

## Magnitude and Sign Correlations in Heartbeat Fluctuations

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We propose an approach for analyzing signals with long-range correlations by decomposing the signal increment series into magnitude and sign series and analyzing their scaling properties. We show that signals with identical long-range correlations can exhibit different time organization for the magnitude and sign. We find that the magnitude series relates to the nonlinear properties of the original time series, while the sign series relates to the linear properties. We apply our approach to the heartbeat interval series and find that the magnitude series is long-range correlated, while the sign series is anticorrelated and that both magnitude and sign series may have clinical applications.

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A broad class of physical and biological systems exhibits complex dynamics, associated with the presence of many components interacting over a wide range of time or space scales. These often-competing interactions may generate an output signal with fluctuations that appear “noisy” and “erratic” but reveal scale-invariant structure. One general approach to study these systems is to analyze the ways that such fluctuations obey scaling laws [1–3].

Here, we take into account that the fluctuations in the dynamical output of any system can be characterized by their magnitude (absolute value) and their direction (sign). These two quantities reflect the underlying interactions in a system—the resulting “force” of these interactions at each moment determines the magnitude and the direction of the fluctuations. For an important representative of complex dynamics—human heartbeat intervals—we find unexpected results for the time ordering of the heartbeat interval fluctuations by studying the scaling properties of their magnitude and sign. We also demonstrate that fluctuations following identical long-range correlations can exhibit very different time ordering for the magnitude and sign.

We consider the time series formed by consecutive cardiac interbeat intervals (Fig. 1a) and focus on the correlations in the time *increments* between consecutive beats. This time series is of general interest, in part because it is the output of a complex integrated control system, including competing stimuli from the neuroautonomic nervous system [4]. These stimuli modulate the rhythmicity of the heart’s intrinsic pacemaker, leading to complex fluctuations. Previous reports indicate that these fluctuations exhibit scale-invariant properties, and are anticorrelated over a broad range of time scales (i.e., the power spectrum follows a power-law where the amplitudes of the higher frequencies are dominant) [5,6].

The time series of the fluctuations in heartbeat intervals can be “decomposed” into two different time series. We analyze separately the time series formed by the magnitude and the sign of the increments in the time intervals

between successive heartbeats (Figs. 1b and 1c). We use 2nd order detrended fluctuation analysis [6] (and not the conventional power spectrum) since it has the ability to accurately estimate correlations in the heartbeat fluctuations even when they are masked by linear trends [7]. We find

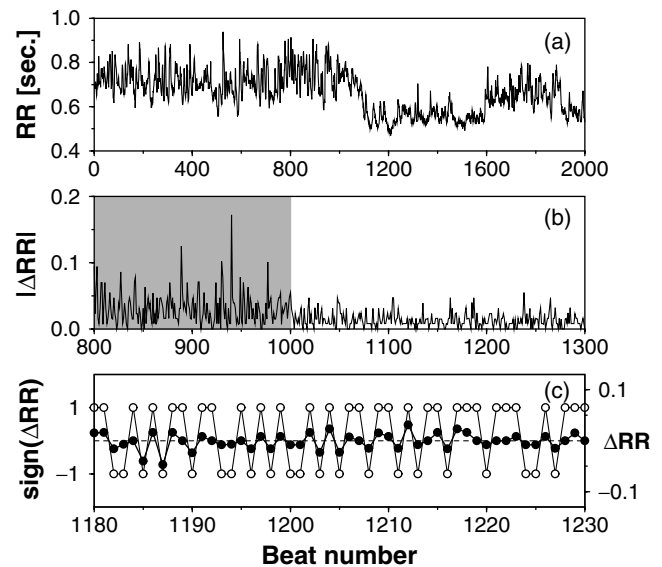


FIG. 1. (a) An example of 2000 heartbeat (RR) intervals of a healthy subject during daytime. (b) The magnitude series of a portion of the RR series (beat numbers 800–1300) shown in (a). Patches of more “volatile” increments with large magnitude (beat numbers 800–1000) are followed by patches of less volatile increments with small magnitude (beat numbers 1000–1300), consistent with our quantitative conclusion that there is correlation in the magnitude time series. (c) The sign series (○), as well as the  $\Delta RR$  series (●) of a portion of the RR series (beat numbers 1180–1230) shown in (a). The positive sign (+1) represents a positive increment, while the negative sign (−1) represents a negative increment in the RR series of interbeat intervals. The tendency to alternation between +1 and −1 is consistent with our quantitative conclusion that there is (multiscale) anticorrelation in the sign time series.

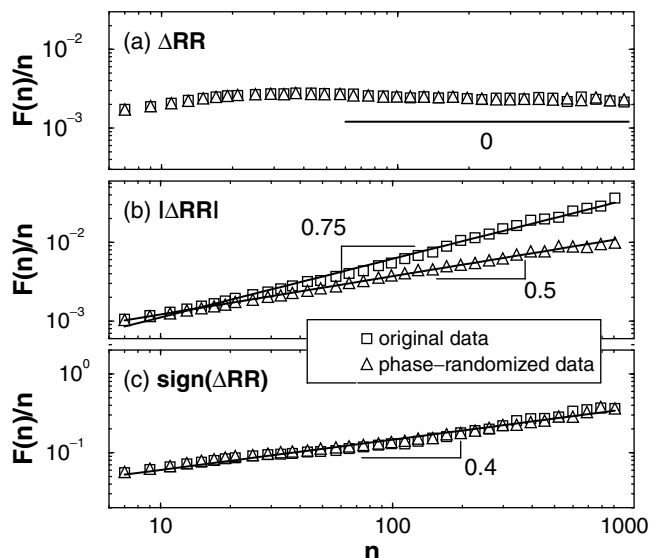


FIG. 2. (a) Root mean square fluctuation,  $F(n)$ , for  $\approx 6$  hour record ( $\approx 32\,000$  data points) for the interbeat interval  $RR_i$  series ( $\square$ ) of healthy subject [9]. Here,  $n$  indicates the time scale (in beat numbers) over which each measure is calculated. The scaling is obtained using second order detrended fluctuation analysis, and indicates long-range anticorrelations in the heartbeat interval increment series  $\Delta RR_i$  [6]. As expected, the scaling properties of the heartbeat interval increment series remain unchanged after the Fourier phase randomization ( $\triangle$ ). (b) The root mean square fluctuation of the integrated magnitude series  $|\Delta RR_i|$  [ $\square$ ] indicates long-range correlations in the magnitude series [ $\square$ ] [group average exponent of  $\alpha - 1 = 0.74 \pm 0.08$  where  $F(n)/n \propto n^{\alpha-1}$ ]. After Fourier phase randomization of the interbeat interval increment series we find random behavior with exponent 0.5 ( $\triangle$ ). This change in the scaling (after removing the nonlinear features in the time series) suggests that the magnitude series carries information about the nonlinear properties of the heartbeat dynamics. (c) The root mean square fluctuation of the integrated sign series ( $\square$ ) indicates anticorrelated behavior in  $\text{sign}(\Delta RR_i)$  [group average exponent of  $\alpha - 1 = 0.42 \pm 0.03$  where  $F(n)/n \propto n^{\alpha-1}$ ]. The scaling properties of the sign series remain unchanged after the Fourier phase randomization ( $\triangle$ ), which suggests that the sign series relates to linear properties of the heartbeat interval time series. We note the apparent crossovers at  $n \approx 20$  beats and  $n \approx 100$  beats. A gradual loss of anticorrelation in the sign series is observed at time scales larger than  $n \approx 100$  beats. We note, however, that heartbeat increments derived from the original time series are anticorrelated up to scales of thousands of heartbeats.

for each subject in a group of 18 healthy individuals [8], that the time series of the magnitudes exhibits correlated behavior (Fig. 2b) (unlike the original heartbeat increment time series, which is anticorrelated, Fig. 2a). The sign series, however, exhibits anticorrelated behavior (Fig. 2c) [9]. Correlation in the magnitude series indicates that an increment with large magnitude is more likely to be followed by an increment with large magnitude. Anticorrelation in the sign series indicates that a positive increment is more likely to be followed by a negative increment. Our result for the temporal organization of heartbeat fluctuations thus suggests that, under healthy conditions, a large increment

in the positive direction is more likely to be followed by a large increment in the negative direction. We find that this empirical “rule” holds over a broad range of time scales from several up to hundreds of beats (Fig. 2) [10].

To show that fluctuations following an identical scaling law can exhibit different time ordering for the magnitude and sign, we perform a Fourier transform on a heartbeat interval increment time series, preserving the amplitudes of the Fourier transform but randomizing the Fourier phases. Then we perform an inverse Fourier transform to create a surrogate series. This procedure eliminates nonlinearities, preserving only the linear features (i.e., two-point correlations) of the original time series [11]. The new surrogate series has the *same* power spectrum as the original heartbeat interval increment time series, with a scaling exponent indicating long-range anticorrelations in the interbeat increments (Fig. 2a). Our analysis of the sign time series derived from this surrogate signal shows scaling behavior almost identical to the one for the sign series from the original data (Fig. 2c). However, the magnitude time series derived from the surrogate (linearized) signal exhibits *uncorrelated* behavior—a significant change from the strongly *correlated* behavior observed for the original magnitude series (Fig. 2b). Thus, the increments in the surrogate series do not follow the empirical “rule” observed for the original heartbeat series, although these increments follow a scaling law identical to the original heartbeat increment series. Moreover, our results raise the interesting possibility that the magnitude series carries information about the nonlinear properties of the heartbeat series, while the sign series relates importantly to linear properties.

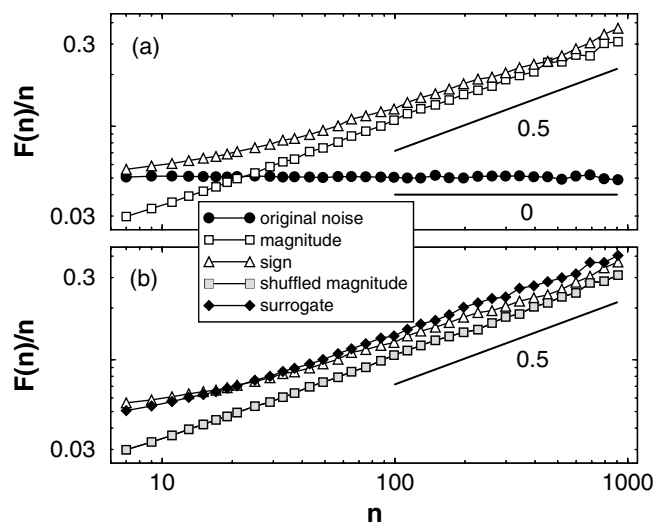


FIG. 3. (a) ( $\bullet$ ) An example of anticorrelated noise (the scaling exponent of the increment series is 0) with ( $\square$ ) uncorrelated magnitude series and ( $\triangle$ ) uncorrelated sign series with exponent 0.5. (Note the sign series is anticorrelated for  $n < 20$  and uncorrelated for  $n > 100$ .) (b) We shuffle the magnitude series from (a) (gray squares) and then multiply its elements by the elements of the sign series from (a). The new surrogate series ( $\blacklozenge$ ) is uncorrelated.

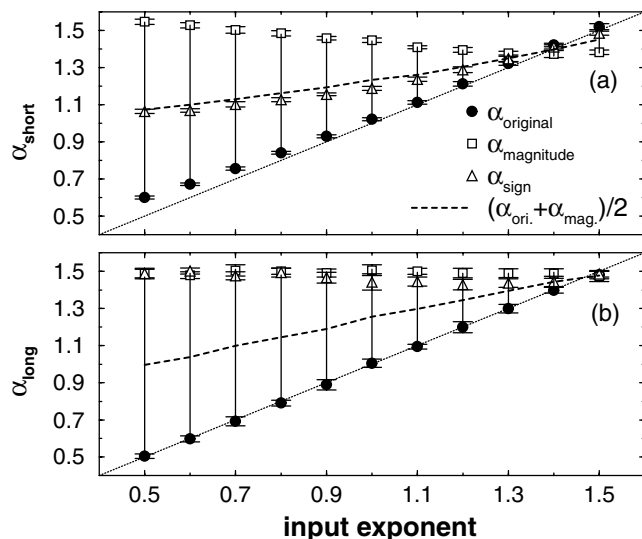


FIG. 4. (a) The relation between the scaling exponents of correlated noise, the integrated magnitude series, and the integrated sign series for the short-range regime ( $n < 16$ ). We generate 10 series of length 32768 with different correlations (input exponent) and then calculate the scaling exponents of the original series ( $\bullet$ ), of the integrated magnitude series ( $\square$ ), and of the integrated sign series ( $\triangle$ ). In the figure we show the average  $\pm 1$  standard deviation. The dashed line indicates the approximate empirical relation between the different scaling exponents [ $\alpha_{\text{sign}} \approx (\alpha_{\text{original}} + \alpha_{\text{magnitude}})/2$ ]. This empirical approximation is good for the short-range regime only ( $n < 16$ ). (b) Same as (a) for the long-range regime ( $n > 64$ ). Here the approximation does not hold anymore. In this regime the scaling exponents of the magnitude and sign series are uncorrelated no matter what is the exponent of the original series.

Next, we investigate the relation between the scaling exponent of the original series and the scaling exponents of the magnitude and the sign series. For this purpose, we test our approach on well-defined signals with built-in correlated behavior that show uncorrelated behavior for the magnitude and sign. First, we consider a particular example of correlated noise with scaling exponent equal to 1, for which the increment series is anticorrelated with scaling exponent equal to 0 (Fig. 3a). Surprisingly, at large time scales, we find that the magnitude series and the sign series of the increments exhibit uncorrelated behavior (scaling exponent of 0.5) although the original increment series, which is the multiplication of the elements of these two series, is strongly anticorrelated. Moreover, we find that for linear colored noise with correlation exponent less than 1.5 (i.e., with anticorrelations for the increment series), the magnitude and sign series of the increments are uncorrelated (Fig. 4b). Next, we shuffle the magnitude series by randomly exchanging pairs of elements. After multiplication of the elements of the shuffled magnitude series with the elements of the sign series, we find that the resulting time series is uncorrelated, in contrast to the original increments time series which is strongly anticorrelated. Note that the scaling exponents of the magnitude and sign series remain the same as before the shuffling (Fig. 3b). This test indicates that the correlations in a time

series are not related to the correlations in the magnitude and sign series, but rather to the particular pairing of the elements of the magnitude and sign series.

At small time scales, however, we find an empirical approximate relation for the scaling exponents (Fig. 4a),  $\alpha_{\text{sign}} \approx \frac{1}{2}(\alpha_{\text{original}} + \alpha_{\text{magnitude}})$ . We observe that for the heartbeat series this relation is valid over a larger range of scales (i.e., for time scales  $n < 100$ ).

Finally, we test our analysis on a group of 12 subjects with congestive heart failure [8]. Compared to the healthy subjects, the magnitude exhibits weaker correlations with a scaling exponent closer to the exponent of an uncorrelated series. The change in the magnitude exponent for the heart failure subjects is consistent with a previously reported loss of nonlinearity with disease [12,13]. The sign time series of heart failure subjects shows scaling behavior similar to that observed in the original time series, but significantly different from the healthy subjects (Table I).

TABLE I. Comparison of the statistics of the root mean square fluctuation,  $F(n)$  (calculated using the second order detrended fluctuation analysis method [6] where  $n$  is the time scale in beat numbers over which each measure is calculated), and the scaling exponents for 18 healthy subjects and 12 subjects with heart failure [8] (obtained from 6-h records during the day). The scaling features of the magnitude and sign change significantly for the subjects with heart failure, raising the possibility of bedside applications.  $\alpha$  is the best fit to the range  $6 < n < 1024$ .  $F(n)$  is estimated at the crossover position ( $n = 16$ ) (Fig. 2b) where the largest separation between the two groups is estimated. Since we observe two apparent crossovers in the scaling behavior of the sign series, we calculate the scaling exponents in three different regions: (i) the short-range regime for time scales  $6 < n < 16$  with scaling exponent  $\alpha_1$ ; (ii) the intermediate regime for time scales  $16 \leq n \leq 64$  with scaling exponent  $\alpha_2$ ; and (iii) the long range regime for time scales  $64 < n \leq 1024$  with scaling exponent  $\alpha_3$ . For each measure, the group average  $\pm 1$  standard deviation is presented. The values which show highly significant differences ( $p \leq 0.01$  by student's  $t$ -test) between the healthy and heart failure groups are indicated in boldface. We note, surprisingly, that the short-range and the intermediate range scaling exponents  $\alpha_1$  and  $\alpha_2$  of the sign series may provide even more robust separation between healthy and heart failure compared to previous reports [6] based on the scaling exponents of the original heartbeat series.

Magnitude			
Measure	Healthy	Heart failure	$p$ Value
$\log_{10} F(n)$	<b><math>-1.49 \pm 0.16</math></b>	<b><math>-1.92 \pm 0.17</math></b>	$1 \times 10^{-7}$
$\alpha$	<b><math>1.74 \pm 0.08</math></b>	<b><math>1.66 \pm 0.06</math></b>	0.01
$\alpha_1$	$1.55 \pm 0.08$	$1.6 \pm 0.08$	0.13
$\alpha_2$	$1.66 \pm 0.08$	$1.61 \pm 0.08$	0.14
$\alpha_3$	<b><math>1.82 \pm 0.1</math></b>	<b><math>1.71 \pm 0.1</math></b>	$4 \times 10^{-3}$
Sign			
Measure	Healthy	Heart failure	$p$ Value
$\log_{10} F(n)$	<b><math>0.14 \pm 0.05</math></b>	<b><math>0.02 \pm 0.06</math></b>	$1 \times 10^{-6}$
$\alpha$	$1.42 \pm 0.03$	$1.44 \pm 0.02$	0.08
$\alpha_1$	<b><math>1.43 \pm 0.12</math></b>	<b><math>1.15 \pm 0.12</math></b>	$7 \times 10^{-7}$
$\alpha_2$	<b><math>1.27 \pm 0.07</math></b>	<b><math>1.41 \pm 0.07</math></b>	$1 \times 10^{-5}$
$\alpha_3$	$1.53 \pm 0.065$	$1.49 \pm 0.04$	0.04

We conclude that series with identical correlation properties can have completely different time ordering, which can be characterized by different scaling exponents for the magnitude and sign series. Moreover, we show that the magnitude series carries information regarding the nonlinear properties of the original series while the sign series carries information regarding the linear properties of the original series. The significant decrease in the short-range scaling exponent for the sign series in heart failure may be related to perturbed vagal control affecting relatively high frequency fluctuations. The decrease of the long-range scaling exponent for the magnitude series of the heart failure patients indicates weaker correlations and loss of nonlinearity, which may be related to impaired feedback mechanisms of neurohormonal cardiac regulation. Because information obtained by decomposing the original heartbeat time series into magnitude and sign time series likely reflects aspects of neuroautonomic regulation, this type of analysis may help address the challenge of developing realistic models of heart rate control in health and disease.

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- [8] MIT-BIH Normal Sinus Rhythm Database and BIDMC Congestive Heart Failure Database available at <http://www.physionet.org/physiobank/database/#ecg>
- [9] The magnitude/sign decomposition consists of the following steps: (i) given  $RR_i$  series we create the increment series,  $\Delta RR_i = RR_{i+1} - RR_i$ ; (ii) we decompose the increment series into a magnitude series ( $|\Delta RR|$ ) and a sign series [ $\text{sgn}(\Delta RR)$ ]; (iii) to avoid artificial trends we subtract from the magnitude and sign series their average; (iv) because of limitations in the accuracy of the detrended fluctuation analysis method for estimating the scaling exponents of anticorrelated signals ( $\alpha < 0.5$ ), we integrate the magnitude and sign series; (v) we perform a scaling analysis using second order detrended fluctuation analysis on the integrated magnitude and sign series; (vi) to obtain the scaling exponents for the magnitude and sign series we measure the slope of  $F(n)/n$  on a log-log plot, where  $F(n)$  is the root mean square fluctuation function and  $n$  is the scale of analysis (in beat numbers).
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