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Asymmetric intermittency observed in human heart rate dynamics

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***Abstract*— To gain a deeper understanding of intermittent fluctuations observed in complex, real-world systems, we propose positive- or negative-directional non-Gaussian statistics. As a numerical example of asymmetric intermittent fluctuations, we heuristically introduce a random cascade-type model. Using our method, it is demonstrated that the asymmetric properties of heart rate variability depend on aging. This provides new insight into the physiological mechanism controlling heart rate dynamics in health and in autonomic disorder.**

I. INTRODUCTION

Understanding the physics of intermittent fluctuations has been an important problem, not only in the field of hydrodynamic turbulence but also in a wide range of complex systems, such as econophysics, geophysics, and physiology. Recently, we demonstrated that the intermittent property of heart rate variability (HRV) is related to the risk factor for cardiac death in heart failure patients [1]. Sudden cardiac death is a major public health problem, accounting for 300,000 to 400,000 deaths annually in the United States. Therefore, an accurate and reliable identification of patients who are at high risk of sudden cardiac death is an important and challenging problem.

It is known that HRV is negotiated by both vagal and sympathetic modulation of the sinus node [3], and that the vagal and sympathetic effects are related, respectively, to deceleration and acceleration of heart rate. This fact suggests that heart rate dynamics reflects the asymmetric mechanism generating the fluctuations, possibly altered by aging and autonomic disorder [4]. Thus, our working hypothesis in this paper is that the balance of the vagal and sympathetic modulation is reflected in the asymmetric properties in HRV.

Such an asymmetric mechanism is to be expected in other complex, real-world systems. To study the asymmetric nature of the dynamics of complex time series, it is necessary to develop a method to quantify the asymmetric intermittency. To this end, we heuristically introduce a random cascade-type model exhibiting asymmetric intermittent fluctuations. Based on this model, we propose positive- or negative- directional non-Gaussian statistics, where the term "directional" means the positive or negative side of the median of the time series. Using this approach, we demonstrate age dependence of the asymmetric properties of heart rate variability, possibly reflecting the autonomic imbalance due to aging [4]. This provides new insight into the physiological mechanism controlling heart rate dynamics.

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II. CHARACTERIZATION OF ASYMMETRIC INTERMITTENCY

A standard approach to characterize intermittent time series is to describe how the shape of the PDF changes across scales. That is, from an observed time series $\{X_i\}$, consider the PDF of the partial sum $\Delta_s Z_i = \sum_{j=1}^{s} X_{i+j}$, where s indicates the scale. In other words, $\Delta_s Z_i$ is equal to the increment of the integrated series $Z_n = \sum_{i=1}^{n} X_i$. However, the coarse graining procedure using the partial sum cannot characterize separately the positive- and negative-directional deviations in the asymmetric intermittency. To overcome this problem, we here introduce a coarse graining procedure using local mean-absolute-deviation.

Here, let us consider an observed time series $\{X_i\}$ with zero median. As the first step of the coarse graining procedure, the time series is divided into segments of equal length. In each subinterval $[i, i+s]$ with scale s, we define the local mean-absolute-deviation in the positive direction as

$$\Delta_s^{(+)} Z_i = \frac{1}{N_+} \sum_{j=1}^{N_+} X_{i+n_j}, \tag{1}$$

where X_{i+n_j} represents positive values, and N_+ is the total number of the positive values in the subinterval. For negative values in the subinterval, we define the local mean-absolute-deviation in the negative direction as

$$\Delta_s^{(-)} Z_i = \frac{1}{N_-} \sum_{j=1}^{N_-} -X_{i+n_j}, \tag{2}$$

where N_- is the total number of the negative values in the subinterval. Under the assumption of zero median, we can expect that $\langle N_+ \rangle = \langle N_- \rangle = s/2$, where the angle brackets represent an average over all segments. In our approach, we study scale dependence of the statistical properties of the local mean-absolute-deviations in positive and negative directions. To quantify the asymmetric intermittency of the local mean-absolute-deviations, we propose three types of statistics, directional correlation r, one-sided non-Gaussian index, and one-sided root-mean-square deviation.

To quantify the correlation between positive and negative local deviations, we define the directional correlation r_d as

$$r_d = \frac{\left\langle \left(L_s^{(+)}\right)\left(L_s^{(-)}\right) \right\rangle - \left\langle L_s^{(+)} \right\rangle \left\langle L_s^{(-)} \right\rangle}{\left\langle \left(L_s^{(+)} - \langle L_s^{(+)} \rangle\right)^2 \right\rangle \left\langle \left(L_s^{(-)} - \langle L_s^{(-)} \rangle\right)^2 \right\rangle}, \tag{3}$$

where the angle brackets represent an average over all segments and $L_s^{(+)} = \ln \Delta_s^{(+)} Z_i$ and $L_s^{(-)} = \ln \Delta_s^{(-)} Z_i$.

To describe how far values lie from the median, we define the one-sided mean square deviation on the positive side as

$$\sigma_{(+)}^2 = \frac{\pi s \left\langle \Delta_s^{(+)} Z_i^2 \right\rangle}{2s + 2(\pi - 2)}. \quad (4)$$

When we approximate the local distribution on the positive side in each segment by a half-Gaussian distribution, $\sqrt{2/\pi} \exp\left(-x^2/2\sigma_h^2\right)/\sigma_h$ for $x > 0$, this notation can be derived as an estimate of σ_h^2. On the negative side, $\sigma_{(-)}^2$ is defined by the same form as Eq. (4), using $\Delta_s^{(-)} Z_i$ instead of $\Delta_s^{(+)} Z_i$.

To quantify the non-Gaussian shape of the PDF, we define the one-sided non-Gaussian index on the positive side as

$$\lambda_{(+)}^2 = 2 \left(\ln \sqrt{\frac{2}{\pi}} - \ln \frac{\left\langle \Delta_s^{(+)} Z_i \right\rangle}{\sigma_{(+)}} \right). \quad (5)$$

On the negative side, $\lambda_{(-)}^2$ is defined by the same form as Eq. (5) using $\Delta_s^{(-)} Z_i$ instead of $\Delta_s^{(+)} Z_i$. The one-sided non-Gaussian index is derived as a comparable value of the non-Gaussian parameter λ^2 in multiplicative log-normal models. Hence, $\lambda_{(\pm)}^2 = 0$ means a Gaussian shape of the PDF, and the greater $\lambda_{(\pm)}^2$ indicates the fatter non-Gaussian tail of the PDF. In addition, when we analyze symmetric intermittent time series generated by a multiplicative log-normal model, our approach can reproduce the non-Gaussian statistics obtained from the multiscale PDF analysis using partial sums as the coarse graining procedure.

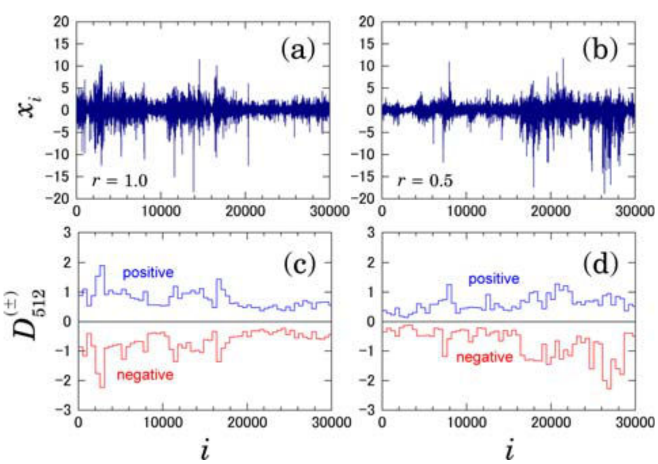

Fig. 1. Numerical examples of the intermittent process [Eq. (6)] for two values of the directional correlation $r = 1.0$ (a) and $r = 0.5$, together with the coarse grained time series at the scale of 512 data points, respectively (c) and (d).

III. Asymmetric random process

Here we introduce a heuristic model generating asymmetric intermittent time series. In our previous studies, we proposed a random cascade-type model generating symmetric intermittent time series. To generate asymmetric intermittency, we modify the cascade model. Based on this model, we discuss the statistical properties of the asymmetric intermittency.

The numerical procedure to generate the time series is as follows: First, we generate a time series $\{W_i\}_{i=1}^{2^m}$ of Gaussian white noise with zero mean and unit variance, where m is the total number of cascade steps. In the first cascade step ($j = 1$), we divide the whole interval into two equal subintervals. Depending on the sign of W_i, we multiply W_i in each subinterval by random weights $\exp[Y_{\pm}^{(1)}(k)]$ ($k = 0, 1$), where $Y_+^{(j)}$ and $Y_-^{(j)}$ are identical independent random variables for, respectively, positive and negative values of W_i, in the first cascade step $j = 1$. In the asymmetric process, the correlation coefficient r between $Y_+^{(j)}$ and $Y_-^{(j)}$ is a parameter, which is assumed to be a constant through the cascade steps j. In the next cascade step ($j = 2$), we further divide each subinterval into two equal subintervals, and apply the random weights $\exp[Y^{(2)}(k)_{\pm}]$ ($k = 0, 1, 2, 3$) depending on the sign of W_i. The same procedure is repeated, and after m cascade steps, the time series $\{X_i\}$ is given by

$$X_i = \begin{cases} A_+ \sigma_+ W_i \exp \sum_{j=1}^{m} Y_+^{(j)} \left(\left\lfloor \frac{i-1}{2^{m-j}} \right\rfloor \right) & \text{if } W_i > 0 \\ A_- \sigma_- W_i \exp \sum_{j=1}^{m} Y_-^{(j)} \left(\left\lfloor \frac{i-1}{2^{m-j}} \right\rfloor \right) & \text{if } W_i < 0 \end{cases}, \quad (6)$$

where $\lfloor \cdot \rfloor$ is the floor function, σ_+ and σ_- are the root mean square deviation from zero, and A_+ and A_- are the normalization constant without σ_+ and σ_-. When $r = 1$ and $\sigma_+ = \sigma_-$, this process is the same as the multiplicative log-normal model generating symmetric intermittent time series.

When we assume that $Y_+^{(j)}$ obeys a Gaussian distribution with zero mean and variance λ_+^2, and $Y_-^{(j)}$ obeys a Gaussian distribution with zero mean and variance λ_-^2, the normalization constants are given by $A_+ = \exp(-m\lambda_+^2)$ and $A_+ = \exp(-m\lambda_-^2)$. Under this assumption, the PDF of X is given by

$$f(x) = \begin{cases} \int_0^\infty \frac{1}{2\pi s \bar{\lambda}_+} e^{\left[-\frac{x^2}{2s^2} - \frac{\left(\ln s/\sigma_+ - \bar{\lambda}_+^2\right)^2}{2\bar{\lambda}_+} \right]} d(\ln s) \text{ if } x > 0 \\ \int_0^\infty \frac{1}{2\pi s \bar{\lambda}_-} e^{\left[-\frac{x^2}{2s^2} - \frac{\left(\ln s/\sigma_- - \bar{\lambda}_-^2\right)^2}{2\bar{\lambda}_-} \right]} d(\ln s) \text{ if } x < 0 \end{cases}, \quad (7)$$

where $\bar{\lambda}_+^2 = m\lambda_+^2$ and $\bar{\lambda}_-^2 = m\lambda_-^2$. In this case, each side of the PDF [Eq. (7)] is of the same form as the multiplicative log-normal model. So far, it has been demonstrated that multiplicative log-normal models using a Gaussian process assumption can provide a good approximation of the observed non-Gaussian PDF. Hence, we here assume $Y_+^{(j)}$ and $Y_-^{(j)}$ are both Gaussian.

Numerical examples of the intermittent processes [Eq. (6)] are shown in Figs. 1 (a) and (b), together with the coarse grained time series at the scale of 512 data points [Fig. 1 (c) and (d)]. The synchronization properties of the local positive- and negative-directional deviations are different depending on the parameter r. If r is equal to 1, the local positive- and negative-deviations are completely synchronized, as shown in Fig. 1. On the other hand, if r is close to zero, the positive- and negative-directional deviations are independent. In the model, r is constant through the cascade process.

If $\lambda_+ \neq \lambda_-$, as shown in Fig. 1 (a) and (b), the PDF of x is asymmetric non-Gaussian. The asymmetric non-Gaussian properties can be quantified by the one-sided non-Gaussian index, $\lambda^2_{(+)}$ and $\lambda^2_{(-)}$. In the model, as in the symmetric case of the multiplicative log-normal model, the scale dependence of the one-sided non-Gaussian index can be estimated as

$$\lambda^2_{(+)}(s) \approx m\lambda^2_+ (m - \log_2 s) \quad (8)$$

$$\lambda^2_{(-)}(s) \approx m\lambda^2_+ (m - \log_2 s)\,. \quad (9)$$

As shown in Fig. 2, our approach can reproduce the theoretical values. In the range of $s < 20$, the estimated values are larger than the theoretical values. This is because the number of samples, $n_\pm$, included in $\Delta_s^{(\pm)} Z_i$ fluctuates highly around the expectation value $s/2$ for the smaller scales.

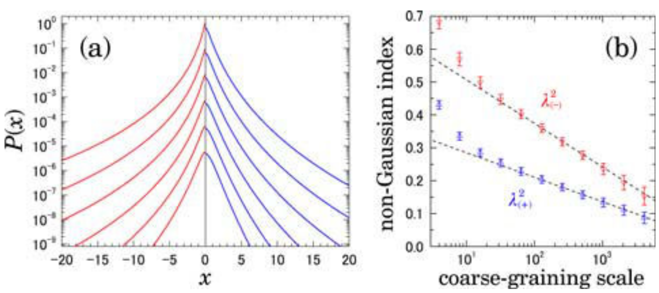

Fig. 2. Estimated PDF is shown for an asymmetric cascade process for a range of scales $s = 1, 4, 16, 64, 256, 1024$ (a) and the values of λ_+ and λ_- are plotted as a function of scale s (b). The solid lines reflect the theoretical values.

IV. Data

We analyzed a dataset of heart rate of 109 individuals (23 women and 86 men; ages $21-80$ years) without any known disease affecting autonomic control of heart rate. They underwent ambulatory monitoring during normal daily life, and the long-term heart rate data were measured as sequential heart interbeat intervals. Details of the recruitment of the subjects, screening for medical problems, protocols, and the data collection and preprocessing are described in Sakata et al. [2], [3]. Here, we analyzed whole-day data containing periods of sleep and waking (in Ref. [3] only daytime results were used). We analyze full day-long sequences of data, comprising over 100,000 data points, of the intervals between two successive R waves of sinus rhythm, i.e. HRV.

V. Asymmetric intermittency of healthy human heart rate

To demonstrate that our approach can provide new insight in real-world systems, we here analyze the human heart rate variability of the healthy subjects. In this section, we study the relation between asymmetric properties of HRV and the effect of aging on the autonomic control.

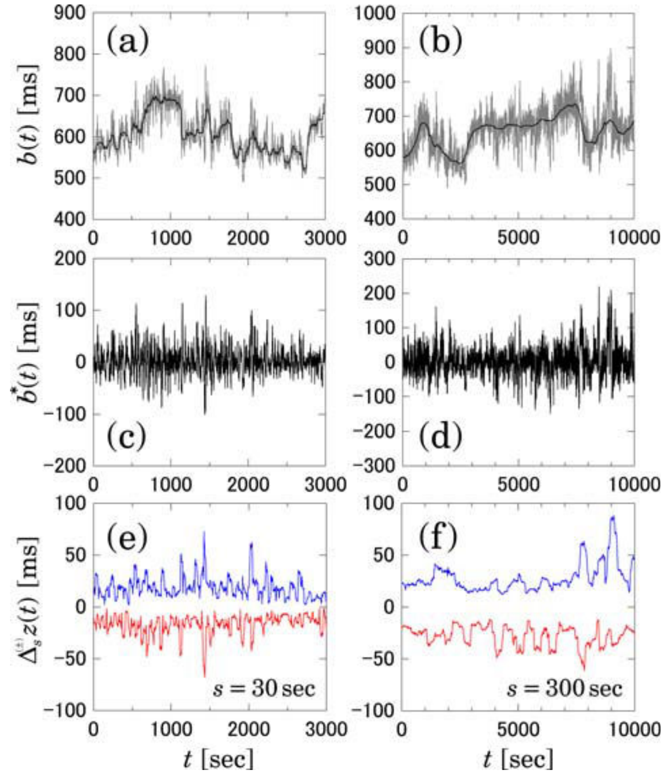

Fig. 3. Examples of the heart rate pre-processed at two different scales $s = 30$ sec. (a) (c) (e), and $s = 300$ sec. (b) (d) (f). The heart rate time series (gray) with the moving median filter shown by the solid (black) lines in panels (a) (b). The deviations $b^*(t)$ from the moving median filter are shown in (c) and (d), respectively, for the intervals shown in (a) and (b). Local mean-absolute-deviations, positive $\Delta_s^+ Z_i$ and $\Delta_s^- Z_i$ negative for (a) and (b) are shown in (e) and (f), respectively.

In order to obtain a temporal representation of the heart rate intervals, the N-N interval time series are interpolated and resampled at a predefined sampling interval. Time series of N-N intervals are interpolated with a cubic spline function and resampled at an interval (Δt) of 500 ms (2 Hz). To remove the non-stationary trends of the time series $\{b(t)\}$, we use the moving median filter in the range $[t-s, t+s]$, where s is the scale of analysis ($s = 30$ sec. for λ_{30sec}). The detrended time series $\{b^*(t)\}$ is measured as the deviation from the moving median, as shown in Fig. 3.

The subjects were divided into three age groups: $21-40$, $41-60$ and $61-80$ years of age. For each of the groups, the directional correlation r_d and the directional non-Gaussianity indices $\lambda^2_{(-)}$ and $\lambda^2_{(+)}$ were calculated for a range of scales from $s = 10$ sec. to $s = 1000$ sec. There is a pronounced difference between the age groups in both the directional correlation across the scales and in the directional λ coefficients. In Fig 4 (a), the directional correlation r_d appears to be the greatest for the youngest group across the entire range of time scales. Middle-aged individuals show a rapid drop in the directional correlation r_d for time scales shorter than 10 min. Compared with the middle-aged individuals, the oldest group further develops a lack of directional correlations for time scales larger than 30 sec. In Fig 4(b) and (d), we show the directional correlation r_d for fixed characteristic time scales of 30 sec. and 10 min. respectively. All the groups show significant differences of the directional correlation at these scales, as indicated. Similarly, in Fig. 5 (a) (b) (c) we show the positive non-Gaussianity index $\lambda^2_{(+)}$ for all three age groups, first in multiscales (a), then for the selected time scales of 30 sec. (b) and 10 min. (c). There are significant differences between the groups at a 10 min. temporal resolution, as indicated in Fig. 5 (c). Analogically, we plot the results for the negative non-Gaussianity index $\lambda^2_{(-)}$ in Fig. 5 (d) (e) (f), noting that the significant differences between the age groups are again observed at the time scale of 10 min. [Fig. 5 (f)].

VI. Discussion

These results appear to confirm the previously posed hypothesis of 'autonomic aging' [4], however providing a new, much higher level of selectivity in assessing the 'antagonistic' autonomic balance of the sympathetic and parasympathetic control branches, in particular as a function of age. A rapid decrease is observed in all the time scales of the correlation index with progressing age. Passing middle age appears selectively to degenerate the directional correlation for time scales greater than 30 sec., attributed to predominantly sympathetic stimulus. The directional non-Gaussianity indices supplement this scenario, $\lambda^2_{(+)}$, reflecting positive fluctuations – 'accelerations' negotiated by dominating sympathetic activity – increasing rapidly in the middle-age and the oldest groups with respect to the youngest age group for time scales greater than 30 sec. However, the negative non-Gaussian fluctuation index $\lambda^2_{(-)}$ – capturing 'decelerations' negotiated by weakened sympathetic and elevated vagal tone – increases selectively but monotonically in the separate frequency bands between the different age groups (range 10 sec. to 100 sec.), but shows consistent marked increases with age outside of this range, indicating elevated intermittency in the vagally dominated (impaired sympathetic) negative fluctuations of HRV. The age dependent increase of the non-Gaussianity of both the negative and the positive fluctuations, at a degree of directional correlation progressively decreasing with age, is a newly established insight into the aging behavior of the HRV, indicating a growing disparity between the functioning of the autonomic control branches of the cardiac regulatory system at higher non-linearity (evidenced through non-Gaussianity) of each selective branch.

In the analysis framework presented, accelerations and decelerations have an essentially straightforward geometrical interpretation defined by the median. Respective asymmetry should be more straightforward to interpret directly in terms of increase or decrease of the autonomic (or humoral, etc.) stimuli and the presence/violation of their homeostasis, responsible for the HRV regulatory response within the considered frequency bands. Thus the above results are an illustration of the capability of the directional fluctuation methodology to assess intermittency properties of heart rate fluctuations. A full exploration of these capabilities, in a wide range of data including autonomic dysfunction, will be presented in a forthcoming article.

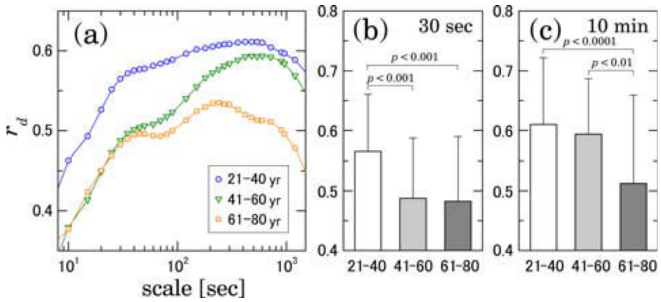

Fig. 4. Directional correlation r_d for the age groups: $21-40$, $41-60$ and $61-80$, for scales from 10 sec. to 1000 sec. (a), for 30 sec. (b), and for 10 min. (c).

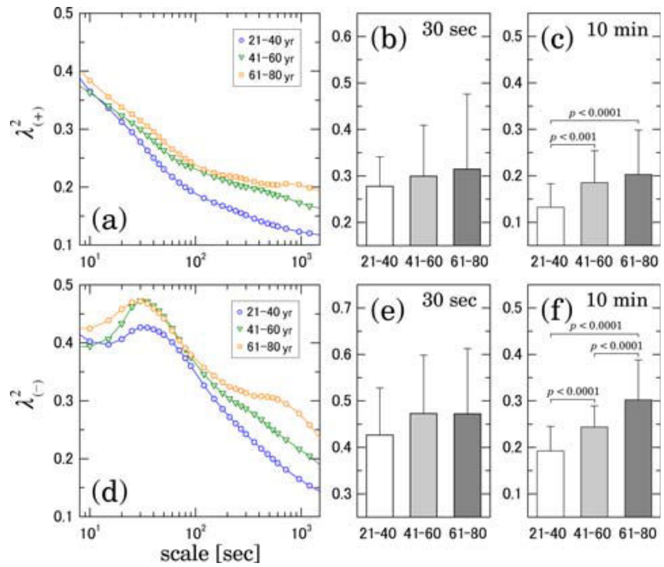

Fig. 5. Directional non-Gaussianity indices $\lambda^2_{(-)}$ and $\lambda^2_{(+)}$ for the age groups: $21-40$, $41-60$ and $61-80$, for scales from 10 sec. to 1000 sec. in (a) and (d), respectively, for 30 sec. in (b) and (e) respectively, and for 10 min. in (c) and (f) respectively.

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