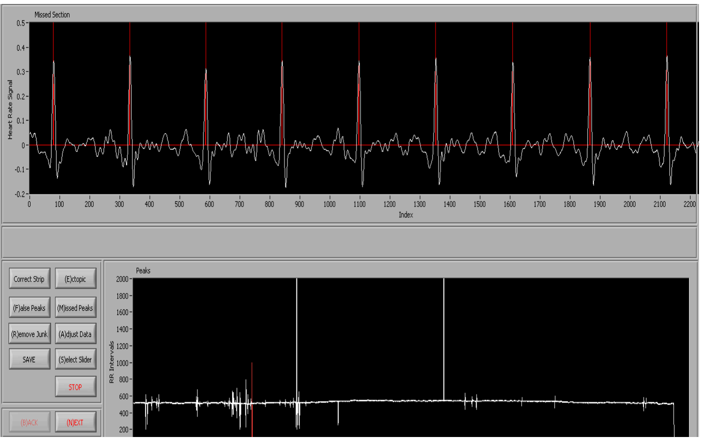
eFigure 1

eFigure 1: Performing Detrended Fluctuation Analysis

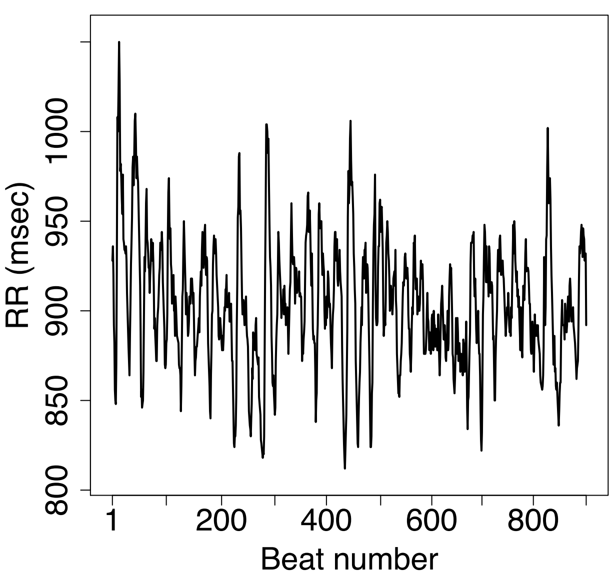
Identify QRS complexes on Lead II EKG

A. Identify QRS complexes

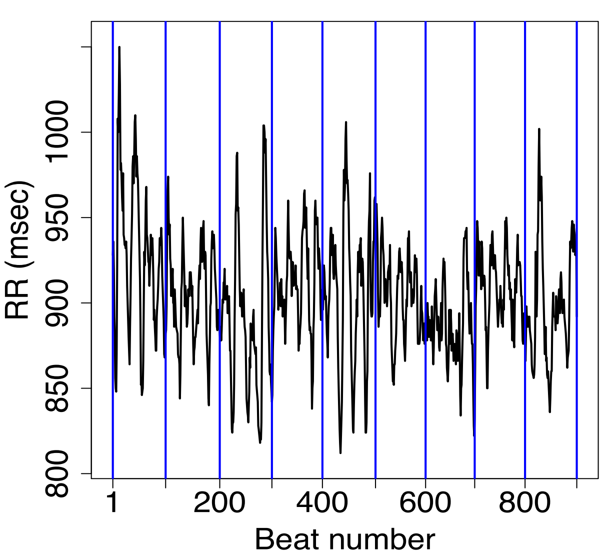


Plot time between successive QRS complexes, RR

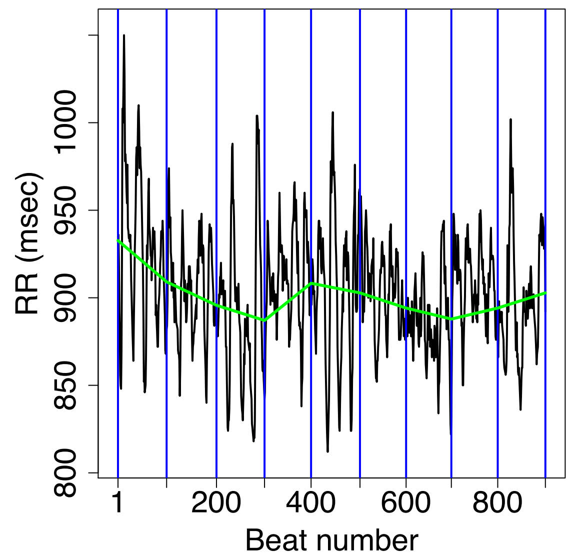
B. Tachogram



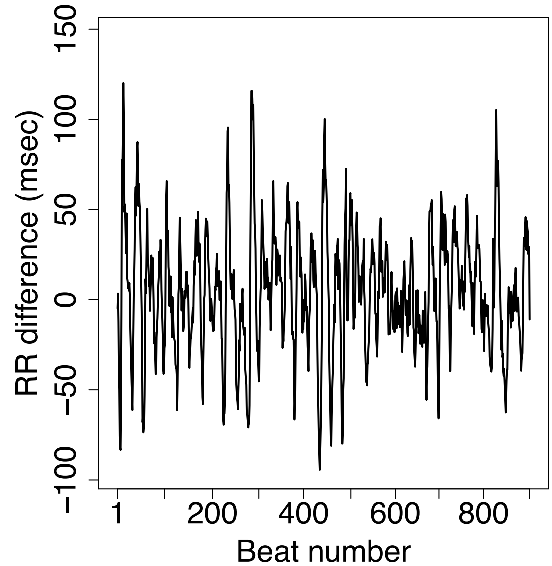
C. Tachogram segmented at 100–beat intervals



D. Tachogram with segmented linear regression

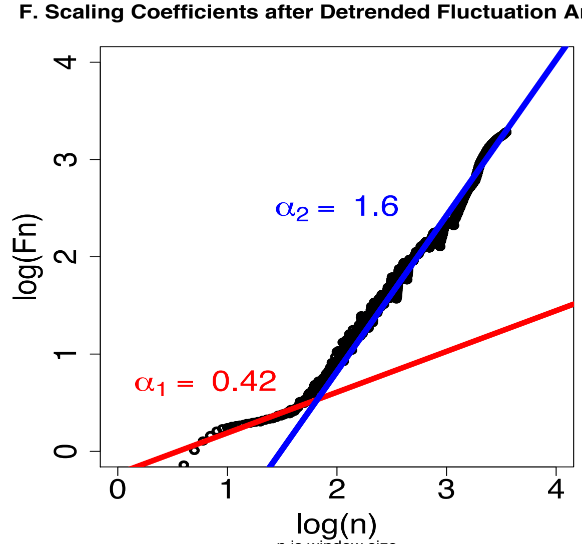


E. Tachogram with regression lines subtracted

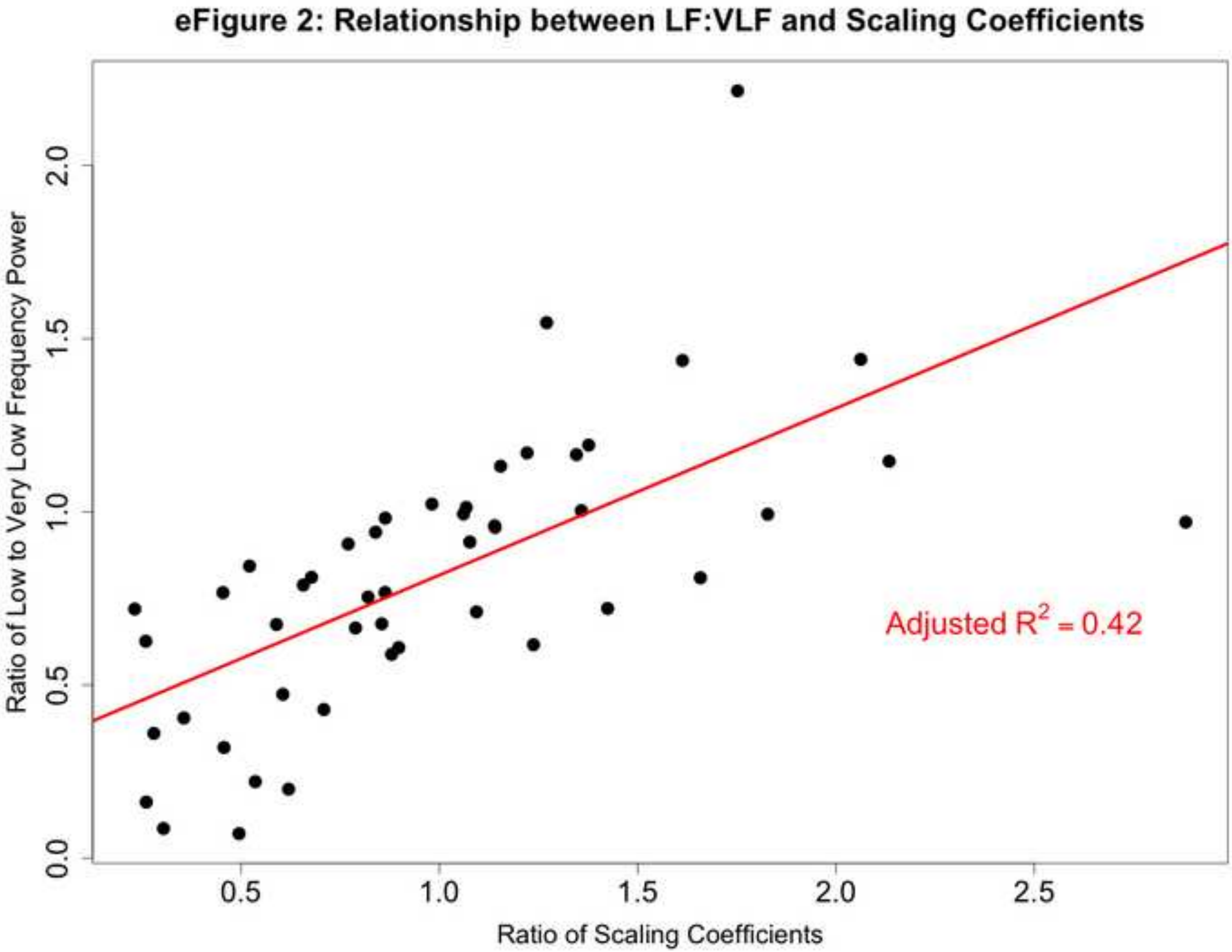


Generate log-log plot of window size vs. fluctuation

F. Scaling Coefficients after Detrended Fluctuation Analysis



eFigure 2


eFigure 2: Relationship between LF:VLF and Scaling Coefficients
Ratio of Low to Very Low Frequency Power
0.0
0.5
1.0
1.5
2.0
0.5
1.0
1.5
2.0
2.5
Ratio of Scaling Coefficients
Adjusted R2 = 0.42

Appendix: Time, Frequency, and Complexity Domain Metrics from tachogram

Time Domain:

The mean μ was calculated as

$$\mu = \sum_{i=0}^{n-1} \frac{x_i}{n}$$

where n is the number of samples in $\boldsymbol{X}$. The variance is calculated as

$$\sigma^2 = \sum_{i=0}^{n-1} \frac{(x_i - \mu)^2}{n-1}$$

The square root of the variance is the standard deviation of the signal. The root mean square (*RMS*) value of the signal is calculated as

$$RMS = \sqrt{\frac{1}{n}\sum_{i=0}^{n-1} |x_i|^2}$$

Frequency Domain:

Welch's method was used to estimate the power spectra.[1] This method separates the time signal into K successive blocks of length M samples each, multiplies each block with a window function w(n), calculates the squared magnitude of the Fourier transform of each windowed block, and then averages the results to obtain the estimated power spectrum $\hat{S}_k^W(f_k)$is defined as follows:

$$\hat{S}_k^W(f_k) = \frac{1}{K\sum_{n=0}^{M-1} w(n)^2} \sum_{m=0}^{K-1} \left| \sum_{n=0}^{M-1} x_m(n) e^{-j2\pi nk/N} \right|^2$$

where $x_m(n)$ represents the mth block of data and N is the FFT size. The original time series was sampled at f_s = 500 Hz, and $f_k = \frac{kf_s}{N}$. We used, K=8 and each block maintained a 50% overlap with adjacent blocks in our analysis.

We also calculated the power spectral density (PSD) using an auto-regressive function

$$S(f) = \frac{\sigma^2}{\left|\sum_{q=0}^{l-1} a(k) e^{-\frac{i2\pi q f_k}{f_s}}\right|^2}$$

where *S(f)* is equal to the PSD of the original time series. The variance of the noise for the estimated AR model is given as σ^2. The variable *a* contains the AR model coefficients, where $a = [a_0 = 1, a_1, a_2, \dots a_l]$ and l=16 is the order of the AR estimation. The AR coefficients were estimated by minimizing the sum of the squared Lth order forward prediction errors over the length of the data.

VLF (Very Low Frequency) range: 0.0-0.04 Hz

LF (Low Frequency) range: 0.04-0.15 Hz

HF (High Frequency) range: 0.15-0.4 Hz

Complexity Domain:

Sample Entropy [2,3]: Sample Entropy is a nonlinear dynamic analysis method. It can be defined as the negative natural logarithm of the Conditional Probability in a data set of length 'N' that a dataset will repeat itself for 'm+1' points given that the dataset has repeated itself for 'm' points with a tolerance 'r'.

We computed sample entropy in the following steps.

1. The RR interval series (x_i), is normalized by the following equation.

$$y_i = \frac{x_i - \mu}{\sqrt{\left({}^{1}/_{N}\,\Sigma(x_i - \mu)^2\right)}}$$

μ is the mean of the RR interval series.

2. The resulting series y_i is then inspected for the number of matches within the tolerance range 'r' for up to a length of m and m+1 points.
3. The number of matches of m+1 points is divided by the matches of m points, which gives the conditional probability of m+1 points matching with respect to m points.
4. The negative natural logarithm of the above ratio is sample entropy.

Scaling coefficients (α) from detrended fluctuation analysis [4]

Following the techniques of Peng et al, we first integrated the tachogram. The integrated tachogram is then divided into *P* intervals of equal length, and a least-squares line fit $y_p(r)$ is found for each interval. The integrated tachogram y(r) is detrended by subtracting $y_p(r)$ from y(r). The root mean-square fluctuation of this detrended signal is then calculated as

$$F(p) = \sqrt{\frac{1}{R}\sum_{r=1}^{R}[y(r) - y_r(r)]^2}$$

The fluctuation plot is the graph of the log of F(n) vs. the log of window size (n). We estimated the short-term scaling coefficient α1 as the slope of the straight line approximation of the fluctuation plot for window sizes from 4 to 31 beats ($10^{0.5}$ to $10^{1.5}$).

The long-term scaling exponent α2, was similarly found as the slope of the straight line approximation of the fluctuation plot for window sizes greater than 100 beats (10^2).

1. Welch PD: **The Use of Fast Fourier Transform for the Estimation of Power Spectra: A Method Based on Time Averaging Over Short, Modified Periodograms**. *IEEE Transactions on Audio and Electroacoustics 1967*, **15**(2):70-73.
2. Lake DE, Richman JS, Griffin MP, Moorman JR: **Sample entropy analysis of neonatal heart rate variability**. *Am J Physiol Regul Integr Comp Physiol* 2002, **283**(3):R789-797.
3. Richman JS, Moorman JR: **Physiological time-series analysis using approximate entropy and sample entropy**. *Am J Physiol Heart Circ Physiol* 2000, **278**(6):H2039-2049.
4. Peng CK, Havlin S, Stanley HE, Goldberger AL: **Quantification of scaling exponents and crossover phenomena in nonstationary heartbeat time series**. *Chaos* 1995, **5**(1):82-87.