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Scale Invariance in the Nonstationarity of Human Heart Rate

Pedro Bernaola-Galván,^{1,2} Plamen Ch. Ivanov,^{1,3} Luís A. Nunes Amaral,^{1,3} and H. Eugene Stanley¹

¹*Center for Polymer Studies and Department of Physics, Boston University, Boston, Massachusetts 02215*

²*Departamento de Física Aplicada II, Universidad de Málaga, E-29071, Spain*

³*Cardiovascular Division, Harvard Medical School, Beth Israel Deaconess Medical Center, Boston, Massachusetts 02215*

(Received 17 May 2000; published 2 October 2001)

We introduce a segmentation algorithm to probe the temporal organization of heterogeneities in human heartbeat interval time series. We find that the lengths of segments with different local mean heart rates follow a power-law distribution and show that this scale-invariant structure is not a simple consequence of the long-range correlations present in the data. The differences in mean heart rates between consecutive segments display a common functional form, but with different parameters for healthy individuals and for heart-failure patients. These findings suggest that there is relevant physiological information hidden in the heterogeneities of the heartbeat time series.

DOI: 10.1103/PhysRevLett.87.168105

PACS numbers: 87.19.Hh, 05.40.-a, 87.80.Vt, 89.75.Da

A time series is stationary if the mean, standard deviation, and all higher moments, as well as the correlation functions, are invariant under time translation [1]. Signals that do not obey these conditions are nonstationary. Nonstationarity is a prominent feature of biological variability that can be associated with regimes (segments) of different statistical properties. The borders between different segments can be gradual or abrupt (Fig. 1).

A major challenge in contemporary physiology is the nonstationarity of time series generated under free-running conditions [2]. Physiological signals obtained under widely varying conditions raise serious difficulties to both technical and fundamental aspects of time series analysis. By filtering out effects of nonstationarity, much work has focused on “intrinsic properties” of physiological signals [3]. This approach is based on the implicit assumption that the nonstationarity arises simply from changes in environmental conditions—e.g., different daily activities—so environmental “noise” may be treated as a “trend” and distinguished from the more subtle fluctuations that may reveal intrinsic correlation properties of the dynamics. Indeed, important scale-invariant features in physiological processes were recently revealed after filtering out masking effects of nonstationarity [4]. However, nonstationarity itself is also an important feature of physiological time series and is known to change from healthy to pathological conditions [5], suggesting more than only environmental conditions are reflected in the phenomena. Thus one would expect that there is a nontrivial structure associated with the nonstationarity in physiological signals, which may change with disease. To test this hypothesis we focus on one statistical property, the mean heart rate, which is related to physiologic responses and is used for medical evaluation.

The problem we address is the partition of a nonstationary time series, which is composed of many segments with different mean value, in such a way as to maximize the difference in the mean values between adjacent seg-

ments. We apply the following procedure: We move a sliding pointer from left to right along the signal. At each position of the pointer, we compute the mean of the subset of the signal to the left of the pointer (μ_{left}) and to the right (μ_{right}). To measure the significance of the

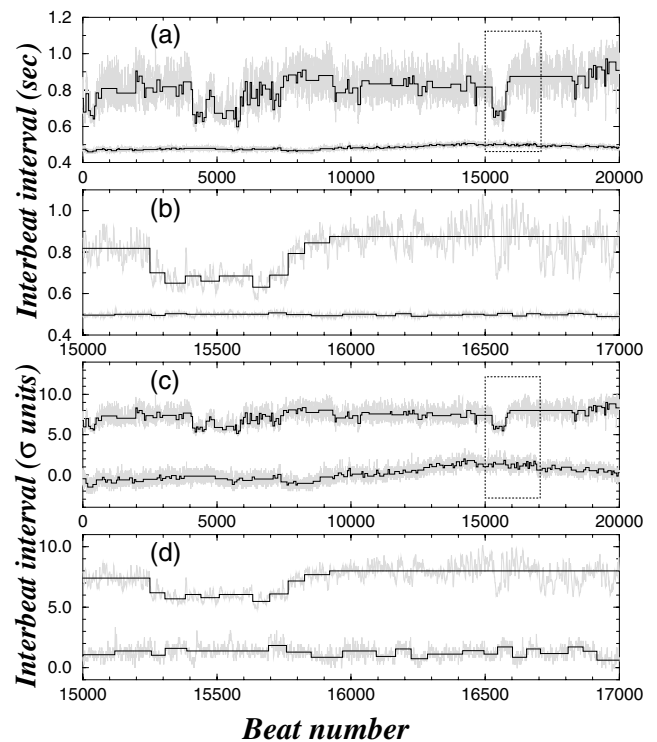


FIG. 1. (a) Plot of 20 000 interbeat intervals (≈ 6 h) for a healthy subject (upper curve) and a subject with heart failure (bottom curve). Note the larger variability and patchiness for the healthy record. (b) Magnification of a small fraction (2000 beats) of the signals in (a). (c) Same signals as displayed in (a) after subtracting the global average and dividing by the global standard deviation; after this normalization both signals appear very similar. (d) Magnification of a small fraction (2000 beats) of the signals in (c).

difference between μ_{left} and μ_{right} , we compute the statistic $t \equiv |(\mu_{\text{left}} - \mu_{\text{right}})/s_D|$, where $s_D = [(s_{\text{left}}^2 + s_{\text{right}}^2)/(N_{\text{left}} + N_{\text{right}} - 2)]^{1/2}(1/N_{\text{left}} + 1/N_{\text{right}})^{1/2}$ is the pooled variance [6] and s_{left} and s_{right} are the standard deviations of the data to the left and to the right of the pointer, respectively, and N_{left} and N_{right} are the number of points to the left and to the right of the pointer.

We next determine the position of the pointer for which t reaches its maximum value, t_{max} , and compute the statistical significance of t_{max} . The significance level $\mathcal{P}(\tau)$ of a possible cutting point with $t_{\text{max}} = \tau$ is defined as the probability of obtaining the value τ or lower values within a random sequence: $\mathcal{P}(\tau) = \text{Prob}\{t_{\text{max}} \leq \tau\}$. Thus, a series of N random numbers of fixed mean would remain unsegmented with probability $\mathcal{P}(\tau)$.

We check if this significance exceeds a selected threshold \mathcal{P}_0 , usually taken to be 95%. If so, then the signal is cut at this point into two subsequences; otherwise the signal remains undivided. If the sequence is cut, the procedure continues recursively for each of the two resulting subsequences created by each cut. Before a new cut is accepted, we also compute t between the right-hand new segment and its right neighbor (obtained by a previous cut) and t between the left-hand new segment and its left neighbor (also obtained by a previous cut) and check if both values of t have a statistical significance exceeding \mathcal{P}_0 . If so, we proceed with the new cut; otherwise we do not cut. Thus all resulting segments have a statistically significant difference in their means. The process stops when none of the possible cutting points has a significance exceeding \mathcal{P}_0 , and we say that the signal has been segmented at the “significance level \mathcal{P}_0 ” (Fig. 2).

As we could not obtain $\mathcal{P}(\tau)$ in a closed analytical form, we have developed a suitable approximation by means of Monte Carlo simulations. $\mathcal{P}(\tau) \approx \{1 - I_{[\nu/(\nu+\tau^2)]} \times (\delta\nu, \delta)\}^\gamma$, where $\gamma = 4.19 \ln N - 11.54$, $\delta = 0.40$, N is the size of the sequence or subsequence to be split, $\nu = N - 2$ is the number of degrees of freedom, and $I_x(a, b)$ is the incomplete beta function [6]. To check the validity of this approximation, we have carried out the following experiments: We generate 100 000 random series of given length N and fixed mean, and we segment them at significance level \mathcal{P}_0 . In all experiments the ratio between the number of series which remain undivided and the total number of series is very close to \mathcal{P}_0 , independently of N .

Our method leads to partitioning of a time series into segments with well-defined means, each significantly different from the mean of the adjacent segments (Fig. 1), and we probe the nonstationarity in a signal through the statistical analysis of the properties of the segments.

Here we consider 47 datasets from 18 healthy subjects, 17 records of cosmonauts during orbital flight, and 12 patients with congestive heart failure [7]. We separately analyze 6-h long subsets of each dataset, corresponding to the periods when the subject is awake or sleeping. Figure 1 shows a representative dataset of a healthy subject, and a

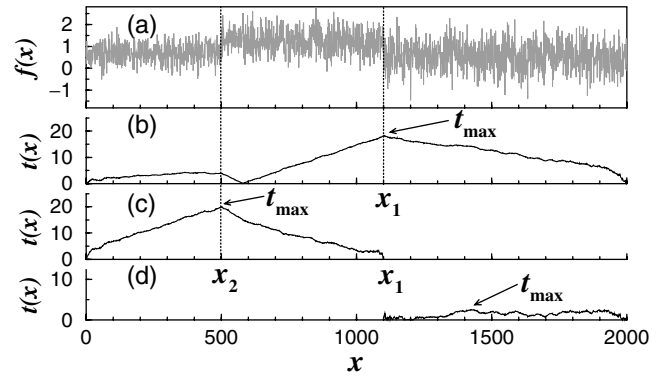


FIG. 2. (a) An artificial time series $f(x)$ composed of three segments with different mean values. (b) Values of the statistic t obtained by moving the pointer along the time series. Note that t_{max} is reached at x_1 . We find that if $\mathcal{P}(t_{\text{max}}) \geq \mathcal{P}_0 = 95\%$, and so we cut the series at x_1 . (c) We iterate the procedure with the segment $[0, x_1]$. We find that $\mathcal{P}(t_{\text{max}}) \geq 95\%$ and we also find that the significance of t computed between $[x_2, x_1]$ and $[x_2, 2000]$ is greater than 95%, so the series is cut at x_2 . (d) We iterate the procedure with the segment $[x_1, 2000]$. Now, $\mathcal{P}(t_{\text{max}}) \leq 95\%$, so this segment is not cut. Our procedure has a limitation for the extreme case of a long segment with a given mean, followed by a short segment with a different mean, which again is followed by a long segment with a mean identical to the mean of the first segment. First, we note that this is a very unlikely event in real data. However, even in this extreme case, the algorithm could provide a good segmentation, if we lower sufficiently the significance level, \mathcal{P}_0 . In fact, more often one can find in real data a situation when the second long segment has a mean value very close but not identical to the mean value of the first long segment; in such a case the procedure works accurately.

subject with heart failure. Superposed on the interbeat interval series, we also plot the segments obtained by means of our segmentation algorithm.

To quantify the nonstationarity in heart rate variability, we study the statistical properties of the segments corresponding to parts of the signal with significantly different mean values. To characterize the segments, we analyze two quantities: (i) the length of the segments and (ii) the absolute values of the differences between the mean values of consecutive segments, called jumps.

(i) *Distribution of segment lengths.*—Healthy subjects typically exhibit nonstationary behavior associated with large variability, trends, and segments with large differences in their mean values, while data from heart-failure subjects are characterized by reduced variability and appear to be more homogeneous (Fig. 1) [5]. Thus, one might expect that signals from healthy subjects will be characterized by a large number of segments, while signals from heart-failure subjects will exhibit a smaller number of segments (i.e., the average length of the segments for healthy subjects could be expected to be smaller than for heart-failure subjects).

We find that the distribution of segment lengths for the healthy subjects is well described by a power law with

similar exponents, indicating absence of a characteristic length for the segments. Surprisingly, we also find that this power law remains unchanged for records obtained from cosmonauts during orbital flight (under conditions of microgravity) and for patients with heart failure (Fig. 3). A similar common type of behavior is also observed from 6-h records during sleep for all three groups [8].

To verify the results of the segmentation procedure, we perform several tests. First, we check the validity of the observed power law in the distribution of segment lengths. We generate a surrogate signal formed by joining segments of white noise with standard deviation $\sigma = 0.5$, and mean values chosen randomly from the interval $[0, 1]$. We choose the lengths of these segments from a power-law distribution with a given exponent. Even when the difference between the mean values of adjacent segments is smaller than the standard deviation of the noise inside the segments, we find that our procedure partitions the surrogate signal into segments with lengths that reproduce the original power-law distribution [Fig. 4(a)]. This test shows that the distributions, obtained after segmenting surrogate data with similar values of their exponents, appear clearly different from each other, confirming that the distributions obtained for the lengths of the segments for the healthy, cosmonauts, and congestive heart-failure subjects (Fig. 3) follow indeed an identical distribution.

Second, we test if the observed power-law distribution for the segment lengths is simply due to the known presence of long-range correlations in the heartbeat interval series [9]. We generate correlated linear noise [10] with the same correlation exponent as the heartbeat data and find that the distribution of segment lengths obtained for

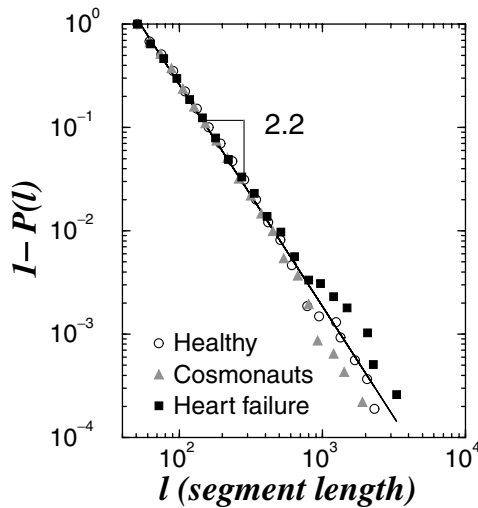


FIG. 3. Probability of finding segments with a length ℓ larger than a given value for the segments obtained from all subjects in the healthy, cosmonauts, and heart-failure groups during daily activity. The significance level is fixed to $\mathcal{P}_0 = 95\%$, and the imposed minimum length of the segments is $\ell_0 = 50$ beats. For all three groups we find a power law in the distribution of segment lengths with exponent $\beta \approx 2.2$.

the linear noise differs from the distribution obtained for the heartbeat data [Fig. 4(b)]. For the noise, the distribution decays faster, which means that these signals are more segmented than the heart data. For different linear noises with a broad range of correlation exponents, we do not find power-law behavior in the distribution of the segments. Thus, we conclude that the linear correlations are not sufficient to explain the power-law distribution of segment lengths in the heartbeat data.

(ii) *Differences between the mean values of consecutive segments (jumps).*—Different healthy records can be characterized by different overall variance, depending on the activity and the individual characteristics of the subjects. Moreover, subjects with heart failure exhibit inter-beat intervals with lower mean and reduced beat-to-beat variability (lower standard deviation). Thus, one can assume that these larger jumps in healthy records are due only to the fact that their average standard deviation is larger [Figs. 1(a) and 1(b)]. In order to systematically compare the statistical properties of the jumps between different individuals and different groups, we normalize each

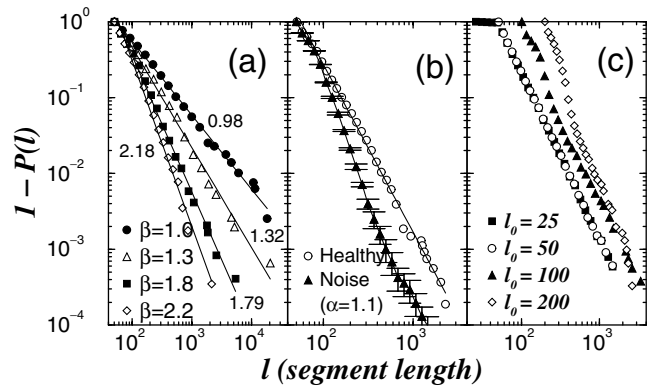


FIG. 4. (a) To test the validity of the observed power-law behavior in the distribution of segment lengths, we generate surrogate signals formed by joining segments of white noise with standard deviation $\sigma = 0.5$ and average values chosen randomly from the interval $[0, 1]$. We chose the lengths of these segments from a power-law distribution with a given exponent β and find excellent agreement between the given values of β and the values estimated from the segmentation. (b) To test the effect of long-range correlations in the signal on the segmentation process, we generate ten realizations, each with a length of 26 000 points, of a monofractal Gaussian-distributed correlated noise with power spectrum decaying as f^{-1} [10]. We find that the distribution of segment lengths for the correlated noise does not follow the power law found for the heartbeat data, suggesting that the observed scale-invariant behavior in the distributions of segment lengths in the heartbeat is not simply due to the correlations. To verify that the curvature found in the distribution of segments for the noise is not due to finite size effects, we also repeated the test with longer realizations of the noise (1 000 000). (c) To test the effect of the selected value of ℓ_0 on the segmentation process, we generate surrogate signals, as in (a), with power-law distribution of segment lengths with an exponent $\beta = 2.2$ and a cutoff at $\ell_{\min} = 50$. We test for different values of ℓ_0 and find that the correct behavior is obtained only when $\ell_0 = \ell_{\min}$.

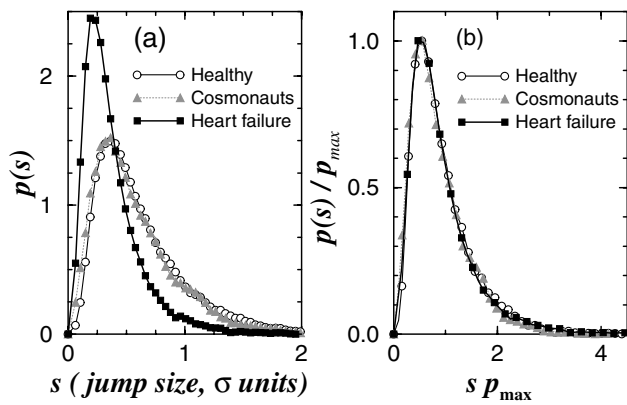


FIG. 5. (a) Probability density functions of the absolute value of the difference between the mean values (jumps) of consecutive segments. Both healthy and cosmonaut subjects follow an identical distribution while the heart-failure subjects follow a quite different distribution with higher probability for small jumps consistent with reports of smaller variability in heart-failure subjects [5]. All distributions are normalized to unit area. Note that the distributions are plotted in units of standard deviation, and that the results present a striking difference between the healthy and the heart-failure group, which are not as apparent by eye in the raw data after normalization [Fig. 1(d)]. (b) Same probability distributions as in (a), after rescaling $P(s)$ by P_{\max} , and s by $1/P_{\max}$. This transformation preserves the normalization to unit area.

time series by subtracting the global average (over 6 h) and dividing by the global standard deviation. In this way, all individual time series have zero mean and unit standard deviation [Figs. 1(c) and 1(d)]. Such a normalization does not affect our segmentation procedure.

We find that both the healthy subjects and the cosmonauts follow identical distributions, but the distribution of the jumps obtained from the heart-failure group are markedly different—centered around lower values—indicating that, even after normalization, there is a higher probability for smaller jumps compared to the healthy subjects [Fig. 5(a)]. Note that the distributions for all groups appear to follow an identical homogeneous functional form, so we can collapse these distributions on top of each other by means of a homogeneous transformation [Fig. 5(b)]. The ratio between the scaling parameters used in this transformation gives us a factor by which this feature of the heart rate variability is reduced for the subjects with heart failure as compared to the healthy subjects. This finding indicates that, although the heart rate variability is reduced with disease, there may be a common structure to this variability, reflected in the identical functional form. These observations agree with previously reported results for the distribution of heartbeat fluctuations obtained by means of wavelet and Hilbert transforms [11].

An important question raised by our results regards the physiologic meaning of the finding of identical distribu-

tions of segment length for both diseased and healthy subjects. This finding is unexpected because these two groups have radically distinct levels of physical activity and of neuroautonomic control of the heart rate [12]. This is a very intriguing finding for which there is no clear explanation. In fact, it raises a new scientific question: What is the origin of the mean heart rate nonstationarity? One possible explanation is that, for both healthy and heart-failure subjects, the effects of intrinsic (neuroautonomic) and external stimuli on the heart rate are reflected in segments with different local mean, the characteristics of which exhibit surprising universal features—i.e., identical power-law distribution for the length of the segments and identical functional form for the distribution of the jumps. However, the smaller mean value for the jumps observed in the heart-failure subjects, even after normalization, indicates decreased reflexive-type responsiveness compared to healthy subjects.

We thank A. L. Goldberger, I. Grosse, C.-K. Peng, and Z. Struzik for helpful discussions and suggestions, and Grants No. Spain/BIO99-0651-CO2-01 and No. NIH/NCRR (P41RR13622) for support.

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