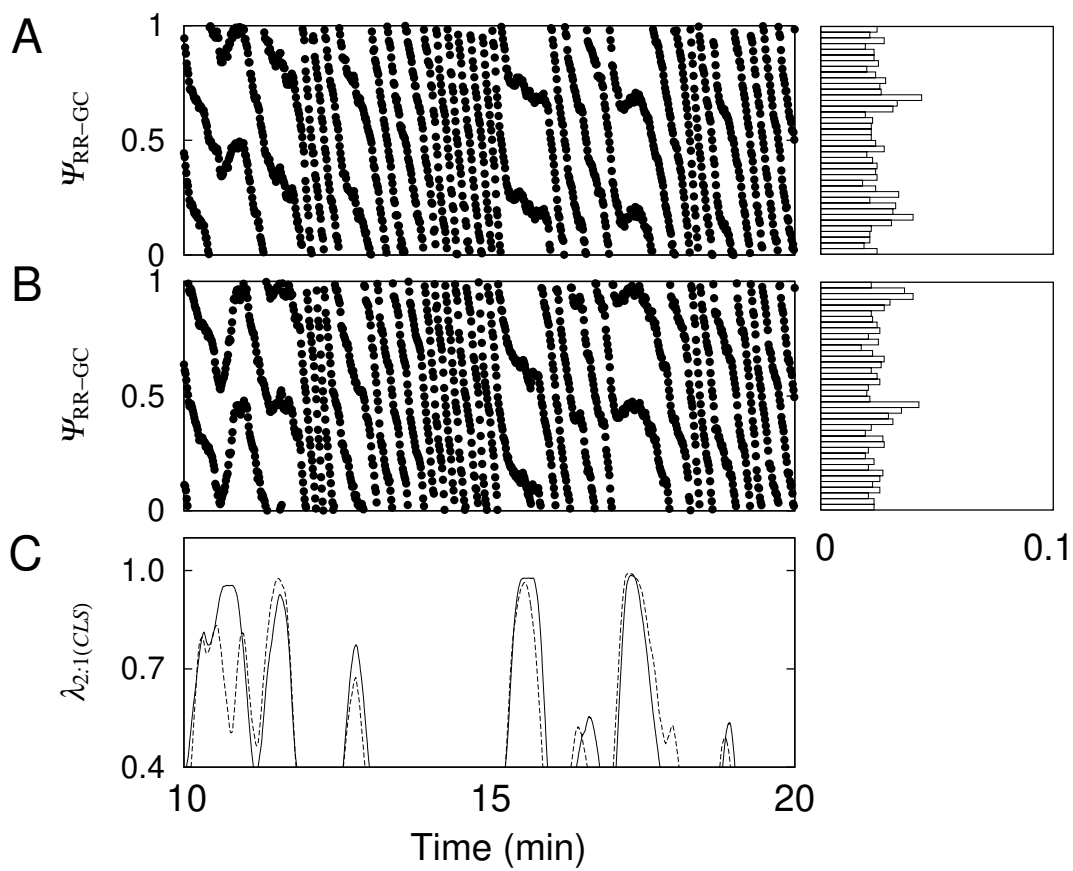


Fig. 5

