

## Phase Transition in a Healthy Human Heart Rate

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A healthy human heart rate displays complex fluctuations which share characteristics of physical systems in a critical state. We demonstrate that the human heart rate in healthy individuals undergoes a dramatic breakdown of criticality characteristics, reminiscent of continuous second order phase transitions. By studying the germane determinants, we show that the hallmark of criticality—highly correlated fluctuations—is observed only during usual daily activity, and a breakdown of these characteristics occurs in prolonged, strenuous exercise and sleep. This finding is the first reported discovery of the dynamical phase transition phenomenon in a biological control system and will be a key to understanding the heart rate control system in health and disease.

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It has been suggested that the underlying mechanism behind human heart rate regulation shares the general principles of other complex systems [1,2]. Indeed, fractal concepts [3], chaotic dynamics, and the statistical theory of turbulence [2], have been shown to provide useful paradigms for characterizing heart rate fluctuations, applicable in the prognosis and diagnosis of cardiovascular diseases [4,5]. Nevertheless, the nature of heart rate complexity has eluded satisfactory explanation. Recently, critical phenomena have been proposed as the likely paradigm to explain the origins of heart rate fluctuations [6,7], suggesting that the theory of phase transitions and critical phenomena in nonequilibrium systems [8–10] may be useful in elucidating the mechanism of complex heart rate dynamics. Characteristic features at a critical point of a second order phase transition are the divergence of the relaxation time with strongly correlated fluctuations and the scale invariance in the statistical properties. Indeed, a healthy human heart rate has been confirmed robustly to show these types of behavior [1,5,7,11,12].

Here we seek a phase transition phenomenon in heart rate in order to support the criticality hypothesis more strongly. We provide evidence that a clear transition of heart rate dynamics between distinct, stable “phases” can be revealed in heart rate fluctuations in healthy individuals. Within these phases—observed in experimentally controlled behavioral states of sleep and prolonged strenuous exercise—healthy human heart rate fluctuations undergo a dramatic breakdown of critical characteristics, in particular, long-range correlations.

Using a modified random walk method with a detrending procedure, we study: (1) the correlation properties of the interbeat intervals, (2) the scale dependence of the non-Gaussian probability density function (PDF), and (3) the magnitude correlation function which characterizes the correlation properties of the local energy fluctuations

across different scales. All of these quantities confirm that strongly correlated behavior is observed only in the state of usual daily activity, and a breakdown of these characteristics occurs in other states. In particular, an essential difference among distinct states, which has not been observed previously [1,5], is only observed by using (3), i.e., the magnitude correlation function, suggesting the need to account for the scalewise local energy correlations in studying complex heart rate dynamics, and possibly other complex real-world signals.

We analyze seven records of healthy subjects (mean age: 25.3 yr) in three behavioral states: (1) usual daily activity, (2) experimental exercise, and (3) sleep. The data set consists of the interbeat intervals between consecutive heartbeats measured over 24 h [Fig. 1], in which the subjects were initially asked to ride on a bicycle ergometer for 2.5 h, as the exercise state, and maintain their heartbeat intervals at 500–600 ms. After the exercise, the data were continuously measured during usual daily activity in the daytime and sleep at night, with regular sleep schedules. As shown in Fig. 1, the data set is classified in four states:

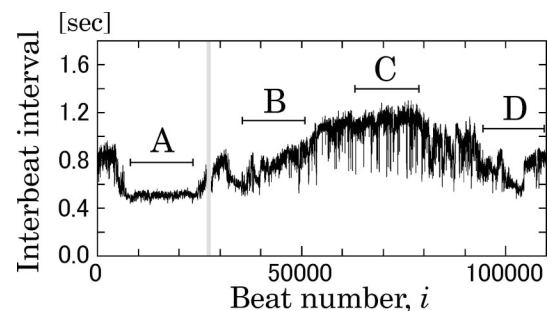


FIG. 1. A representative record of heart interbeat intervals for a healthy subject measured over 24 h (13:00–). For analyses, we selected four subintervals during different states from the records of seven healthy subjects [22].

(A) constant exercise, (B) usual daily activity after the exercise, (C) sleep, and (D) usual daily activity the next morning. The data for each state contains over 15 000 heartbeat intervals.

In order to characterize the heart rate fluctuations, we use a detrended random walk method. We consider a time series of sequential heart interbeat intervals,  $\{b(i)\}$  ( $i = 1, \dots, N_{\max}$ ), where  $i$  is the beat number and the time series is normalized to have zero mean and unit variance. Because the original time series of the interbeat intervals is not a diffusive random walk, we first integrate the time series  $\{b(i)\}$ , and analyze the “walk” of  $B(i)$ :

$$B(i) = \sum_{j=1}^i b(j). \quad (1)$$

To eliminate the  $(d - 1)$ th order polynomial trends included in the time series  $\{b(i)\}$ , in each subinterval  $[1 + s(k - 1), s(k + 1)]$  of length  $2s$ , where  $k$  is the index of the subinterval, we fit  $B(i)$  using a polynomial function of the order  $d$ , which represents the trend in the corresponding segment. The fluctuation statistics show no significant difference with respect to the order of detrending polynomials if the order is greater than two [7]. Thus, in the following analysis, we use the third order detrending ( $d = 3$ ). After this detrending procedure, we define heart rate increments at a scale  $s$  as  $\Delta_s B(i) = B^*(i + s) - B^*(i)$ , where  $1 + s(k - 1) \leq i \leq sk$  and  $B^*(i)$  is a deviation from the polynomial fit.

One of the widely used methods to characterize long-range power-law correlations is a scaling analysis of the mean square displacement [13],  $S_2(s) = \langle |B(i + s) - B(i)|^2 \rangle$ , where  $\langle \cdot \rangle$  denotes a statistical average; the  $S_2(s)$  is related to the so-called Hurst exponent  $H$  [14] as  $S_2(s) \sim s^{2H}$ . Consider a stationary stochastic process with  $\langle b_i \rangle = 0$ ,  $\langle b_i^2 \rangle = \sigma^2$ . If the walk of  $B(i)$  is totally random, as in ordinary Brownian motion, no correlations of  $b(i)$  exist and  $H = 1/2$ . If the autocorrelation function  $C(\tau)$  of  $b(i)$  scales as  $C(\tau) \sim \tau^{-\alpha}$  ( $0 < \alpha < 1$ ) for a large time lag  $\tau$ , the mean square displacement is evaluated as  $S_2(s) \sim s^{2-\alpha}$ . Thus, the  $H$  represents the long-range power-law correlation properties of the signal as  $H = (2 - \alpha)/2 > 1/2$ .

The scale dependence of the square root of  $S_2(s)$  in each of the behavioral states is shown in Fig. 2. For the usual daily activity [Figs. 2(b) and 2(d)], we can see scaling behavior with a slope 1, which implies  $1/f$  scaling in the power spectrum and the long-range correlated behavior in a wide range of scales. On the other hand, constant exercise [Fig. 2(a)] and sleep [Fig. 2(c)] states exhibit a crossover in the scaling behavior. The crossover point is about 3 minutes for both states, and the slopes for larger scales  $s$  approach 0.5, which signifies uncorrelated behavior. This result demonstrates an almost complete breakdown of the long-range correlated behavior in these states with higher (exercise) and lower (sleep) heart rates.

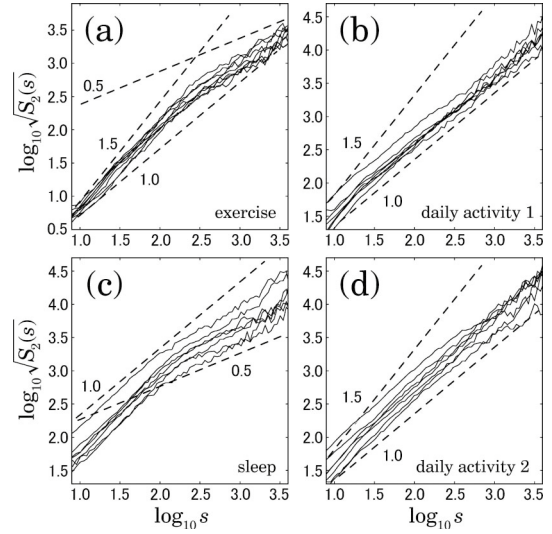


FIG. 2. Scale dependence of the square root of the second order structure function of seven records from healthy subjects during: (a) constant exercise, (b) usual daily activity after the exercise, (c) sleep, and (d) usual daily activity the next morning.

We previously reported [7] the robust scale-invariance in the non-Gaussian PDF of  $\Delta_s B(i)$  for a healthy human heart rate, which is preserved not only in a quiescent waking state, but also during usual daily activity. In Refs. [15–18], it has been demonstrated that a non-Gaussian PDF with fat tails can be modeled by random multiplicative processes. Let us represent the increment  $\Delta_s B$  by the following multiplicative form [18]:

$$\Delta_s B(i) = \xi_s(i) e^{\omega_s(i)}, \quad (2)$$

where  $\xi_s$  and  $\omega_s$  are random variables, independent of each other. If we assume  $\xi_s$  to be a fractional Gaussian noise and the variance of  $\omega_s$  is small enough, the correlation property (or the Hurst exponent  $H$ ) of  $\Delta_s B$  is approximated by that of  $\xi_s$ . This follows from the observation that for fractional Brownian motion, a long-range correlation property is generated from the sign of their increments rather than from the amplitudes [19]. Note that, in Eq. (2), the sign of  $\Delta_s B$  is determined only by the sign of the  $\xi_s$ , and the amplitudes of  $\xi_s$  are modulated by  $\exp(\omega_s)$  ( $> 0$ ).

In addition, non-Gaussian PDF’s can be described by the PDF form of Eq. (3). If we assume the PDF of  $\omega_s$  to be Gaussian, the PDF of  $\Delta_s B(i)$  is expressed by

$$P_s(\Delta_s B) = \int F_s\left(\frac{\Delta_s B}{\sigma}\right) \frac{1}{\sigma} G_s(\ln\sigma) d(\ln\sigma), \quad (3)$$

where  $F_s$  and  $G_s$  are both Gaussian with zero mean and variance  $\sigma_s^2$  and  $\lambda_s^2$ , respectively [18]. In this case,  $P_s$  converges to a Gaussian when  $\lambda \rightarrow 0$ . On the contrary, as  $\lambda$  increases, fat tails and a peak around the mean value become evident.

For a quantitative comparison, we fit the data to the above function [Eq. (3)] and estimate the variance  $\lambda_s^2$  of

$\omega_s$  in Eq. (2) [15]. The deformation of the standardized PDF's of the increment  $\Delta_s B$  across scales is shown in Fig. 3(a) for the usual daily activity, showing the non-Gaussian PDF [Fig. 3(a)], which is well described by Eq. (3), as reported in our previous study [7]. The scale dependence of  $\lambda^2$ , as shown in Fig. 3(b), indeed exhibits distinctive features. The non-Gaussian PDF's for the two records of daily activity show a striking resemblance. The scale invariance of the non-Gaussian PDF in a range of 20–1000 beats, however, disappears in sleep states, in which non-Gaussian fluctuations at a characteristic scale of  $\sim 100$  beats are dominant. The  $\lambda^2$  for constant exercise is much smaller than for the other states, implying near Gaussianity.

It is important to note that, from the point of view of the increment PDF and multifractal formalism, the non-Gaussian noise with uncorrelated  $\omega_s$  in Eq. (2) and multifractal random walk-type process with long-range correlated  $\omega_s$  are indistinguishable because their one-point statistics at a given scale can be identical; e.g., we can see similar non-Gaussian PDF's at certain scales for both usual daily activity and sleep states [Fig. 3(b)]. Thus, to find the origin and possible mechanisms of the non-Gaussian fluctuations, we have to establish another aspect such as correlation properties of  $\omega_s$  in Eq. (2). To do this, we further introduce an alternative method to study correlation functions of the local energy fluctuations [20].

At a scale  $s$ , we define the local energy and its magnitude as

$$\sigma_s^2(i) = \frac{1}{s} \sum_{j=1+s(i-1)}^{si} \Delta_s B(j)^2, \quad (4)$$

and

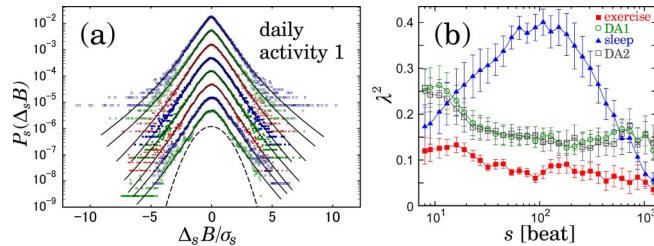


FIG. 3 (color online). (a) Deformation of standardized PDF's (the standard deviation has been set to one) of the increment  $\Delta_s B$  across scales, where the  $\sigma_s$  is the standard deviation of  $\Delta_s B(i)$ . The standardized PDF's (in logarithmic scale) for different time scales are shown for (from top to bottom)  $s = 8, 16, 32, 64, 128, 256, 512, 1024$  beats. The PDF's are estimated from all the records for usual daily activity after the exercise. The dashed line is a Gaussian PDF for comparison. In solid lines, we superimpose the deformation of the PDF using Castaing's equation [15] with the log-normal self-similarity kernel, providing an excellent fit to the data. (b) Dependence of the fitting parameter  $\lambda^2$  on the scale  $s$  during constant exercise, usual daily activity after the exercise (DA1), sleep, and usual daily activity the next morning (DA2).

$$\bar{\omega}_s(i) = \frac{1}{2} \log \sigma_s^2(i), \quad (5)$$

respectively. Using the magnitude  $\bar{\omega}_s$  we evaluate the fluctuation properties of  $\omega_s$  in Eq. (2). The local energy fluctuations computed from data from a single subject (Fig. 1) are shown in Fig. 4(a) as the function of the beat number and the scale. In Fig. 4(a), we see quite different patterns in the local energy fluctuations depending on the behavioral states. Further, by using the magnitude correlation function as defined by

$$C(\tau; s_1, s_2) = \langle [\bar{\omega}_{s_1}(i) - \langle \bar{\omega}_{s_1} \rangle][\bar{\omega}_{s_2}(i + \tau) - \langle \bar{\omega}_{s_2} \rangle] \rangle, \quad (6)$$

we are able to study nontrivial correlation properties of heart rate fluctuations. Higher values of  $C(\tau; s_1, s_2)$  imply more correlated behavior of  $\omega_s$ . Thus, the  $C(\tau; s_1, s_2)$  quantifies clustering of the local energy fluctuations.

The “one-scale ( $s_1 = s_2$ )” and “two-scale ( $s_1 < s_2$ )” magnitude correlation functions for each state are shown in Figs. 4(b) and 4(c), respectively. This analysis clearly reveals the difference in the origin of the non-Gaussian fluctuations between the usual daily activity and sleep states. The magnitude fluctuations for the daily activity state are strongly correlated, not only at a fixed scale but also at different scales, which means the magnitude fluctuations at a short time scale strongly influence the subsequently generated magnitude fluctuations across a wide range of time scales [Fig. 4(c)]. On the other hand, the magnitude correlations for the sleep state are very weak between different time scales, although correlated behavior is observed at small scales  $< 30$  beats. This fact shows that, for the sleep state, the non-Gaussian fluctuations at a characteristic scale of  $\sim 100$  beats have a different mechanism from that for the waking state.

To date, no significant difference in the multifractal scaling property [5] or the PDF of the local energy fluctuations [1] between sleep and waking states has been observed. In contrast, using the magnitude correlation functions, we demonstrate that there is indeed an essential difference between sleep and waking states. This result indicates that one-point statistics are not sufficient fully to characterize heart rate fluctuations. Similarly, no significant change in the correlation properties of the magnitude of increment has been reported for exercise and resting conditions [21], whereas we now demonstrate a striking difference between constant exercise and usual daily activity.

In conclusion, we have demonstrated that a healthy human heart rate exhibits phase transitionlike dynamics between different behavioral states, with a dramatic departure from criticality. We have discussed relevant characteristics in the significant behavioral states, showing that strongly correlated fluctuations—a hallmark of criticality—are observed only in the narrow region of usual daily activity, while a breakdown follows the transition to other

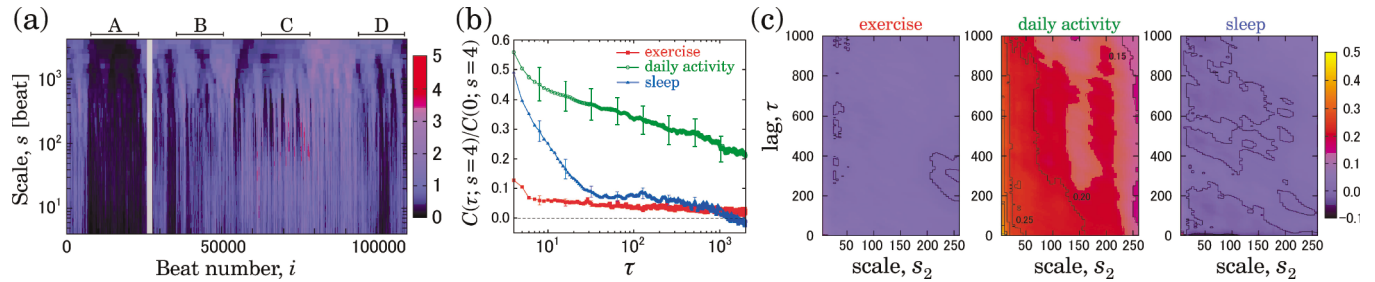


FIG. 4 (color). (a) Local energy fluctuations  $\sigma_s^2(i)/\langle\sigma_s^2(i)\rangle$  of the heart rate increments  $\Delta_s B_s(i)$  obtained from a representative record (Fig. 1) at each scale (resolution)  $s$ ; (b) one-scale magnitude correlation functions,  $C(\tau; 4, 4)/C(0; 4, 4)$ ; (c) two-scale magnitude correlation functions for each state. The color scales and contour lines (at 0.05 resolution increment levels) represent values of  $C(\tau; 4, s_1)/\sigma_4\sigma_{s_2}$ . For exercise and sleep states, contour lines of only  $C(\tau; 4, s_2) = 0$  can be seen, as the correlation levels remain within  $|C(\tau; 4, s_2)| \leq 0.05$ . The one-scale and two-scale magnitude correlation functions are estimated from all the records for each state.

states. This transition is reminiscent of a second order phase transition, and supports the hypothesis [7] that a healthy human heart rate is controlled to converge continually to a critical state during usual daily activity. We believe this feature to be a key to understanding the heart rate control system [6].

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