Deviations from uniform power law scaling in nonstationary time series

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A classic problem in physics is the analysis of highly nonstationary time series that typically exhibit long-range correlations. Here we test the hypothesis that the scaling properties of the dynamics of healthy physiological systems are more stable than those of pathological systems by studying beat-to-beat fluctuations in the human heart rate. We develop techniques based on the Fano factor and Allan factor functions, as well as on detrended fluctuation analysis, for quantifying *deviations* from uniform power-law scaling in nonstationary time series. By analyzing extremely long data sets of up to $N=10^5$ beats for 11 healthy subjects, we find that the fluctuations in the heart rate scale approximately uniformly over several temporal orders of magnitude. By contrast, we find that in data sets of comparable length for 14 subjects with heart disease, the fluctuations grow erratically, indicating a loss of scaling stability. [S1063-651X(97)05101-5]

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I. INTRODUCTION

A major challenge in biological physics is the analysis of time series that are typically highly nonstationary [1] (Fig. 1). Such nonstationarities may be due to stable physiologic scaling associated with ''fractal'' properties or to instabilities related to internal or external perturbations. This highly irregular behavior has recently motivated investigators [2–7] to apply time-series analyses that derive from statistical physics, especially methods for the study of critical phenomena where fluctuations at all length (time) scales occur. These studies show that under healthy conditions, many physiological time series exhibit long-range power-law correlations reminiscent of physical systems near a critical point [8]. However, the hypothesis [9] that normal physiological systems behave consistently over a wider range of time scales than diseased systems has *not* been thoroughly tested, and there has been no study of *deviations* from stable power-law scaling in nonstationary time series. Here we put this idea to an experimental test by studying the scaling stability of human heartbeat fluctuations.

The healthy heartbeat is traditionally thought to be regulated according to the classical principle of homeostasis whereby physiologic systems operate to reduce variability and achieve an equilibriumlike state [1]. However, more recent studies [2,7] reveal that under normal conditions, beat-to-beat fluctuations in the human heart rate display the kind of long-range correlations typically exhibited by dynamical systems far from equilibrium. In contrast, heart rate time series from patients with severe heart disease may show a breakdown of this long-range correlation behavior [2,4]. Here we develop techniques based on the *Fano factor* [10] and *Allan factor* [11] functions, as well as *detrended fluctuation analysis* (DFA) [12], to quantify scaling stability in human heart rate fluctuations for lengthy data sets (comprising as many as 10^5 successive heartbeats).

II. METHODS

We analyze the heartbeat data sets using two independent and complementary approaches. One treats the heartbeat as a *point process,* while the other treats it as a *sequence* of interbeat intervals [5,13]. Our intention is not to compare these two approaches, but rather to test, by using two independent methods based on different descriptions of the data, the hypothesis that there may be a loss of scaling stability under pathological conditions.

A. Fano factor and Allan factor methods

We first develop techniques to quantify scaling stability based on the Fano factor [10] and Allan factor functions [11]. We choose these methods because they are well suited to the study of point processes [5]. A heartbeat time record can be treated as a point process, i.e., as a sequence of events (beats) distributed on the time axis [14]. We divide the entire time axis into nonoverlapping ''boxes'' or windows of size t seconds and count how many beats are in each box. We compute these counts separately for each box and then we compute the Fano factor $f(t)$, defined as the *variance* of the counts divided by their *mean*. In general, for a fractal point

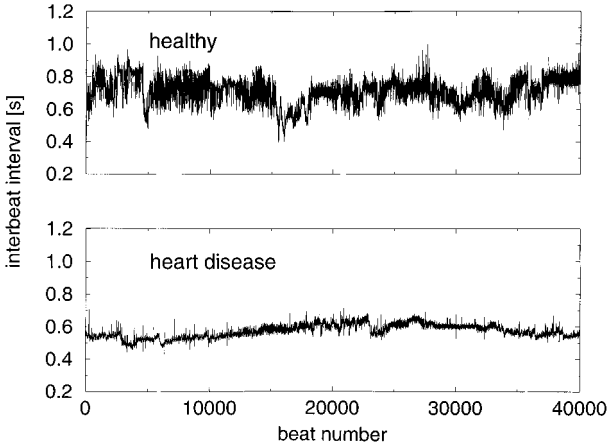

FIG. 1. Interbeat interval time series for a healthy subject (top curve) and a subject with congestive heart failure (bottom curve). Such data are typically highly nonstationary.

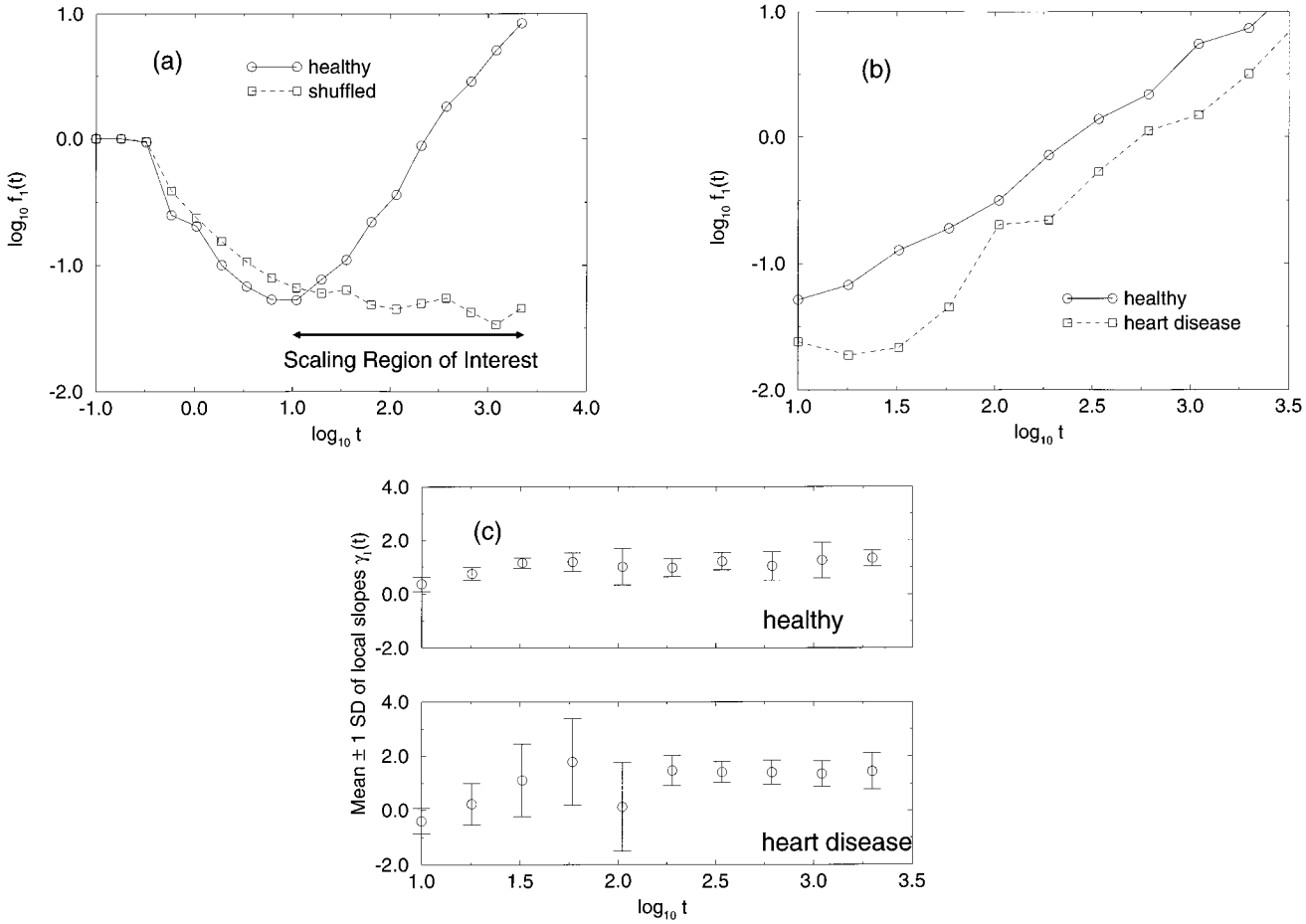

FIG. 2. (a) Double log plot of the Allan factor function $f_1(t)$ for a representative healthy subject and the surrogate data obtained by randomly shuffling the interbeat interval time series. Successive values of t increase by a factor of 1.8. The shuffled data have the same mean, variance, and higher moments as the original data, but temporal correlations are lost. The region of interest is for $t>10$ s, where the original data and surrogate differ considerably. To obtain good statistics, we use a minimum of 300 nonoverlapping boxes. However, for large t, we partially overlap the boxes to obtain 300 boxes. The scaling region is chosen so that there is no significant difference in the scaling stability of the shuffled surrogate data obtained from normal and disease subjects (see the text). (b) Allan factor function $f_1(t)$ for a representative healthy and a diseased subject, where the subscript indicates linear detrending (see the text). We find that the function $f_1(t)$ scales more uniformly for the normal data than for data from subjects with heart disease. Specifically, $f_1(t)$ has more curvature for disease vs health. (c) Mean $\pm$ 1 standard deviation of the local slopes $\gamma_1(t)$ for normal (top curve) and disease data (bottom curve). We find that there is greater variation in $\gamma_1(t)$ for disease data sets than for normal ones, especially for $t<100$ s, suggesting a loss of scaling stability with heart disease.

process with persistent correlations, $f(t)$ will increase when we increase the size of the box t. When plotting the function $f(t)$ versus t on a double log scale, good linear behavior indicates the existence of scaling (fractal) properties in the time series.

The box-counting method requires important modifications for studying nonstationary data [5,15–17]. If there are trends in the data (e.g., if the average heart rate steadily increases or decreases over a given time period), then the above method gives spurious results. To correct for trends and patchiness in the data, we use a modification of the Fano factor known as the Allan factor, originally developed to study the stability of atomic-based clocks [11] (see also [18,19]). The Allan factor $f_1(t)$ is defined as the variance of the *difference* between the number of beats in two successive boxes divided by twice the mean box count. This modification eliminates all *linear* trends in the data because taking successive differences of a linearly increasing quantity produces a constant, stationary variable [20].

In the asymptotic region (large-t value), we can define the scaling exponent $\gamma_1(t)$ as $\gamma_1(t)\equiv d\log f_1(t)/d\log t$, i.e., $\gamma_1(t)$ is the ''local'' derivative (slope) of the log-log plot of $f_1(t)$ (Fig. 2). In actual calculation, we estimate $\gamma_1(t)$ by taking the slope $\Delta\log f_1(t)/\Delta\log t=\Delta\log f_1(t)/\log 1.8$, where 1.8 is the ratio of successive values of t that we used. If $\gamma_1(t)$ is constant for different t then the scaling is consistent and stable. Substantial variation in $\gamma_1(t)$ with t indicates that the scaling properties of the system are not consistent, and are unstable even when linear trends in the data are removed.

We next describe how we select the scaling region for our analysis. It is known that the scaling behavior of the Allan factor appears only at relatively large time scales (asymptotic region). However, for biological data, it is impractical to study the properties of any function in this region. Therefore,

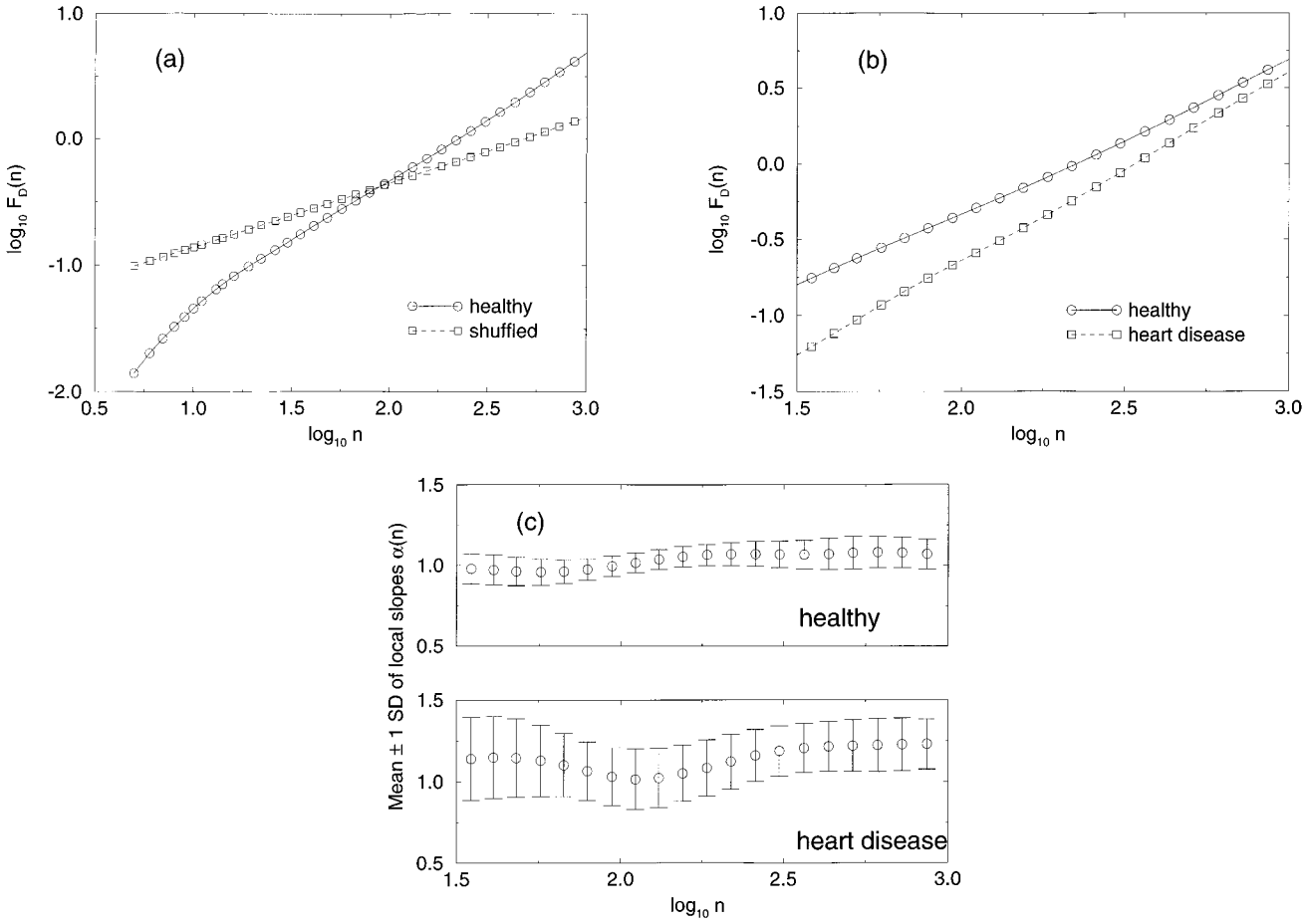

FIG. 3. (a) Double log plot of the DFA function $F_D(n)$ for a representative subject and surrogate data obtained by randomly shuffling the same interbeat interval time series. The DFA function does not have the ''dip'' observed in the Allan factor. We obtain $\alpha=1/2$ for the shuffled data because of the absence of temporal correlations. The scaling region shown is approximately equal to the scaling region of interest used for the Allan factor (see the text). Successive values of n differ by a factor of $2^{1/4}$. (b) DFA function $F_D(n)$ for the same representative healthy and diseased subjects as in Fig. 2. We note the consistently higher values of α in disease, consistent with previous studies of heartbeat dynamics [2]. Moreover, the scaling instability indices are able to detect subtle deviations from uniform power-law behavior that are otherwise difficult to see directly by visual inspection. (c) Mean ± 1 standard deviation of the DFA scaling exponents (local slopes) $\alpha(n)$ computed for the normal (top curve) and diseased (bottom curve) groups of subjects. We find greater variability of $\alpha(n)$ for the diseased subjects than for the healthy ones, confirming the loss of scaling stability with disease.

we need to carefully select a region that exhibits the scaling behavior of interest. To this end, we use shuffled time series as controls.

When we shuffle the interbeat intervals for each time series, we find that the Allan factor function $f_1(t)$ steadily decreases and then flattens for $t>10$ s for both healthy and disease data sets (Fig. 1), indicating a loss of long-range correlations [5]. For small time scales [see region $\log_{10}t\leqslant 10$ in Fig. 2(a)], the Allan factor function is different for these shuffled data sets due to the strong influence of the probability distributions of the interbeat intervals (not their dynamical properties).

In contrast, for very large time scales, the scaling behavior is the same for the shuffled data from different subjects, i.e., $f_1(t)$ is constant and the scaling exponent is zero. Thus we can define a scaling region of interest where there are no significant differences in scaling stability between the healthy and disease data sets after shuffling. This requirement makes it more likely that any observed difference in scaling between the original normal and disease data sets is not due to differences in the probability distributions of the interbeat intervals, but rather arises from intrinsic differences in the scaling behavior of long-range temporal correlations. We find this region of interest to be $1.0\leqslant\log t\leqslant 3.5$.

B. Detrended fluctuation analysis (DFA) method

The above treatment of the heartbeat time series as a point process has possible limitations that arise from parametrizing the time series in terms of real time t. The Allan factor $f_1(t)$ has a ''dip'' near $t=10$ s due to the anticlustering (i.e., regularity) of the heartbeat on these scales [5]. This effect is partially caused by the ''dead time'' following each heartbeat during which the heart is refractory to stimulation [5]. The dip causes the Allan factor to have curvature even up to $t\approx 100$ s. For these reasons, the Allan factor may not always reliably separate effects due to the shape of the interbeat interval distribution from those arising from long-range correlations. DFA [12,4], which treats the heartbeat as a time series parametrized by beat number j rather than by time t, is

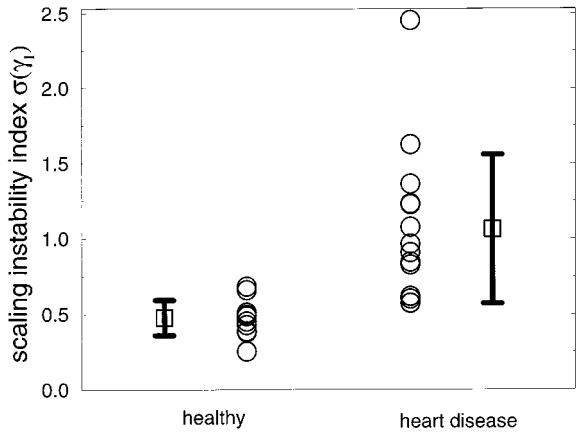

FIG. 4. Scaling instability index $\sigma[\gamma_1(t)]$ for each subject. We find that $\sigma[\gamma_1(t)]$ is considerably greater for diseased subjects than for healthy subjects. Furthermore, there is more intragroup variability in the subjects with heart disease, consistent with a wide range in the degree of pathologic disturbances. The values of the scaling instability index for the healthy and disease data sets are significantly different ($p<0.0002$, Wilcoxon rank sum test). However, if each time series is randomly shuffled, then the resulting values of the scaling instability index are no longer different. This finding indicates that there is a significant loss of scaling stability with heart disease. Furthermore, this loss of scaling stability cannot be detected by measuring only the mean and variance of the interbeat interval time series, i.e., the physiologically important scaling stability information is contained in the temporal ordering of the interbeat intervals rather than in their probability distribution.

not susceptible to these limitations and can be used to complement our Allan factor analysis [21].

The DFA method [12] has been systematically compared with other algorithms for measuring fractal correlations by Taqqu *et al.* [22] and was found to be the best of the computationally efficient methods. It is summarized as follows. First, the interbeat interval time series $u(j)$ (where j is the beat number) is integrated to give a function $y(j)\equiv\sum_{i=0}^{j}u(i)$, which can be thought of graphically as a one-dimensional random walk. The sequence $y(j)$ is then divided into a number of sub sequences of length n. For each subsequence, linear regression is used to calculate an interpolated ''detrended'' walk $y'(j)\equiv a+b(j-j_0)$. We define the ''DFA fluctuation'' by $F_D(n)\equiv\sqrt{\langle(\delta y)^2\rangle}$, where $\delta y\equiv y(j)-y'(j)$ and the angular brackets denote averaging over all points $y(j)$. We use a moving window to obtain better statistics [23]. The DFA exponent $\alpha(n)$ is defined by

$$\alpha(n)\equiv\frac{d\log F_D(n)}{d\log(n+3)}, \tag{1}$$

where the $+3$ term is a correction important for small n [23]. We estimate $\alpha(n)$ by taking the slope $\Delta\log F_D(n)/\Delta\log n$, where $\Delta\log n=2^{1/4}$ and $2^{1/4}$ is the ratio of successive values of n. Uncorrelated data give rise to $\alpha=1/2$, as expected from the central limit theorem, while correlated data give rise to $\alpha\neq1/2$. A constant value of $\alpha(n)$ indicates stable scaling, while departures indicate loss of scaling stability.

We choose the scaling region of interest $1.5\leqslant\log n\leqslant3.0$ corresponding approximately to the one used for the Allan factor. However, the two scaling regions cannot be matched exactly since the Allan factor $f_1(t)$ is of necessity referenced to real time, while the DFA function $F_D(n)$ is referenced to beat number.

III. ANALYSIS

Our analysis is based on the digitized electrocardiograms of beat-to-beat heart rate fluctuations over very long time scales (up to 24 h $\approx10^5$ beats) recorded with an ambulatory monitor. We truncate each time series to 69 000 beats to eliminate spurious effects due to variations in data set lengths and we remove data points due to nonsinus beats associated with interbeat intervals greater than 1.8 s (Fig. 1). These deleted beats comprise a very small fraction of our records (less than 0.1%)

We study data from a group of 11 healthy subjects (mean age, 32; range, 20–45) (Fig. 2). We find that the Allan factor scaling exponent $\gamma_1(t)$ is approximately constant for the healthy data for different values of t as well as for different subjects. Typically, we find for healthy subjects that $\gamma_1(t)$ lies in the range $0<\gamma_1(t)<2$ in the region of interest.

We perform the identical analysis on 14 subjects with a life-threatening form of heart disease known as *congestive heart failure* (mean age, 56; range, 22–71). We find wide variations in $\gamma_1(t)$, indicating that fluctuations grow erratically and nonuniformly with time scale t, consistent with scaling instabilities in the dynamics of the system.

We verify these findings using DFA. Figure 3 compares the DFA scaling exponent $\alpha(n)$ for the normal and diseased subjects. We find that there is greater variation in $\alpha(n)$ for diseased subjects than for healthy subjects.

We next define two *scaling instability indices* for quantifying departures from stable power-law scaling: $\sigma[\gamma_1(t)]$ and $\rho[\gamma_1(t)]$ are the standard deviation and range (i.e., maximum minimum), respectively, of the scaling exponents $\gamma_1(t)$ in the region of interest $1.0\leqslant\log t<3.5$. Small values of the scaling instability indices indicate uniform, stable scaling, while large values indicate deviations from stable scaling (Fig. 4). We further define $\sigma[\alpha(n)]$ and $\rho[\alpha(n)]$ to be the standard deviation and range, respectively, of the DFA exponent $\alpha(n)$ in the scaling region $1.5\leqslant\log n\leqslant3.0$. We find statistically significant differences between healthy and diseased groups [24]. Specifically, as indicated in Figs. 2(c) and 3(c), there is an underlying loss of uniform power-law scaling in disease. The observed differences between heart failure and healthy control groups was not related to age effects.

IV. DISCUSSION

Our results suggest that the scaling properties of the dynamics for a group of healthy subjects are more uniform than those from subjects with congestive heart failure (Fig. 4). The greater scaling consistency found for healthy subjects suggests that the fluctuations in heart rate scale in a more stable fashion than in disease. The hypothesis that scaling *instabilities* may be indicative of perturbed behavior is plausible for several reasons.

(i) Many systems, such as those regulating the heartbeat, are under neurophysiological control.

(ii) Healthy neurophysiological control mechanisms regulate their activity over a wide range of effective time scales.

Fluctuations on such widely different time scales are remarkably similar to each other, leading to stable power-law scaling spanning several decades in healthy cases.

(iii) The inability of a pathologic or aging [25] neurophysiological system to regulate itself over particular time scales may lead to a breakdown or instability of scaling on those time scales [7,26].

V. CONCLUSION

In summary, we developed techniques to quantify scaling uniformity and its deviations in nonstationary physiological time series and applied these techniques to complex cardiac interbeat interval time series obtained under healthy and pathologic conditions. These techniques may generalize to the analysis of a wide variety of nonstationary time series.

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[1] W. B. Cannon, Physiol. Rev. **9**, 399 (1929).
[2] C.-K. Peng, J. Mietus, J. M. Hausdorff, S. Havlin, H. E. Stanley, and A. L. Goldberger, Phys. Rev. Lett. **70**, 1343 (1993).
[3] R. G. Turcott and M. C. Teich, Proc. SPIE **2036**, 22 (1993).
[4] C.-K. Peng, S. Havlin, H. E. Stanley, and A. L. Goldberger, CHAOS **5**, 82 (1995).
[5] R. G. Turcott and M. C. Teich, Ann. Biomed. Eng. **24**, 269 (1996).
[6] M. Meesman, F. Grüneis, P. Flachenecker, and K.-D. Kniffki, Biol. Cybern. **68**, 299 (1993).
[7] A. L. Goldberger, Lancet **347**, 1312 (1996).
[8] H. E. Stanley, *Introduction to Phase Transitions and Critical Phenomena* (Oxford University Press, London, 1971); *Fractals and Disordered Systems*, edited by A. Bunde and S. Havlin (Springer-Verlag, Berlin, 1991); *Fractals in Science*, edited by A. Bunde and S. Havlin (Springer-Verlag, Berlin, 1994).
[9] A. L. Goldberger and B. J. West, Yale J. Biol. Med. **60**, 421 (1987).
[10] U. Fano, Phys. Rev. **72**, 26 (1947).
[11] J. A. Barnes and D. W. Allan, Proc. IEEE **54**, 176 (1996).
[12] C.-K. Peng, S. V. Buldyrev, S. Havlin, M. Simons, H. E. Stanley, and A. L. Goldberger, Phys. Rev. E **49**, 1691 (1994).
[13] There is an active debate about whether it is preferable to analyze biological time series such as the heartbeat with reference to real time or to beat number. We adapt two methods that analyze the data from each perspective. The first approach treats the heartbeat as the *event* of interest and assumes that there is an objective ''clock'' for the timing of the event. The second approach emphasizes the interbeat interval and uses the beat number as an index of the biological time.
[14] R. W. DeBoer, J. M. Karemaker, and J. Strackee, IEEE Trans. Biomed. Eng. **BME-31**, 384 (1984).
[15] S. B. Lowen and M. C. Teich, Fractals **3**, 183 (1995).
[16] S. B. Lowen and M. C. Teich, J. Acoust. Soc. Am. (to be published).
[17] M. C. Teich, C. Heneghan, S. B. Lowen, and R. G. Turcott, in *Wavelets in Medicine and Biology*, edited by A. Aldroubi and M. Unser (CRC, Boca Raton, FL, 1996).
[18] M. C. Teich, R. G. Turcott, and R. M. Siegel, IEEE Eng. Biol. Med. Mag. (to be published).
[19] R. G. Turcott, P. D. R. Barker, and M. C. Teich, J. Stat. Comput. Simul. **52**, 253 (1995).
[20] We can also achieve higher-order detrending, which we indicate by $f_i(t)$, where the subscript gives the order of detrending.
[21] For time series with long-range power-law correlations, the Allan factor exponent γ_1 is related to the DFA exponent α by $\gamma_1 = 2\alpha - 1$.
[22] M. S. Taqqu, V. Teverovsky, and W. Willinger, Fractals **3**, 785 (1995).
[23] S. V. Buldyrev, A. L. Goldberger, S. Havlin, R. N. Mantegna, M. E. Matsa, C.-K. Peng, M. Simons, and H. E. Stanley, Phys. Rev. E **51**, 5084 (1995).
[24] We find a significant loss of scaling stability evidenced by the higher values of the two indices for disease. Statistical significance is defined as $p < 0.05$ using the Wilcoxon rank sum test. We obtain similar results using other indices that measure departures from stable power-law scaling, such as the root-mean-square curvatures of $\gamma_1(t)$ and $\alpha(n)$.
[25] N. Iyengar, C.-K. Peng, R. Morin, A. L. Goldberger, and L.A. Lipsitz, Am. J. Physiol. **271**, 1078 (1996).
[26] P. Ch. Ivanov, M. G. Rosenblum, C.-K. Peng, J. Mietus, S. Havlin, H. E. Stanley, and A. L. Goldberger, Nature **383**, 323 (1996).