

Effect of Physical Contact (Hand-Holding) on Heart Rate Variability

T. Pishbin, S.M.P. Firoozabadi, N. Jafarnia Dabanloo, F. Mohammadi and S. Koozehgari

Abstract—Heart's electric field can be measured anywhere on the surface of the body (ECG). When individuals touch, one person's ECG signal can be registered in other person's EEG and elsewhere on his body. Now, the aim of this study was to test the hypothesis that physical contact (hand-holding) of two persons changes their heart rate variability. Subjects were sixteen healthy female (age: 20-26) which divided into eight sets. In each sets, we had two friends that they passed intimacy test of J.sternberg. ECG of two subjects (each set) acquired for 5 minutes before hand-holding (as control group) and 5 minutes during they held their hands (as experimental group). Then heart rate variability signals were extracted from subjects' ECG and analyzed in linear feature space (time and frequency domain) and nonlinear feature space. Considering the results, we conclude that physical contact (hand-holding of two friends) increases parasympathetic activity, as indicate by increase SD1, SD1/SD2, HF and MF power ($p < 0.05$) and decreases sympathetic activity, as indicate by decrease LF power ($p < 0.01$) and LF/HF ratio ($p < 0.05$).

Keywords—Autonomic nervous system (ANS), Hand- holding, Heart rate variability (HRV), Power spectral density analysis.

I. INTRODUCTION

As an electric source, heart sends electrical currents to all parts of the body. The heart generates the largest electromagnetic field in our body. The electrical field that measured in an electrocardiogram (ECG) is about 60 times greater in amplitude than electroencephalogram (EEG) [1]-[2]. As a consistent generator of rhythmic information patterns in our body, and possessing an extensive communication system with the brain than do other major organs, the heart exerts a unique and far-reaching influence on the brain and the entire body [3]. The study of communication pathways between

brain and heart has been approached from a rather one-sided perspective, with scientists focusing primarily on the heart's responses to the brain's commands. Now, we have learned that the communication between brain and heart is actually a dynamic, ongoing, two-way dialog, with each organ continuously influencing the other's function. The heart communicates with the brain in four main ways: biophysical communication (pulse wave), neurological communication (nervous system), biochemical communication (hormones) and Energetic communication (electromagnetic fields) [4]. The brain also sends signal to the heart with two branches of autonomic nervous system (ANS).

Figure 1 illustrates how the sympathetic and parasympathetic branches of the ANS influence the sinus node of the heart, thereby modulating heart rate [5].

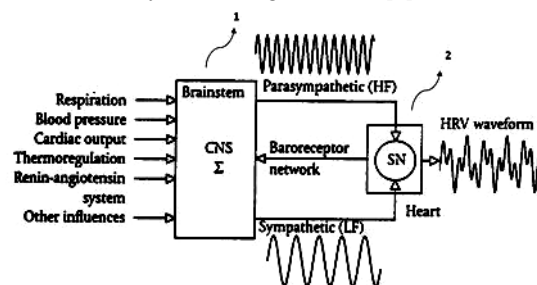


Fig. 1 Nervous system links between the heart and brain [6].

This figure is not describes all of the functions of the autonomic nervous system of a human, but rather provides an exemplar of those signals and functions which are currently believed to be directly related to the operation of the heart. As illustrated in FIG. 1, the brainstem 1 receives various input signals, consisting of control and status information, from throughout the body. The brainstem 1, as the control center of the central nervous system (CNS), continuously summarizes (Σ) all of afferent information and synthesizes appropriate outputs to the heart 1 via either the sympathetic or parasympathetic subsystems [6].

The output control signals of the sympathetic system, is responsible for increased heart rate in some situation, e.g. in response to feel danger, tend to be relatively low frequency (LF) rhythms. In contrast, the parasympathetic system, which works to limit or repress the effects of the sympathetic system, tend to be relatively high frequency (HF) signals. In general, the parasympathetic system tends to produce a relaxed state whereas the sympathetic a more active, excited state. The

T. Pishbin is with the Department of Biomedical Engineering, Science & Research Branch, Islamic Azad University, Tehran, Iran (e-mail: Tahere.pishbin@gmail.com).

S.M.P. Firoozabadi, is with the Department of Biomedical Engineering, Science & Research Branch, Islamic Azad University and the Department of Medical Physics, Medical Sciences Faculty, Tarbiat Modares University, Tehran, Iran (phone: +98-021-82883821; e-mail: Pourmir@modares.ac.ir).

N. Jafarnia Dabanloo is with Department of Biomedical Engineering, Science & Research Branch, Islamic Azad University, Tehran, Iran (phone: +98-021-44474322; e-mail: N_jafarnia@yahoo.com).

F. Mohammadi is with the Department of Biomedical Engineering, Science & Research Branch, Islamic Azad University, Tehran, Iran (e-mail: Fateme.mohammadi86@gmail.com).

S. Koozehgari is with the Department of International Relations, Science & Research Branch, Islamic Azad University, Tehran, Iran (e-mail: koozehgari_saeedeh@yahoo.com).

brainstem 1 also receives afferent information from the baroreceptor network, and other receptor neurons, located throughout the heart and in the aortic arch of the heart 2, which are sensitive to stretch (pressure) and chemical changes within the heart 2. As the heart 2 beats, and its walls swell, various baroreceptors are triggered, providing signals as a function of the heart beat, where increased heart rate is generally reflected by increased baroreceptor signals. In response to the sympathetic and parasympathetic control signals from the brainstem 1, the heart rate 2 varies. The sinus node (SN) of the heart 2 is a group of cells which act as a natural pacemaker to initiate the onset of the heart beat at a rate which is non-linearly related to the relative strengths of these autonomic control signals. It has been determined that the heart beats variability, varies according to the shifting relative balance between the parasympathetic and sympathetic signals [6].

Later, neurophysiologists discovered a neural pathway and mechanism whereby input from the heart to the brain could inhibit or facilitate the brain's electrical activity [7]. Also, they found that during physical contact, one person's ECG signal can be registered in other person's EEG and elsewhere on his or her body (Fig. 2) [1].

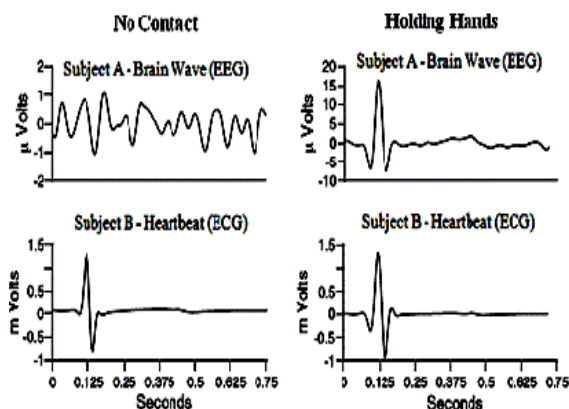


Fig. 2 Signal-averaged waveforms before and while holding hands. Signal averaged waveforms showing a transference of the electrical energy generated by the source's heart to the receiving subject's head. The baseline recording (left side) is from a 10-minute period during which the subjects were seated 4 feet apart without physical contact. The right column shows the recording from a 5-minute period during which the subjects held hands. The EEG data shown here were recorded from the C3 site of the EEG [2].

On the other hand, heart works as an electrical source in our body. The electrical activity of the heart, cause an electrical current in the body (as a volume conductor) and by the physical contact of two persons (contact of two volume conductors) this current can flow in the other's body and vice versa. Therefore, considering the transference of signal during skin-to-skin contact and also communication between heart

and brain, the objective of this study was to determine whether different linear and non-linear HRV measures may change during physical contact or not. The largest amplitude of a single cycle of the normal ECG is referred to as the R-wave manifesting the depolarization process of the ventricle. The time between successive R-waves is referred to as an RR-interval, and an RR-tachogram is then a series of RR-intervals that shows naturally-occurring, beat-to-beat changes in heart rate, which are reflective of heart-brain interactions and autonomic nervous system dynamics [3]-[20]. On the other hand, researches have revealed that heart rate variability is influenced by a variety of factors, including physical movement, mental and emotional states [5]-[8]. So the subjects of this study were eight healthy friend sets that got quorum grade of standard intimacy test (intimacy test of Robert J.sternberg).

II.METHODS

A. Subjects

From thirty-eight volunteers (nineteen friends groups) that filled out a health questionnaire and intimacy test of Robert J.sternberg, sixteen female subjects (eight friend groups) had participated in this study. These subjects (age: 20-26) divided into eight sets. In each sets, we had two friends that were healthy and got quorum grade of intimacy test. No subject was taking any medication that affect heart rate variability and no subject had diseases such as heart disease, diabetes mellitus or depression and for all subjects signal quality was normal for analysis.

B. Experimental Protocol

To test the hypothesis that when 2 people touch, their heart rate variability properties change because of the exchange of electrical energy produced by their hearts, in this project the experiments were done as followed:

Eight friend sets had participated in this experiment. A total of experiments for each set were conducted on a separate day at the same time (8:30 AM). Each set was seated in comfortable, high-back chair and fitted with ECG electrodes. Prior to each experiment, subjects were asked to turn off their mobile phones and refrain from talking, engaging in exaggerated body movement and from intentionally altering their respiration. The two friends were simultaneously monitored using a 5-minute baseline period during which they seated without any physical contact (control group), followed by a 5-minute hand holding period in which friends remained seated but reached out and held the right hand of her friend (experimental group). We asked friends to hold their right hands because researches had shown that in this hand holding orientation, one person ECG appeared with largest amplitude in the other person EEG [1]. Subjects ECG data had saved as text files for further analysis.

C. Signal Acquisition and Analysis

Disposable silver/silver chloride electrodes were used for

bipolar ECG measurement (limb lead). Electrocardiograph was recorded at 250HZ sampling rate by MP100, BIOPAC System Inc. The signals were stored for latter analysis. R-waves were detected from the ECG signals, based on Pan-Tompkins algorithm [9]. Beat-to-beat RRI (R-to-R-interval) signal was constructed as a series of time difference between the successive heart beats. For spectral analysis purposes, the beat-to-beat data were interpolated and re-sampled at 4 Hz using a cubic spline algorithm. HRV analysis was done with Kubios HRV software [10] and in three categories, i.e. time-domain, frequency-domain and nonlinear methods.

Time domain variables were mean RR, SDNN, RMSSD, NN50 of total HR (%) and HRV triangular index. SDNN is the standard deviation of all RR intervals. RMSSD is the square root of the mean of the sum of the squares of differences between adjacent RR intervals. NN50 count means the number of pairs of adjacent RR intervals differing by more than 50 ms in the entire analysis interval. NN50 of total HR (%) is the NN50 count divided by the total number of all RR intervals. The HRV triangular index means the total number of RR intervals divided by maximum height of the histogram excluding boundaries.

Frequency domain analysis was based on power spectral estimation, which was carried out using FFT based methods by Welch method with FFT length of 1024 points [11].

In this domain, the power was calculated for low frequency (LF, 0.01-0.05 Hz), medium frequency (MF, 0.05-0.15 Hz), and high frequency bands (HF, 0.15-0.5 Hz). The LF region is considered a measure of sympathetic activity. In contrast, the HF region is associated with respiratory sinus arrhythmia and is almost exclusively due to parasympathetic activity. Power in the MF region is thought to be mixed sympathetic and parasympathetic activity. In addition the LF/HF and MF/LF+HF ratio were calculated. LF/HF ratio has been associated with the so-called sympathovagal balance and MF/LF+HF has been highly responsive to changing emotional states [5].

The nonlinear properties of HRV have been analyzed using measures such as poincaré plot [12]-[13], approximate entropy (ApEn) [14]-[15], correlation dimension [16] and detrended fluctuation analysis (DFA) [17]-[18]. ApEn measures the complexity or irregularity of the signal. Large values of ApEn indicate more irregular signal and smaller values of ApEn indicate high regularity [10]. Another method for measuring the complexity or strangeness of the time series is the correlation dimension [10]. The correlation dimension is expected to give information on the minimum number of dynamic variables needed to model the system. DFA also measures the correlation within the signal.

D. Statistical Analysis

The group values are summarized as mean±SD. Wilcoxon signed rank test was used to compare HRV properties. Statistical analysis was performed using SPSS version 16.0.

TABLE I
TIME-DOMAIN VARIABLES OF SUBJECT WITHOUT AND DURING
HAND-HOLDING

VARIABLE	CONTROL GROUP	EXPERIMENTAL GROUP	P VALUE
HR Mean (bpm)	76.66±6.16	75.15±6.0	0.25
HR std	4.56±1.20	4.55±1.25	0.64
RR mean (ms)	791.04±65.02	806.51±62.23	0.27
SDNN (ms)	48.24±16.60	49.40±15.15	0.56
RMSSD (ms)	41.10±18.71	45.60±17.97	0.06
RR triangular index	11.91±3.60	12.34±2.90	0.71
pNN50	20.14±19.33	27.65±18.85	0.02*

Values are expressed as mean±SD. * p<0.05.

RMSSD: Square root of the mean squared differences between successive RR Intervals; RR triangular index: The integral of the RR interval histogram divided by the height of the histogram; pNN50: NN50 divided by the total number of RR intervals.

III. RESULTS

A. Time- Domain Results

Time domain methods are based on the beat-to-beat or NN intervals. Table I provides time domain data for the 16 subjects. When the group was analyzed as a whole, time domain variables do not demonstrate any differences between two groups (control and experimental groups) except for pNN50 that increased significantly during hand-holding (20.14±19.33 in control group to 27.65±18.85 in experimental group, p<0.05). Also variables showed an increase close to significance in the RMSSD (p=0.06).

B. Frequency-Domain Results

In the frequency-domain analysis, a power spectrum density (PSD) estimate is calculated for the RR time series. In this study, the HRV spectrum is calculated with FFT based Welch's periodogram method. As described by other investigators [21], we divided the power spectrum into three frequency bands: low frequency (LF, 0.01 to 0.05 HZ), medium frequency (MF, 0.05 to 0.15 HZ) and high frequency (HF, 0.15 to 0.5 HZ). The frequency-domain measures extracted from the PSD estimate for each frequency band include absolute total power (ms²) and relative powers of LF, MF, and HF bands, the LF/HF and MF/(LF+HF) power ratios. The band powers in relative units were obtained from the absolute values (e.g. relative LF power [%] = absolute LF power [ms²]/absolute total power [ms²] × 100%).

Power spectrum analysis results are summarized in Table II. Frequency domain analysis shows significant decreases in LF/HF ratio (0.95±0.60 in control group to 0.65±0.73 in experimental group, p<0.05) and relative LF power (28.16±11.75 to 17.15±7.61, p<0.01) and significant increases in relative MF power (34.99±15.74 to 41.92±15.03, p<0.05) and relative HF power (36.83±15.38 to 41.42±17.78, p<0.05).

TABLE II
FREQUENCY-DOMAIN VARIABLES OF SUBJECT WITHOUT AND DURING
HAND-HOLDING

VARIABLE	CONTROL GROUP	EXPERIMENTAL GROUP	P VALUE
Total power (ms ²)	2190.5±1696.9	2330.9±1780.5	0.53
LF power (%)	28.16±11.75	17.15±7.61	0.003**
MF power (%)	34.99±15.74	41.92±15.03	0.03*
HF power (%)	36.83±15.38	41.42±17.78	0.02*
LF / HF	0.95±0.60	0.65±0.73	0.02*
MF/(LF+HF)	0.65±0.53	0.85±0.70	0.07

Values are expressed as mean±SD. * p<0.05, ** p<0.01.

HF power: high-frequency relative power; MF power: medium-frequency relative power; LF power: low-frequency relative power. LF/HF: low/high frequency power.

C. Non-linear Results

According to the complex control systems of the heart, it is reasonable to suppose that nonlinear mechanisms are involved in the genesis of HRV [10]. The nonlinear properties of HRV have been analyzed using measures such as Poincaré plot, approximate and sample entropy, detrended fluctuation analysis and correlation dimension (Table III). Comparing non-linear results during hand holding with baseline, HRV parameters such as SD1 (29.16±13.26 to 32.48±13.49, p<0.05) and correlation dimension (2.76±1.33 to 3.33±1.13, p<0.01) increased and α_2 decreased significantly (0.83±0.15 to 0.71±0.14, p<0.05).

IV. DISCUSSION & CONCLUSION

The results show that HRV is changed by physical contact (hand-holding). The changes in HRV during hand-holding were detected both by linear and non-linear methods. Among the parameters, the linear variables, pNN50, HF, MF, LF and LF/HF and the non-linear variables SD1, SD1/SD2, α_2 and correlation dimension changed significantly and RMSSD changed close to significance, during this physical contact. Time-domain HRV variables such as SDNN reflects both sympathetic and parasympathetic activity, and RMSSD and pNN50 are determined by parasympathetic activity. So increase of RMSSD (41.10±18.71 in control group to 45.60±17.97 in experimental group, p=0.06) and pNN50 (20.14±19.33 to 27.65±18.85, p<0.05) during hand-holding show increase of parasympathetic activity.

With regard to frequency domain measures, the MF components (0.05-0.15 Hz) in HRV are mediated both sympathetically and parasympathetically and depend on baroreflex. The LF components (0.01-0.05 Hz) are mediated sympathetically and the HF (0.15-0.5 Hz) oscillations of HRV reflects vagal activity only. Our observation suggests that physical contact (hand-holding) caused parasympathetic activation and reduced sympathetic activation, as indicated by increased HF (36.83±15.38 to 41.42±17.78, p<0.05) and MF power (34.99±15.74 to 41.92±15.03, p<0.05) and by decreased LF/HF (0.95±0.60 to 0.65±0.73, p<0.05) and LF

TABLE III
NONLINEAR VARIABLES OF SUBJECT WITHOUT AND DURING HAND-HOLDING

VARIABLE	CONTROL GROUP	EXPERIMENTAL GROUP	P VALUE
ApEn	1.14±0.06	1.44±0.07	0.91
D2	2.76±1.33	3.33±1.13	0.006**
SD1 (ms)	29.16±13.26	32.48±13.49	0.04*
SD2 (ms)	67.17±21.43	65.91±17.67	0.53
Poincare (SD1/SD2)	0.42±0.9	0.48±0.14	0.02*
α_1	1.04±0.23	0.99±0.25	0.16
α_2	0.83±0.15	0.71±0.14	0.017*

Values are expressed as mean±SD. * p<0.05, ** p<0.01.

ApEn: Approximate entropy; D2: Correlation dimension; SD1, SD2: The standard deviation of the Poincaré plot perpendicular to (SD1) and along (SD2) the line-of-identity; α_1 : Short term fluctuation slope; α_2 : Long term fluctuation slope.

power (28.16±11.75 to 17.15±7.61, p<0.01). On the other hand, it has been shown in a number of the study that during mental or emotional stress, there is an increase in sympathetic activity and a decrease in parasympathetic activity and in contrast, positive emotions such as appreciation create increase in parasympathetic activation. Positive emotions change the sympathovagal balance which may be beneficial in the treatment diseases such as hypertension and reduce the likelihood of sudden death in patients with congestive heart failure and coronary artery disease [5]-[6]. The results of work in this area show a significant decrease in the LF/HF ratio and significant increases in LF power (p<0.01), HF power (p<0.01) and in the MF/LF+HF ratio (p<0.01) during positive emotions [5]-[8]. Hence, considering power spectral results and changes in power spectral bands, it seems that subjects (friends) had positive emotions during hand-holding.

Among the non-linear HRV properties, the Poincaré plot has been analyzed quantitatively by calculating the standard deviations of the distances of the RRI(i) to the lines $y = x$ and $y = -x + 2 \cdot \overline{RRI}$, where \overline{RRI} is the mean of all RRI(i). These standard deviations named as SD1 and SD2, respectively. SD1 is related to the fast beat-to-beat variability in the data (used as an indicator of vagal influence), while SD2 describes the longer-term variability of RRI (used as an indicator of sympathetic influence) and the ratio SD1/SD2 describe the relationship between these components [11]. Similar to frequency results, increase of SD1 (29.16±13.26 to 32.48±13.49, p<0.05) and SD1/SD2 (0.42±0.9 to 0.48±0.14, p<0.05), shows increase of parasympathetic activity during hand-holding. Also, compare nonlinear results of control and experimental groups show a significant increase in correlation dimension (2.76±1.33 to 3.33±1.13, p<0.01).

So in this study, we found that physical contact (hand holding) caused parasympathetic activation, as indicated by increased SD1, SD1/SD2, HF and MF power. These HRV changes that occur during skin-to-skin contact (hand holding) may because of heart signal transference from one person to another person. As we said, the electrical activity of the heart, cause an electrical current in the body (as a volume conductor)

and by the physical contact of two persons (contact of two volume conductors) this current can flow in the other's body and vice versa. This signal can change one person's HRV directly by changes her ECG signal or indirectly by affects her sympathetic and parasympathetic signals. Of course we should note that other factors also can play role in these HRV changes. For example as we said, emotions have principal role on the rhythm of the heart and it should be considered and it is possible that when two friends touch, temperature of their hands, and the other feelings or senses that exchange during a touch, influence these changes and many other factors that we don't have any information about them.

The experiments in this study represented an initial attempt to identify HRV changes during physical contact. In future experiments, increase of statistical population in different ages and sexes can give us better results. It is our hope that these data will encourage interested researchers to investigate the answers of many unanswered questions that have been raised by this work.

ACKNOWLEDGMENT

This work was done in the Biomedical Engineering Department, Azad University of Science & Research, Tehran, Iran.

REFERENCES

- [1] R. McCraty, M. Atkinson, D. Tomasino, W. Tiller, "The Electricity of Touch: Detection and measurement of cardiac energy exchange between people," In: K.H. Pribram, ed. *Brain and Values: Is a Biological Science of Values Possible*. Mahwah, NJ: Lawrence Erlbaum Associates, Publishers, 1998: 359-379.
- [2] R. McCraty, "The Energetic Heart: Bioelectromagnetic Communication Within and Between People," Chapter published in: *Clinical Applications of Bioelectromagnetic Medicine*, edited by Rosch P J and Markov M S. New York: Marcel Dekker: 541-562, 2004.
- [3] R. McCraty, "The Scientific Role of the Heart in Learning and Performance," *HeartMath Research Center, Institute of HeartMath*, Publication No. 02-030, Boulder Creek, CA, 2002.
- [4] J.I. Lacey and B.C. Lacey, "Two-way communication between the heart and the brain: Significance of time within the cardiac cycle," *American Psychologist*, February 1978; 99-113.
- [5] W.A. Tiller, R. McCraty, M. Atkinson, "Cardiac coherence: a new, noninvasive measure of autonomic nervous system order," *Alternative Therapies Health Med*, 1996; 2:52-65.
- [6] D. Childre, R. McCraty, M. Atkinson, "Method and Apparatus for Facilitating Physiological Coherence and Autonomic Balance," 2000. Available: <http://www.faq.s.org/patents/app/20090137915>.
- [7] R. McCraty, "Influence of Cardiac Afferent Input on Heart-Brain Synchronization and Cognitive Performance," *International Journal of Psychophysiology*, 45(1-2):72-73, 2002.
- [8] R. McCraty, M. Atkinson, W.A. Tiller, G. Rein, A.D. Watkins, "The effects of emotions on short term heart rate variability using power spectrum analysis," *American Journal of Cardiology*, 1995; 76:1089-1093.
- [9] J. Pan and W.J. Tompkins, "A Real-Time QRS Detection Algorithm," *IEEE Transactions On Biomedical Engineering*, VOL. BME-32, NO. 3, March 1985.
- [10] Mika P. Tarvainen and Juha-Pekka Niskanen. User's Guide of Kubios HRV version 2.0. Biosignal Analysis and Medical Imaging Group (BSAMIG). 2008. Available: <http://kubios.uku.fi>.
- [11] S.L. Marple, "Digital Spectral Analysis," *Prentice-Hall International*, 1987.
- [12] M. Brennan, M. Palaniswami, and P. Kamen, "Do existing measures of Poincaré plot geometry reflect nonlinear features of heart rate variability," *IEEE Trans Biomed Eng*, 48(11):1342-1347, November 2001.
- [13] S. Carrasco, M.J. Cait'an, R. Gonz'alez, and O. Y'anez, "Correlation among Poincaré plot indexes and time and frequency domain measures of heart rate variability," *J Med Eng Technol*, 25(6):240-248, November/December 2001.
- [14] J.A. Richman, and J.R. Moorman, "Physiological time-series analysis using approximate entropy and sample entropy," *Am J Physiol*, 278:H2039-H2049, 2000.
- [15] Y. Fusheng, H. Bo, and T. Qingyu, "Approximate entropy and its application in biosignal analysis," In M. Akay, editor, *Nonlinear Biomedical Signal Processing: Dynamic Analysis and Modeling*, volume II, chapter 3, pages 72-91. *IEEE Press*, New York, 2001.
- [16] B. Henry, N. Lovell, and F. Camacho, "Nonlinear dynamics time series analysis," In M. Akay, editor, *Nonlinear Biomedical Signal Processing: Dynamic Analysis and Modeling*, volume II, chapter 1, pages 1-39. *IEEE Press*, New York, 2001.
- [17] C.-K. Peng, S. Havlin, H.E. Stanley, and A.L. Goldberger, "Quantification of scaling exponents and crossover phenomena in nonstationary heartbeat time series," *Chaos*, 5:82-87, 1995.
- [18] T. Penzel, J.W. Kantelhardt, L. Grote, J.-H. Peter, and A. Bunde, "Comparison of detrended fluctuation analysis and spectral analysis for heart rate variability in sleep and sleep apnea," *IEEE Trans Biomed Eng*, 50(10):1143-1151, October 2003.
- [19] M.P. Tulppo, T.H. Mäkilä, T.E.S. Takala, T. Seppänen, H.V. Huikuri, "Quantitative beat-to-beat analysis of heart rate dynamics during exercise," *Am. J. Physiol*, vol. 271, pp. H244-H252, 1996.
- [20] N. Jafarizadeh-Dabab, D.C. McLernon, H. Zhang, A. Ayatollahi, V. Johari-Majd, "A modified Zeeman model for producing HRV signals and its application to ECG signal generation," *Elsevier Ltd*, 2006.
- [21] S. Akselrod, D. Gordon, F.A. Ubel, D.C. Shannon, A.C. Barger, R.J. Conen, "Power spectrum analysis of heart rate fluctuation: a quantitative probe of beat-to-beat cardiovascular control," *Science*, 1981, 213:220-222.