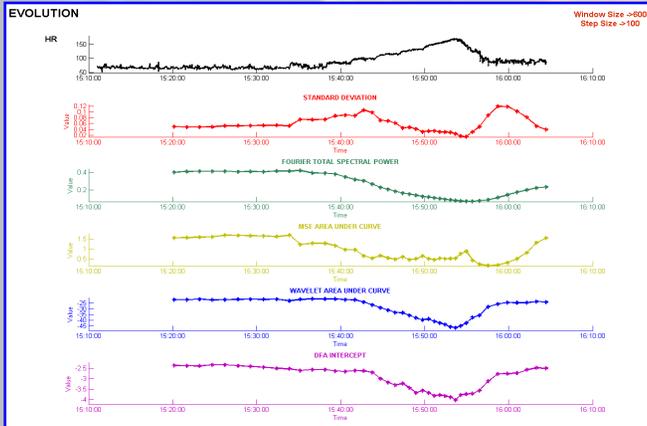
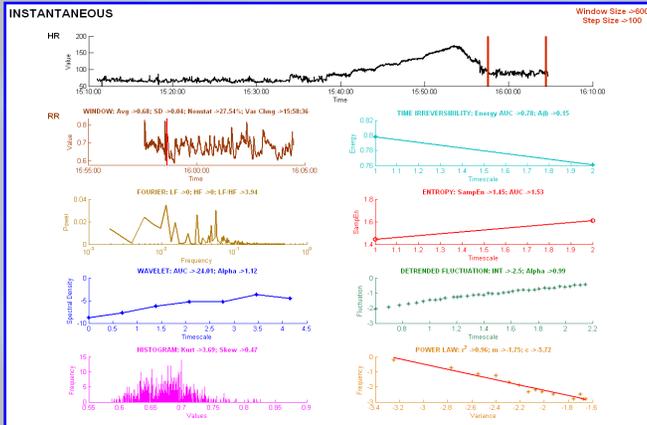


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Objectives

We observe that complex physiologic dynamics are dependent on the integrity of the system generating them. We hypothesize that continuous multiorgan variability analysis offers a technology with which to track the emergent properties of a complex non-linear system¹. Therefore, our objectives are to: (a) develop a novel system for continuous individualized multiorgan variability analysis (CIMVA) integrating cardiac and pulmonary rhythms; and, (b) test the CIMVA system by evaluating changes in cardiopulmonary variability (CPV) during controlled physiologic stress, namely staged incremental exercise in healthy subjects.



Methods

The CIMVA system (developed in Windows® Matlab®) comprises algorithms for computing and normalizing mean, standard deviation, location of non-stationarities, fast Fourier transform (FFT), sample entropy (SampEn), multiscale entropy (MSE), wavelet analysis, detrended fluctuation analysis (DFA), kurtosis, skewness, power law analysis, and time irreversibility statistics. To accomplish continuous variability analysis over time, a *roving window* approach is used, whereby a window of user specified *interval* and *step* marches through the input signal, computing and time-stamping the above variability metrics at each *step*, thus creating multiple variability time series. Interval-in-time variability (instantaneous) and change in variability over time (evolution) are displayed on two parallel monitors. CPV is computed and visualized by synchronizing cardiac and pulmonary variability data streams, followed by plotting their "time evolution" on a normalized X-Y plane. To test the CIMVA system, staged incremental exercise tests were performed on healthy volunteers (N = 8), during which continuous heart rate (Brytech®, 500 Hz EKG System) and respiratory rate (Respironics®, 200 Hz Capnograph System) data were harvested. For analysis, EKG waveforms were converted to RR' time series using Hamilton-Tompkins QRS detection algorithm whereas end-tidal CO₂ waveforms were converted to breath-to-breath time series using a novel *breath detection algorithm*.

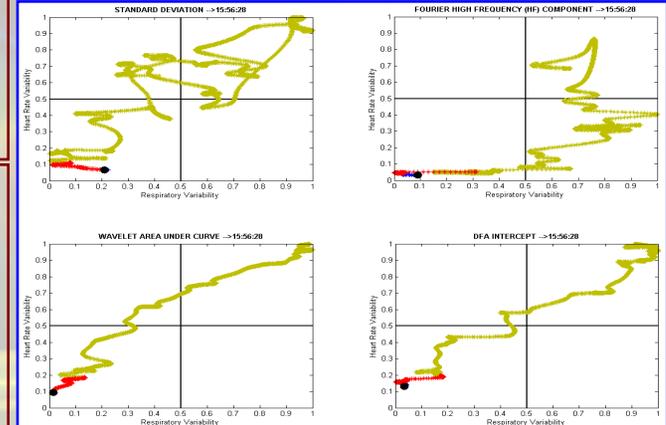
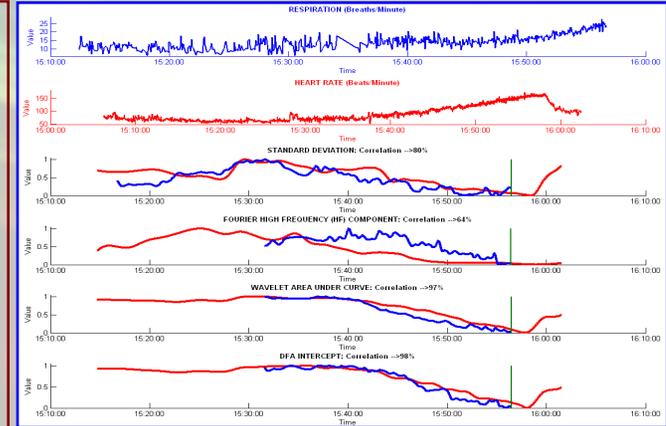
Results

The CIMVA system demonstrated robustness (the speed was satisfactory, there were no system crashes, and the computations were accurate) in continuously analyzing, visualizing, and storing CPV associated with heart and respiratory rate datasets. A reproducible decrease in wavelet, DFA, and power law CPV was observed with exercise for all subjects and this decrease was progressive and continuous. Certain measures of CPV namely FFT, power law, SampEn, and MSE demonstrated higher sensitivity to nonstationarity in the analyzed data, wherein the progressive decrease in CPV was less pronounced and not continuous. The remainder of the variability statistics computed by the CIMVA system, conformed to existing observations regarding characteristic changes in CPV due to mechanical loading or exercise².

Acknowledgments

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Conclusions

We conclude that an automated analysis of continuous individualized multiorgan variability, utilizing a plurality of variability analysis techniques simultaneously is feasible, reproducible, and allows us to study the change in multiorgan variability over time, a novel measure, in a comprehensive and accurate manner. A reduction in overall CPV associated with increasing levels of exercise is evident across the population studied. This software analysis has several clinical applications with promise towards the development of a real-time diagnostic and predictive multiorgan variability analysis system.

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