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A PDA Based Recording System To Investgate Heart Rate

Marcos Efren Bolanos
University of Texas at El Paso, mbolanos@miners.utep.edu

A PDA BASED RECORDING SYSTEM TO INVESTGATE HEART RATE VARIABILITY SIGNAL CHARACTERISTICS AND BLOOD GLUCOSE LEVELS IN HEALTHY AND TYPE 1 DIABETIC INDIVIDUALS

By

MARCOS EFREN BOLAÑOS

Department of Electrical and Computer Engineering

APPROVED:

Homer Nazeran, Ph.D., Chair

Gregory Lush, Ph.D.

Emily Haltiwanger, OTD, MHE, OTR

Pablo Arenaz, Ph.D.
Dean of the Graduate School

Dedication

I would like to dedicate this thesis to my parents Ofelia and Arturo Bolaños who throughout my entire academic career have given me all their love and encouragement and continue to cheer me on as I move onward to getting my Ph.D. I hope to forever make you proud in whatever I do in life. I love you and thank you for helping me get to this point in my life. I'm blessed by the Lord to have such incredible parents.

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MARCOS EFREN BOLAÑOS, B.S.

THESIS

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Abstract

Diabetes is one of most afflicting diseases in society which is caused by the inability of the body to appropriately use insulin to balance sugar levels. Type 1 diabetics require monitoring of their glucose levels to ensure a normal glucose level is maintained between 90 and 130 mg/dL (milligrams per deciliter). Unfortunately, current methods of monitoring are based on invasive and painful sampling of the blood. It was imperative that noninvasive and painless methods of monitoring glucose should be explored. A proven noninvasive technique utilizing infrared light to detect the fluctuations in the heart rate was used to determine if levels of glucose could be accurately determined within regions of safety. The optical absorption properties of blood were used to obtain photoplethysmographic (PPG) data and processed to gather information about the subject's heart rate variations (HRV). The system developed for this study consisted of simultaneously recorded ECG, PPG, and temperature. The data were analyzed on the PDA or through the use of a desktop computer with a custom HRV analysis program written in LabView. Glucose levels were simultaneously measured using a portable glucose monitor. This research study consisted of three primary goals: confirm the reliability of the developed HRV system, determine if HRV data collected from ten subjects without diabetes would correlate to their glucose levels, and finally to determine if HRV data collected from six subjects diagnosed with Type 1 diabetes could be correlated to their glucose levels. The ultimate focus was to develop a complete portable system that could reliably detect changing glucose levels in a non invasive manner. A noninvasive and portable glucose monitor would greatly enhance the lives of diabetics.

The normal blood sugar range of the ten non-diabetic subjects was 70 mg/dL –150 mg/dL. These were the expected values for normal individuals with no history of diabetes or

other glycemic ailments. After evaluating the population means and standard deviations, it was concluded that there were very little variations (coefficients of variation less than 7%) in the maximum, mode, minimum, median, average, and approximate entropy when compared to the rest of the HRV parameters

Side by side box plots of mean, mode, and median reveal that within five of six subjects with diabetes, the normal and hyperglycemic ranges can be clearly distinguishable. Assuming normality, student t-tests reject the null hypothesis of equal means with 95% confidence with a p value < 0.005. Assuming non normality, Mann-Whitney tests reject the null hypothesis of equal means with 95% confidence with very small p values. Side by side box plots of RMSSD, NN50, and SD1 reveal that within two of six diabetics normal and hypoglycemic ranges can be clearly distinguishable. Assuming normality, student t-tests reject the null hypothesis of equal means with 95% confidence with a p value < 0.01. Assuming non normality, Mann-Whitney tests reject the null hypothesis of equal means with 95% confidence with a p value <0.007

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Chapter 1 : Introduction

Diabetes is a disease that changes the daily lifestyle of millions of people everyday including 20.8 million children and adults in the United States[1]. In El Paso, Texas, where this research was performed, 85,000 individuals suffer from the disease[2]. Sufferers of diabetes are constantly at risk unless they monitor their glucose and gather important information that would allow them to make proper judgments on how to maintain a healthy balance of sugar in their body. Individuals with diabetes must be careful as to not become hyperglycemic (sugar levels above 130mg/dL in the blood) and especially more careful not to become hypoglycemic (sugar levels below 70 mg/dL in the blood) otherwise they risk slipping into an insulin coma, risking brain damage, and dying[3]. To prevent such drastic events from occurring, people with diabetes must check their glucose levels and determine whether more sugar intake or an insulin shot is required in order to sustain the balance between 70 and 130 mg/dL.

Glucose reflectance meters are commonly used to check glucose levels. This method involves placing a drop of blood on a test strip to obtain a reading of mg/dL of blood sugar. This method is invasive and painful by taking a sample of blood from the tip or lateral side of the finger using a device that tests the blood. A more sophisticated method used primarily by physicians to ascertain the patterns seen in the blood sugar levels, is a continuous and invasive monitor that is inserted into the subject's abdomen for twenty-four to seventy-two hours. The methods are effective in informing the user in what degree of safety their glucose levels are presently at. Two companies that develop these devices are Medtronic MiniMed and Dexcom. MiniMed developed the CGMS Gold[4] and the Guardian RT[5]. Dexcom developed the Dexcom STS[6]. Also, an advanced monitor by MiniMed known as the Paradigm real-time insulin pump and continuous glucose monitor[7], is the only one of its kind to integrate continuous glucose

monitoring with an insulin pump that assists subjects with diabetes. The devices are all FDA approved and provide records of fluctuating glucose levels in subjects with diabetes.

Glucose monitoring devices remain a financial burden for individuals require monitoring of their glucose levels as part of their daily routine. Many individual with diabetes need to test their glucose levels four to eight times a day, which can result in tremendous costs in supplies and most importantly sore finger tips from the constant pricking. Another tool available in the market known as the GlucoWatch claims to monitor glucose levels non-invasively but lacks in accuracy and dependability[8]. A new and innovative noninvasive and portable glucose monitor would greatly enhance the lives of diabetic sufferers by providing an alternative tool that could compete against the competition and reduce costs in glucose management. Therefore, pain, improvement of accuracy, and reduction of cost are the main issues that this research would address.by using present technology in an innovative way.

Previous research articles have indicated that there may be a relationship between heart rate variability and glucose levels in the blood. A study of abnormal cardiovascular autonomic functions lead to an observation that glycemia was inversely related to the spectral components of HRV[9]. It was also observed that the ratio of the low frequency (LF) and high frequency (HF) components reduced significantly in those with diabetes compared to those without. Another study of cardiovascular autonomic function demonstrated HRV decreased significantly in those with diabetes compared to those without [10]. However, HRV parameters in diabetes sufferers did not have significant differences from each other. A recent study revealed that LF and LF/HF parameters were lower in individuals with abnormal fasting glucose levels (hypoglycemia) than individuals with normal fasting glucose levels[11]. Various parameters of HRV would be analyzed to determine if correlations with glucose levels exist.

The ultimate method of acquiring HRV information would use the infrared absorption properties of blood cells[12] in a finger to obtain photoplethysmographic (PPG) signals. The pulse signals can be used to derive the heart rate variation data of the subject. With simultaneous recordings of PPG and glucose levels of a subject, a correlation between HRV and glucose may be derived and incorporated into a final algorithm. The entire data acquisition and analysis system would ultimately take the form of a light and portable device so that it may be carried in pockets and purses, or even be wearable. The system would be easy to use and allow those with diabetes to determine the range of their glucose levels. With the hopeful discovery of a direct correlation between glucose and HRV, the system could be designed to suit the needs of the user. In a possible design, safe glucose levels could be indicated by a green light, cautionary levels could be indicated by a yellow light and faint warning sound, and dangerously low or high glucose levels could be indicated by a red light and a loud audible alarm.

This research study consisted of five primary goals: develop a PDA acquisition system that records electrocardiogram (ECG), PPG, and temperature data in real time, develop original programming for the acquisition and analysis of HRV information, determine if PPG and ECG resulted in similar HRV information, determine if HRV data collected from individuals without diabetes would correlate to their glucose levels, and finally to determine if HRV data collected from those diagnosed with Type 1 diabetes could be correlated to their glucose levels. The objective of the research was to develop a complete portable system that could reliably detect changing glucose levels in a non invasive manner.

Through this research, the objectives accomplished have been the development of a complete HRV acquisition and analysis system that allows the user to easily record biosignals, convert them to HRV, and analyze the HRV on the PDA and PC. It has successfully been shown

that ECG and PPG can be used to derive similar HRV information in healthy individuals. Variances of twenty-five HRV parameters have been documented for subjects with and without diabetes thus providing a reference to what range of values are expected when testing each population. Lastly, statistical analysis has proven that normal glucose levels are significantly different from hyperglycemic levels in people with diabetes when mean, mode, and median values of HRV are analyzed. It has also been shown that normal glucose levels are significantly different from hypoglycemic levels in individual with diabetes when RMSSD, NN50, and SD1 values of HRV are analyzed. However, this research could not conclude if HRV parameters during hypo and hyperglycemic levels could be distinguished.

Chapter 2 : Background

The exploration of how heart rate variations could be correlated to glucose levels in blood requires the incorporation of various tools. These tools include biological signals, software packages, computer hardware, and medical measuring devices. An understanding of how these tools worked was crucial to the research objective.

2.1 Photoplethysmography

Photoplethysmography (PPG) is the acquisition of pulse signals that correspond to the fluctuating blood volume in the arteries due to the pumping of the heart. It is performed by assembling an infrared emitter and detector inside a probe placed on the forefinger or earlobe. The probe maintains a constant pressure against the finger or earlobe. The infrared light is emitted through the blood vessels in the finger or earlobe and reflected off the bone. The amount of light reflected back to the detector is determined by the amount of blood flowing to the tissue at any given time and converted into a voltage signal. A high volume of blood results in a high voltage and a low volume results in a low voltage (Figure 2-1).

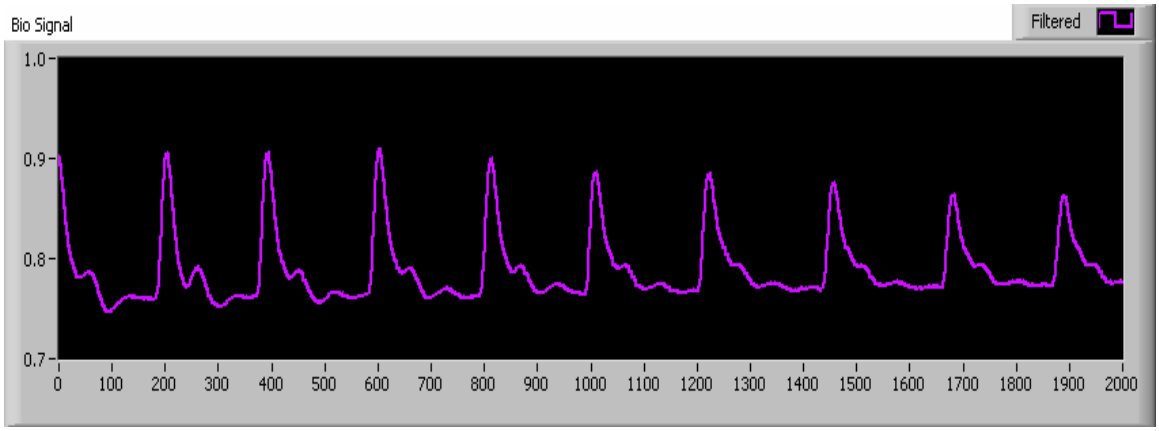

Figure 2-1: Photoplethysmographic Signal

The change in blood volume is directly related to the amount of blood pumped into the aortic valve after ventricular depolarization. This causes fluctuating blood volumes in the arteries which consequently cause the voltage output of the transducer to fluctuate in magnitude. This fluctuating magnitude is the electrical equivalent to the physical pulsating sensation felt when a person presses their fingers up against an artery. The maximum peaks of these signals are called dichrotic peaks.

2.2 Electrocardiography

The electrocardiogram (ECG) is a representation of the electrical activity of the heart. The method of acquisition is noninvasive and is the common method of acquiring HRV data. Its prominent QRS complex makes it ideal for peak detection algorithms to determine occurrences of each heart beat. The QRS complex is the result of the depolarization of the ventricles. ECG signals are acquired by placing Ag/AgCl (silver/silver chloride) electrodes on clearly defined anatomical positions. One lead (channel) of ECG recording requires three electrodes to produce the signal (Figure 2-2) thus requiring three wires to be connected to the subject.

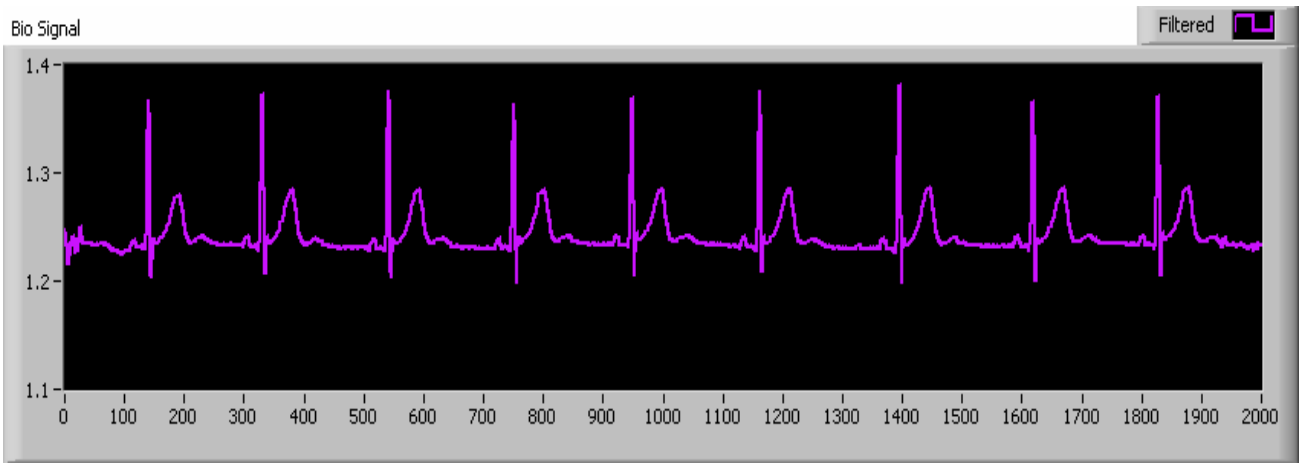

Figure 2-2: Electrocardiogram Signal

2.3 Heart Rate Variations

Heart rate variation is the beat to beat changes in the heart rate and is a reflection of sympathetic and parasympathetic activity in the autonomic nervous system. The parasympathetic nervous system is responsible for slowing down the heart rate, lowering blood pressure, decreasing insulin production in the pancreas, and slowing down the conversion of glycogen into glucose within the liver. The sympathetic nervous system performs the opposite by increasing the heart rate, increasing blood pressure, increasing insulin production, and increasing glycogen to glucose conversion. The organs affected by the autonomic nervous system (Figure 2-3) perform their duties depending which activity is more dominant at a certain point in time: parasympathetic or sympathetic activity[13].

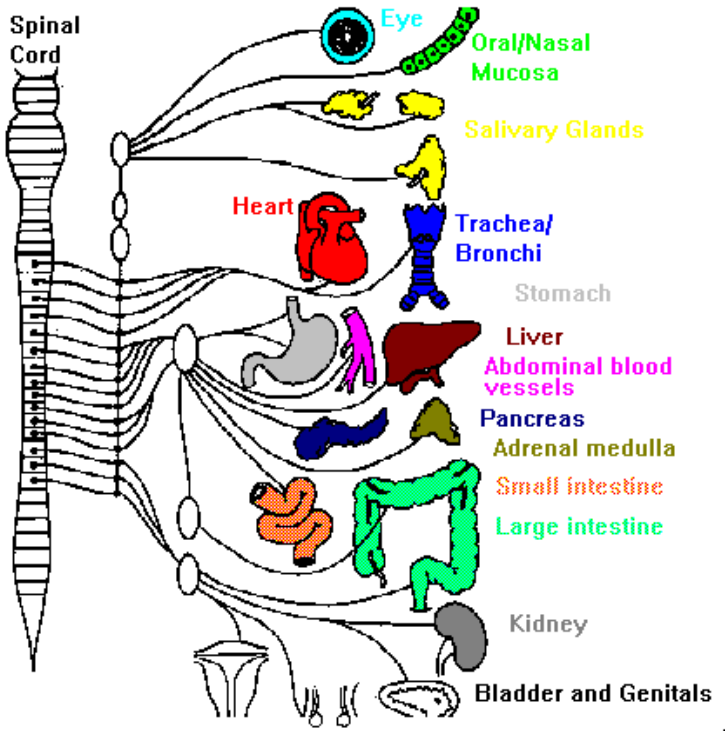

Figure 2-3: Autonomic Nervous System

Courtesy of www.montana.edu/wwwai/imsd/rezmeth/anatomy.htm

HRV data is collected (five minute minimum recordings) [14] by analyzing the changing heart rate and determining the time difference between each heart beat. If the HRV was derived by analyzing electrocardiogram signals, the time differences between each successive beat are referred to as RR intervals because of the R peaks detected in the signal. If the HRV was derived by analyzing photoplethysmographic signals, the time differences between each successive beat are referred to as DD intervals because of the dichrotic peaks detected in the signal. A typical HRV tachogram (Figure 2-4) of a normal individual has much variation and data points that look random.

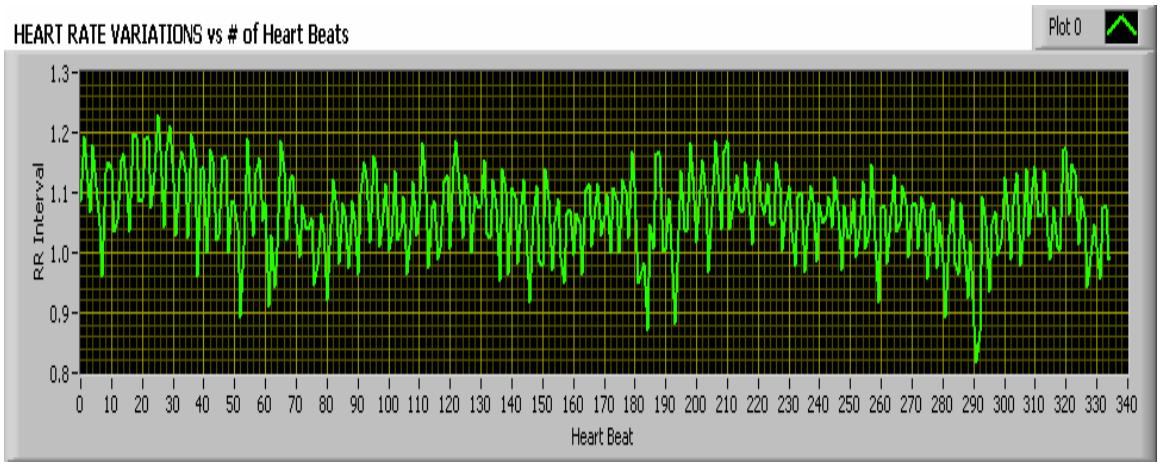

Figure 2-4: Heart Rate Variation signal

The power spectral density of the same tachogram (Figure 2-5) is a visual tool for determining the dominant activity within the autonomic nervous system. The power spectrum of the short term recorded HRV signal can be divided into three frequency bands. The very low frequency (0-0.04 Hz), low frequency (0.04 -0.15 Hz), and high frequency (0.15 – 0.4 Hz) components make up the power spectrum of the HRV signal. The peak to the left represents the power and dominance level of parasympathetic activity (low frequency) and the peak to the right represents the power and dominance level of sympathetic activity (high frequency).

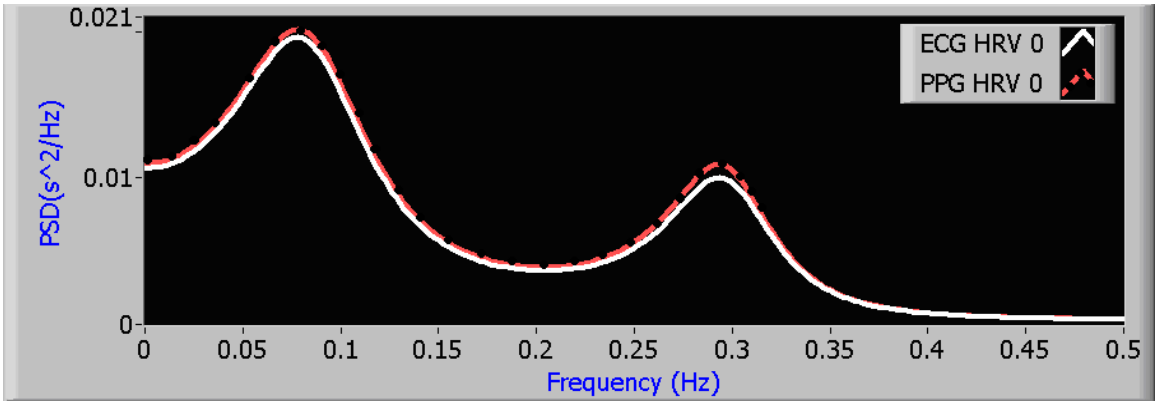

Figure 2-5: HRV power spectrum (AR)

2.4 Glucose Monitoring and Care

In order to control diabetes, sufferers of the disease must maintain constant glucose management and maintenance. Judgments on when to eat, how much insulin to inject, and how much exercise to perform are based on how often the individual tests his or her sugar. People with diabetes need to follow a strict regimen in order to properly manage their glucose. Immediate information about their current glucose levels is required to adhere to their regimen. Glucose monitors are extremely useful in testing for glucose levels during the day and give immediate results after variables such as food intake and exercise change. The downfall to these devices is their invasive methods of operation. The research utilized two types of glucose monitors that had invasive properties. One form of glucose monitoring requires the lancing of the finger in order to obtain a drop of blood. The finger is the preferable location of lancing because changing sugar levels in the blood are more quickly detected in that area than in the arm, for example, where the pain would be minimal because there are fewer nerve endings. Once the finger is pricked with the lancet, the small blood drop (< 4micro liters) is placed onto a glucose strip that is inserted into the glucose monitor. Within five seconds, a glucose reading is displayed on the monitor and the user may take the necessary actions based on the indicated levels. This is

a painful procedure that must be repeated many times a day for the rest of one's life. The typical glucose monitor used in this study was the OneTouch Ultra. Its 95% accuracy in providing glucose measurements during hypoglycemic, normal, and hyperglycemic levels in individuals with Type 1 diabetes made the One Touch Ultra favorable for the research project[15].

The second device used for this research was the MiniMed CGMS Gold system which was mentioned earlier. It is one of four available continuous glucose monitors that was chosen because of its distinctive characteristics that set it apart from the others. The MiniMed GGMS Gold was used because it prevented the wearer of the device from viewing the glucose readings, unlike the Guardian RT, thus preventing any interference in the experiment by the subject. Also, it allowed the recording of a twenty-four hour trend of glucose unlike the Dexcom STS which allowed up to nine hours[16].

Sugar levels are measured in units of milligrams per deciliter (mg/dL). According to the American Diabetes Association, a normal random blood sugar sample will range between 70 to 125 mg/dL. Anything greater than 125 mg/dL indicates hyperglycemia and anything less that 70 mg/dL indicates hypoglycemia.

2.5 LabVIEW Programming Language

The programming language used for all data acquisition and signal processing was the National Instruments LabVIEW graphical language. LabVIEW is a language specially developed for engineers. It is very flexible and simple to use for many data acquisition applications. It is compatible with all NI data acquisition cards which include the CF-6004 which is the data acquisition card used in PDAs. LabVIEW also possesses the signal processing tools required for the project. LabVIEW is a unique programming language simply because it uses graphical representations of commands and lines of code rather than traditional written programming as in

JAVA or C++. Overall, LabVIEW is very flexible and widely versed through its use in both PDA and desktop formats and especially desirable for its real-time capabilities.

Chapter 3 : HRV System Development

3.1 ECG, PPG, & Temperature Acquisition

3.1.1 ECG circuit

The first part of the data acquisition part of the research projects requires the construction of a circuit that acquires electrocardiographic and photoplethysmographic data. ECG signals were acquired through a custom-built low power consumption ECG amplifier. The input to this circuit was provided by three 10-inch long subject wires (packaged inside a subject cable). The subject cable was low-noise, well-shielded, and equipped with snap-on connectors. These wires were connected to disposable Ag/AgCl snap-on skin electrodes. The ECG amplifier was constructed with a gain of 1000, a CMRR of 80dB and a frequency bandwidth of 0.05-100 Hz. The amplifier was first tested by using a Subject Simulator (PS-420, Metron), which was connected to its inputs. The overall performance of the amplifier was then tested acquiring ECG signals from volunteer subjects. These signals were both amplified and filtered to the required specifications. The output waveform from the ECG amplifier was then fed to the rest of the system. Figure 3-1 is the basic block diagram of the ECG circuit and Figure 3-5 is the schematic of the device.

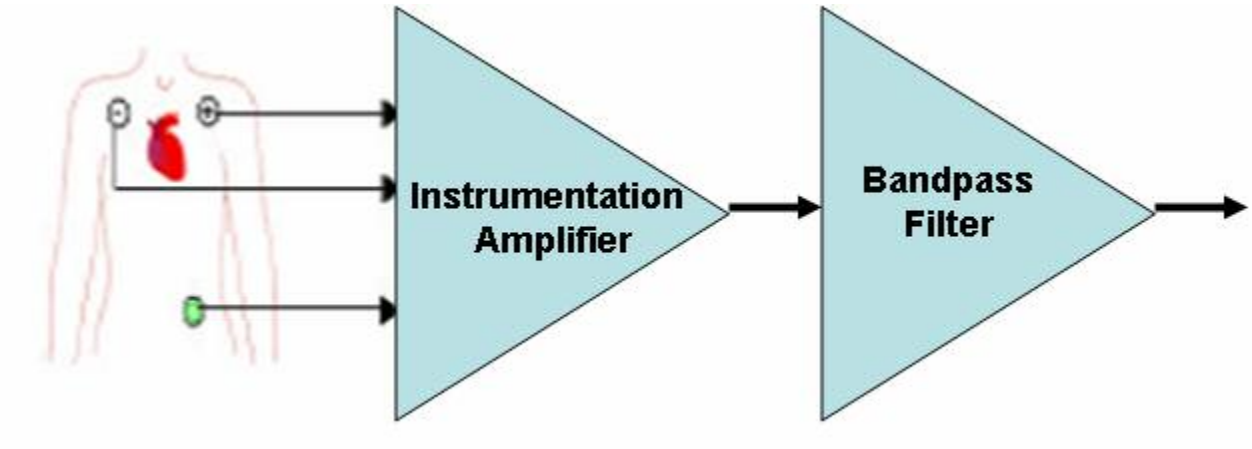

Figure 3-1: Electrocardiogram circuit block diagram

3.1.2 PPG circuit

Blood pressure waveforms were acquired by using the photoplethysmographic method. Photplethysmography is utilization of the reflective and absorbent properties of blood when excited with infrared (IR) light. Blood within the artery of a finger is oxygenated and absorbs infrared light. As the blood pressure within the artery changes, the volume of blood changes and more infrared light is reflected back by the bone in the finger when there is less blood and less light is returned when there is more blood flowing. An optocoupler was utilized to detect the changes in the infrared light reflected back from the finger as a result of blood flow. The optocoupler converted the variations in infrared light into a voltage signal. This light signal was then processed by a band pass filter to reduce noise and remove unwanted DC voltages. The optocoupler provided a high voltage level when there was less blood flowing in the finger. To determine the maximum output voltage corresponding to high blood flow, the light signal was inverted within the bandpass filter. The light sensor in the photoplethysmograph was placed in a protective casing and connected to the rest of the circuit by a three foot long cord. The encasing provided a firm and stable contact between the finger and sensor to prevent stray ambient light

from interfering with the output signal, and to prevent any distortion due to movement of the finger. Figure 3-2 is the block diagram of the PPG circuit and Figure 3-3 is the circuit schematic of the device. The finger probe used in the circuit can be seen in Figure 3-5.

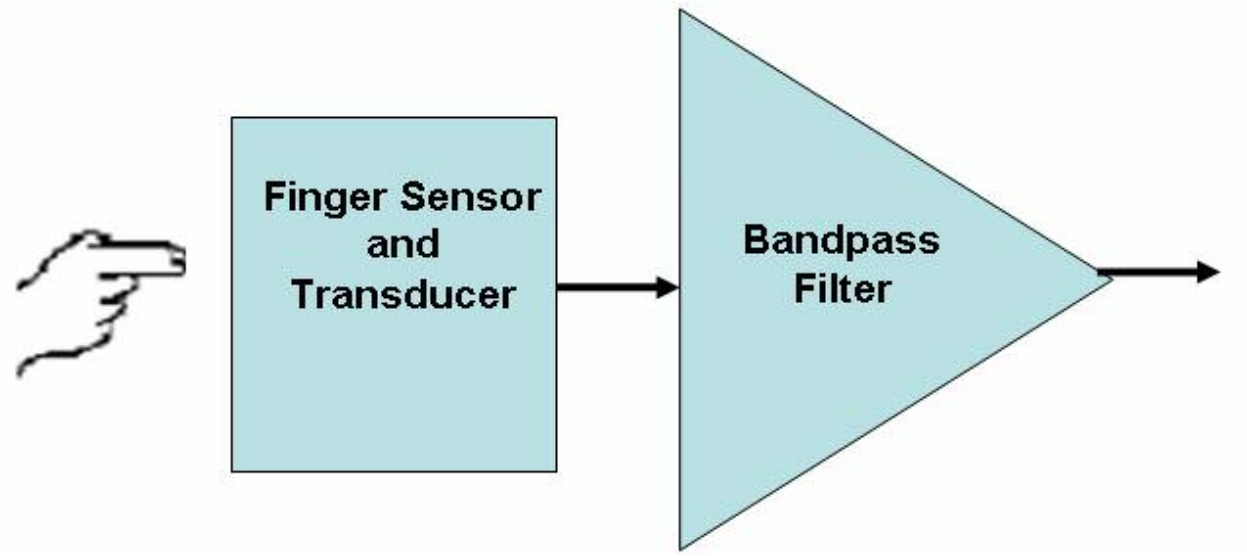

Figure 3-2: Photoplethysmograph circuit block diagram

Figure 3-3: Photoplethysmograph finger probe

3.1.3 Temperature circuit

The temperature sensor was developed through the implementation of the LM 35 temperature transducer (Figure 3-4). The device measures surface and ambient temperature in Celsius. The output of the sensor is sent to the DAQ device.

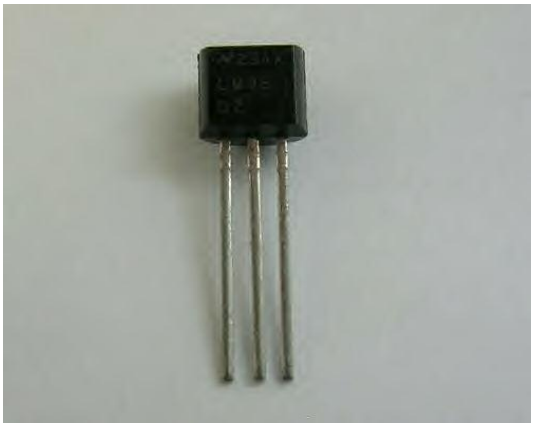

Figure 3-4: LM35 temperature transducer

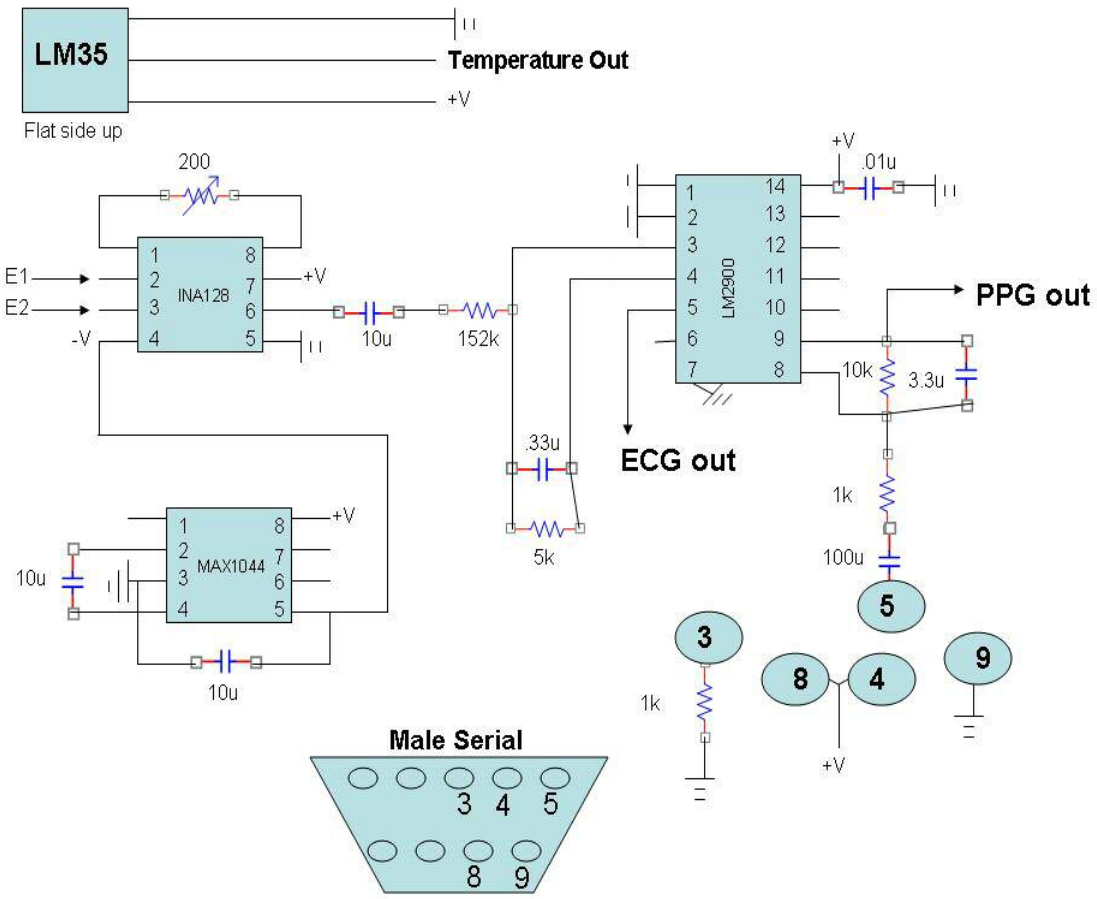

Figure 3-5: ECG, PPG, and temperature signal acquisition schematic

3.1.4 LabVIEW data acquisition program for the PDA

The program written to perform the signal acquisition and recording can be seen on Appendix B.2. Figure 3-6 is the front panel view on the PDA display where the three signals can be viewed as they are recorded. The front panel consists of various user controls: (1) an input for number of samples to be recorded, (2)duration of recording in minutes, (3)start/stop/exit recording controls, (4)the desired file storing location, (5)the command for multiple inputs, and (6)the display screen where the three signals can be viewed and zoomed in on. The user simply presses the start button and a pop up screen asks where to store the data in the PDA memory. At

any time the user can stop the recording process and begin all over again, otherwise the recording will end based on the desired recording duration. Once the data are collected, the user can exit the program and move onto the next recording, subject, analyze the data on the PDA, or upload data to the desktop.

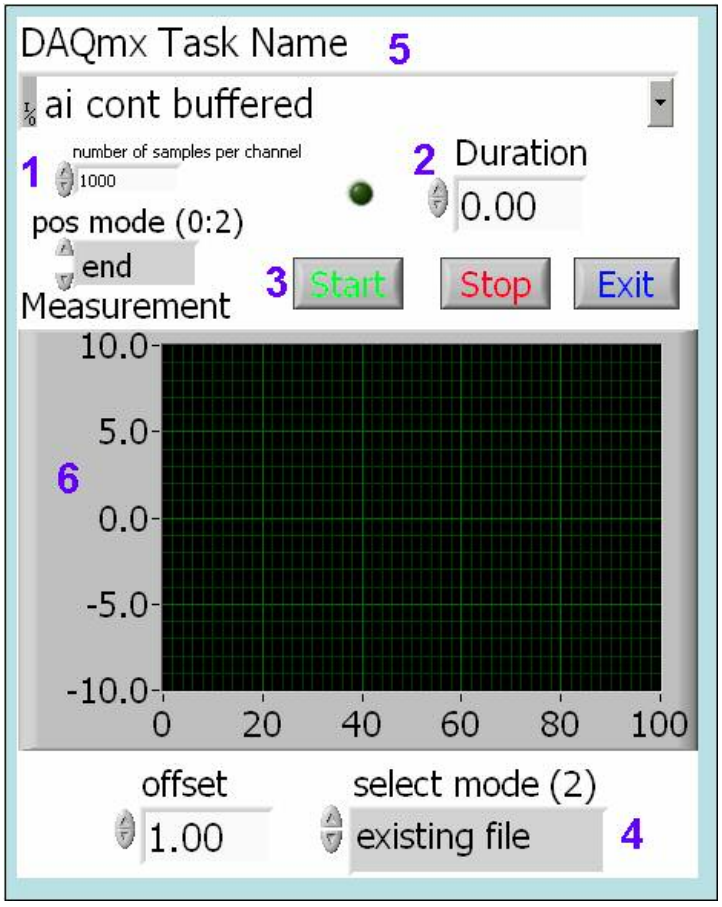

Figure 3-6: PDA front panel signal recording display

3.1.5 PDA and DAQ card interface

A personal digital assistant was used for the design of the HRV acquisition/analysis system because of its advanced computing capabilities contained in a light and portable package. The PDA used in the project was the DELL Axim X50v(Figure 3-7). It was the fastest PDA on

market with a processor speed of 624 MHz and a compact flash II expansion slot. It operates on Windows Pocket PC which allows more functions to be implemented with LabVIEW.

Figure 3-7: Dell PDA used for data acquisition

The signals are interfaced to the PDA through the use of a data acquisition card (DAQ).The DAQ card used was the CF-6004 (Figure 3-8) which takes the form of a compact flash card and compatible with any compact flash II slot. The DAQ card allowed simultaneously sampling of all three signal inputs. The DAQ allows up to 4 inputs at a total sampling rate of 18kS/s. This rate of sampling is more than adequate for the continuous monitoring of ECG and PPG signals.

Figure 3-8: PDA data acquisition card

3.2 HRV Derivation and Analysis in a Pocket PC environment

There are two methods of converting ECG and/or PPG data into HRV information. Both methods implement complex peak detection algorithms in order to detect the prominent peaks in the biosignals. The first method of HRV derivation exists in a Pocket PC environment which allows the user the ability to make their data acquisition and analysis portable. Figure 3-9 is the graphical user interface (GUI) seen on the PDA screen.

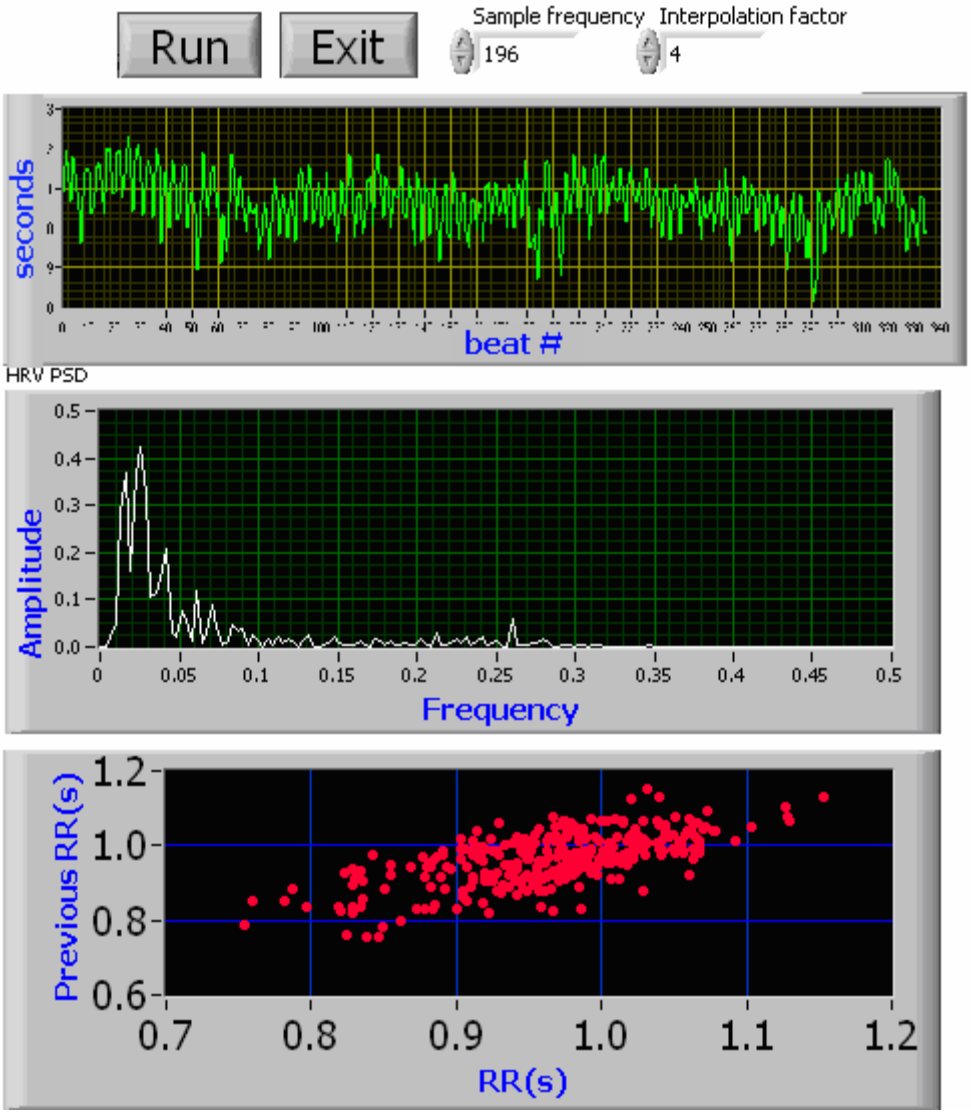

Figure 3-9: Pocket PC HRV Analysis Graphical User Interface

3.2.1 Data Reconstruction

The data was written into text files and separated into groups of data clusters after it was recorded. For example, if 1000 samples were generated per channel, a header was placed in the text files every 1000 data points. The reconstruction part of the program (Figure 3-10), was able

to open the desired signal text file, remove every header in the file, convert the string into an array, and output an entire recording of the biosignal.

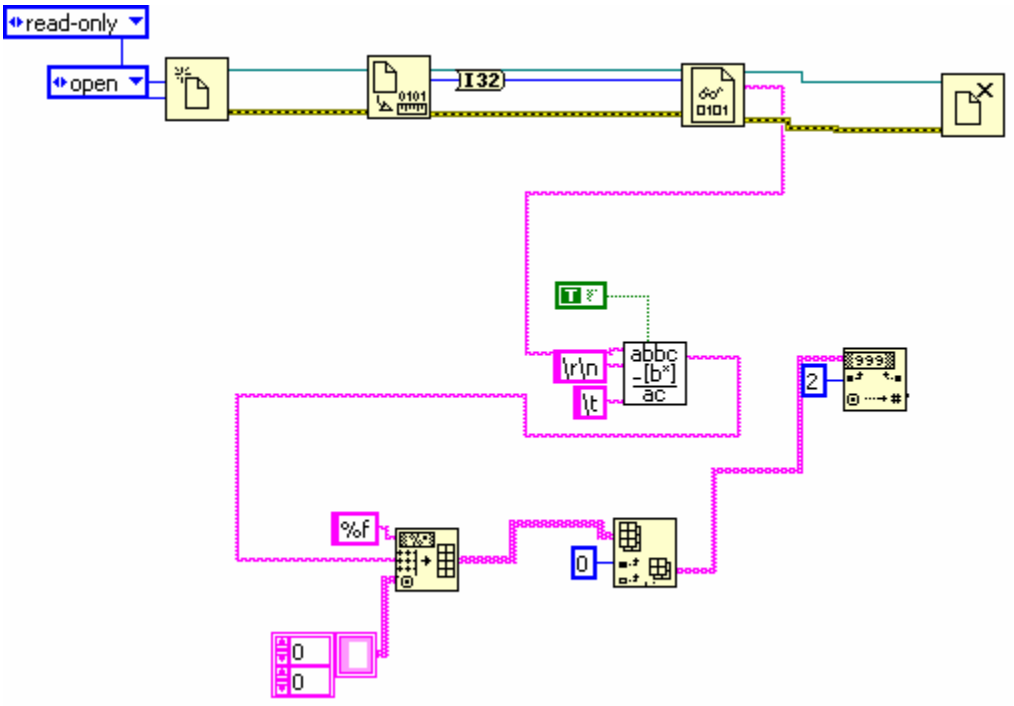

Figure 3-10: PDA Data reconstruction programming

3.2.2 Peak Detection Algorithm

The important part of the HRV derivation process is the detection of the individual peaks in the signal. A peak detection algorithm was used to detect all the major peaks (e.g. QRS complexes), determine their locations (sample in the array), convert the location into seconds, and send the converted locations into an array. Since the time values of the signals were in samples, they were easily converted into seconds by indicating the sampling rate (197 S/s) used to acquire the data in the first place. Figure 3-11 is the programming used to perform the peak detection.

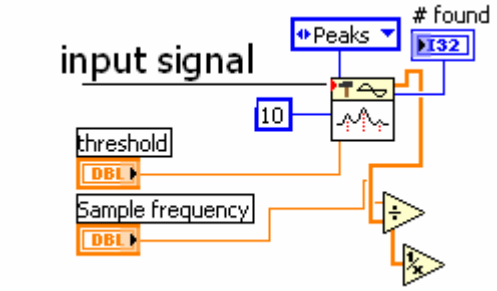

Figure 3-11: PDA biosignal peak detection algorithm

3.2.3 HRV tachogram

The time locations of every major peak in the signals were stored into an array. They were then subtracted from the proceeding time location in order to obtain the time differences. These would be the RR or DD intervals. The RR (DD) time differences were sent and stored into another array. The complete array is the final HRV data set. Figure 3-12 is the programming to obtain the HRV tachogram.

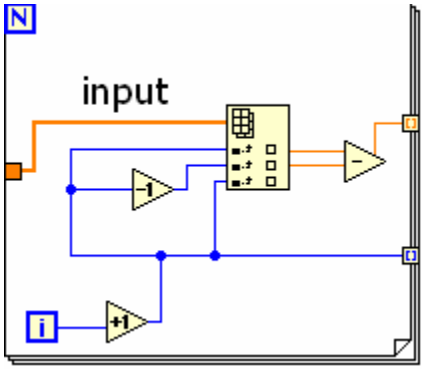

Figure 3-12: PDA HRV tachogram generator

3.2.4 Interpolation

Once the HRV tachogram is created, the HRV data need to be interpolated for purposes of frequency domain analysis. HRV sets are unevenly sampled and therefore require

interpolation. The original time series, however, can be analyzed in the time domain. The recommended value for interpolation is a factor of four which would determine four values between each RR interval. This value can be modified via the GUI if a lower or higher interpolation factor is desired. Figure 3-13 shows the programming written to perform the interpolation.

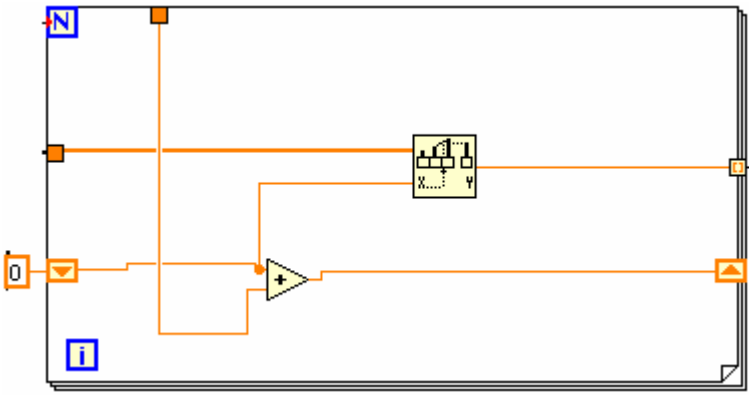

Figure 3-13: PDA HRV interpolation algorithm

3.2.5 FFT Power Spectral Density

The Fast Fourier Transform could be used to determine the spectral density of the HRV data set after it is resampled evenly. The HRV array was inputted into the FFT power spectral density function.

$$P_{FFT}(f) = \sum_{k=0}^{N-1} a_k e^{-j2\pi fk\Delta t}$$

The function used can be seen in Figure 3-14.

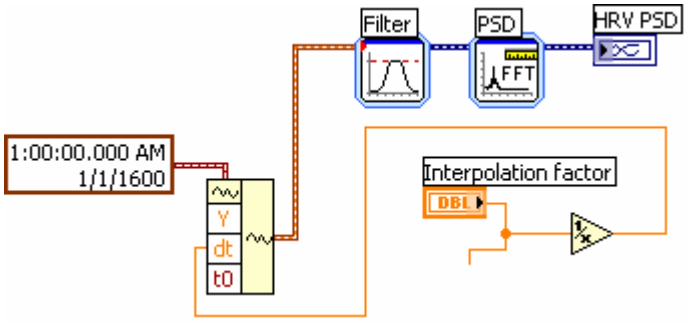

Figure 3-14: PDA Power Spectral Density algorithm

3.2.6 Poincare' Plot

Poincare' plots are useful in monitoring the non linear properties of HRV and determining if the data sets are trustworthy. They use the human ability to visually identify patterns in the data[17]. Poincare' plots plot the HRV data points against their previous data points (e.g. RR_n vs RR_{n-1}). A valuable datum set will have data points clustered together in one region of the Poincare' plot. The programming written to derive the Poincare' plots can be seen in figure 3-15.

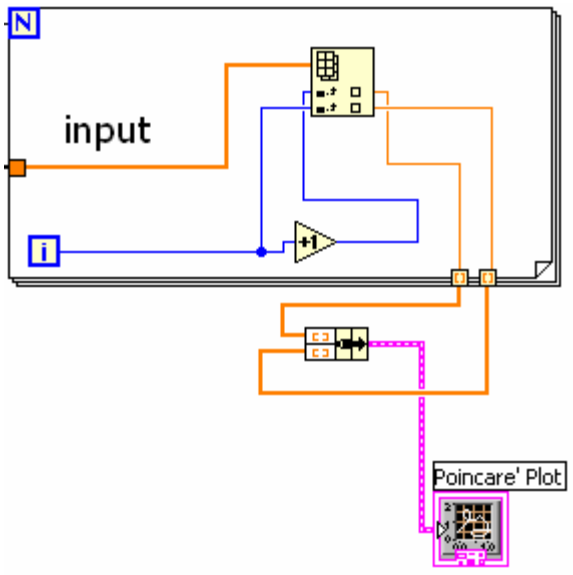

Figure 3-15: PDA HRV Poincare' plot generator

3.3 HRV Derivation in a PC environment

The second alternative to converting ECG or PPG data into HRV information is through a customized conversion program developed for a PC environment. A PC environment is much faster and allows the implementation of algorithms that provide more accurate conversions. The choice between using either the PC program or the Pocket PC program is left to the user's preferences.

3.3.1 Recorded ECG & PPG data upload

The first part of the HRV derivation process was to upload the ECG and PPG data acquired through the PDA. The PDA was interfaced to the desktop computer through its USB cradle and Microsoft ActiveSync (Figure 3-16). The individual files containing the data were transferred to the desktop for analysis in the HRV program.

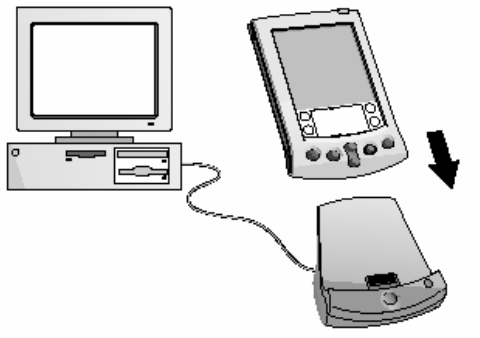

Figure 3-16: Interface between PDA and Desktop

3.3.2 Data Reconstruction

When originally recorded, the data was stored into text files and separated into groups of data clusters. For example, if 1000 samples were generated per channel, a header was placed in the text files every 1000 data points. The reconstruction part of the program (seen below), was able to open the desired signal text file, remove every header in the file, convert the string into an array, and output an entire recording of the biosignal. Figure 3-17 shows the programming implemented to reconstruct the data. Figure 3-18 and Figure 3-19 are the resulting ECG and PPG signal respectively.

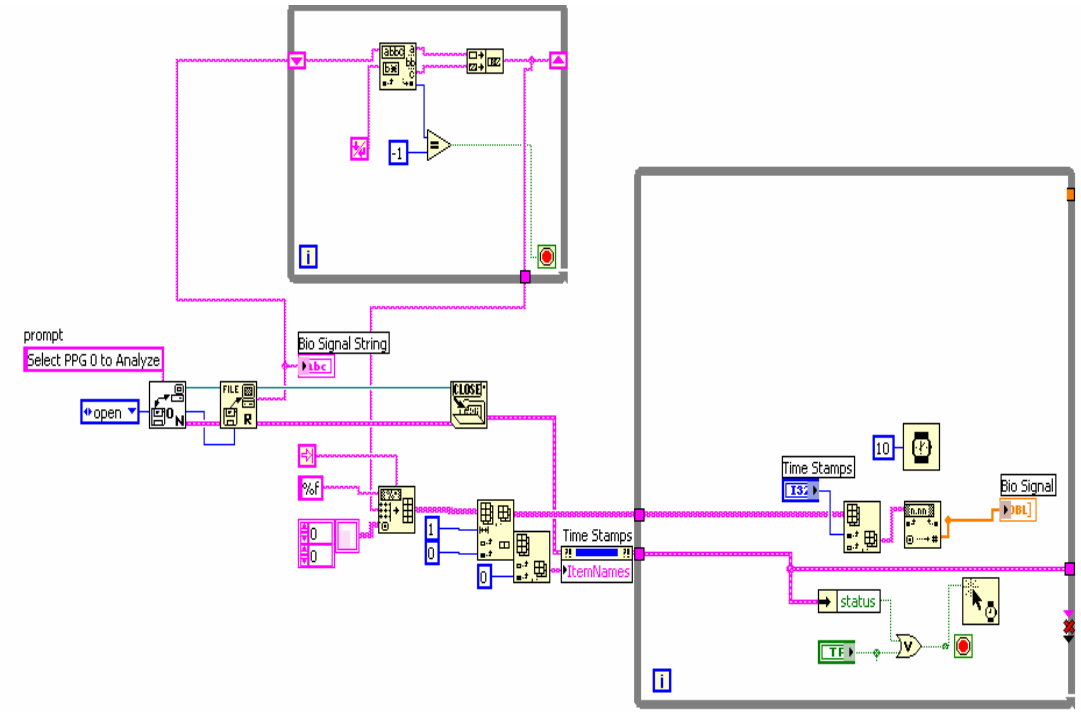

Figure 3-17: Data reconstruction programming

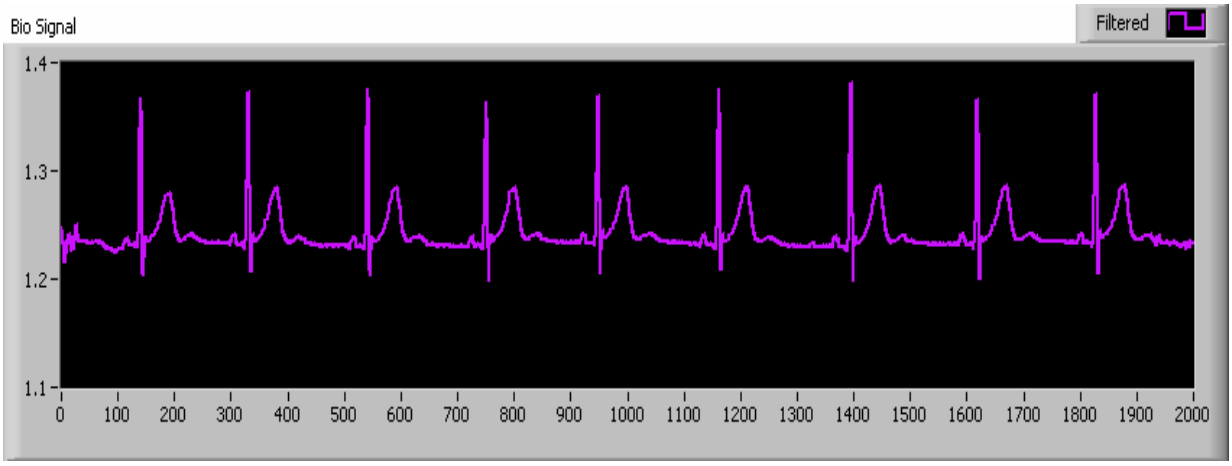

Figure 3-18: ECG reconstructed from PDA upload

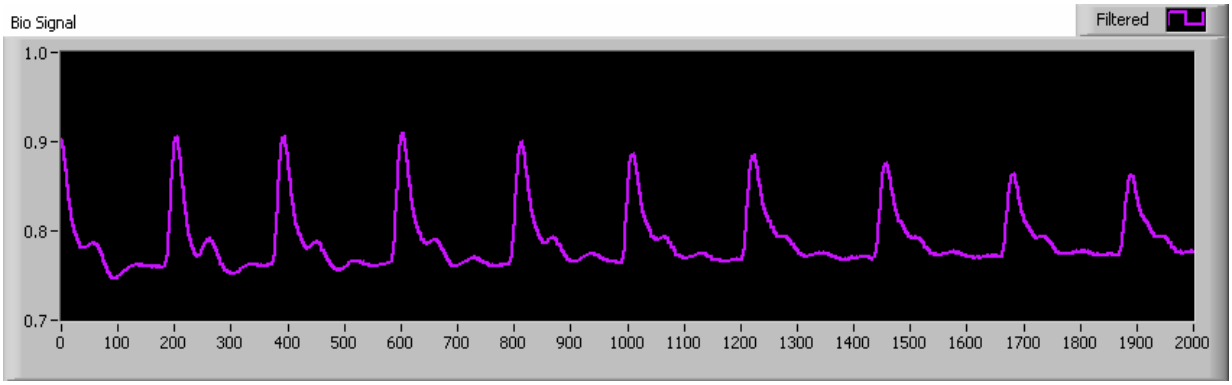

Figure 3-19: PPG reconstructed from PDA upload

3.3.3 Hilbert Transform Algorithm

Since the crucial part of the HRV derivation program is to identify the time of occurrences of each peak in the signals, the peaks need to be identified with minimal error. The ECG signal is a complex signal and possesses three distinct peaks: P wave, QRS complex, and T wave. The desired peak is the QRS complex whose amplitude could be similar to the other two waves in some subjects making it difficult for peak detection algorithms to determine the

difference. This possible confusion is eliminated by implementing the Hilbert Transform Algorithm. The algorithm has proven an effective method in isolating the QRS complex[18].

The Hilbert Transform shifts the frequency components of a signal by - 90 degrees. The definition of the Hilbert Transform is described as

$$H\left[x(t)\right] = \frac{1}{\pi}\int_{-\infty}^{\infty}\frac{x(\tau)}{t-\tau}d\tau = \frac{1}{\pi t} * x(t)$$

Where x(t) is the ECG time signal. The Hilbert Transform is an odd function and will return a value of zero when a maximum or minimum peak in the time signal is detected. When the time signal has a zero crossing, the Hilbert Transform will return a peak. For the purposes of QRS complex detection, the first derivative of the ECG signal is calculated. The derivative crosses zero during the QRS complex occurrence and thus the Hilbert Transform would result in a peak. The same occurs at the T and P waves. However, the slopes of the QRS complex are much more drastic than that of the T and P waves thus resulting in significantly smaller peaks in the Hilbert Transform. The final result is a close reproduction of the original ECG signal but with the significant reduction of the T and P waves.

The signal can be manipulated further and clearly detect the instantaneous QRS peak in the time signal by determining the analytic signal which is defined as

$$x_a(t) = x(t) + H\left[x(t)\right]$$

Where the real part of the conjugate is the input signal (first derivative of the ECG signal) x(t) and the imaginary part is the Hilbert Transform of the input signal H[x(t)]. The maximum amplitude of the signal is determined by finding the complex envelope of the original signal by

$$\left|x_a(t)\right|$$

which is the magnitude of the conjugate.

Figure 3-20 is the code implemented in order to isolate the QRS complex. The array of data is sent into a first derivative function and into the Hilbert Transform. The first derivative acts as the real part of the complex number and the Hilbert output acts as the imaginary part of the complex number. The generated complex number is then converted into polar components. The magnitude is then graphed and is the original ECG signal with very distinct QRS complexes and minimized T and P waves. The exact same process is applied to the PPG signals. Although PPG signals are not as complex as ECG signals, the algorithm still greatly reduces the dichrotic notch from being detected as a secondary peak and eliminates any minor motion artifacts.

Figure 3-20: Hilbert Transform algorithm program

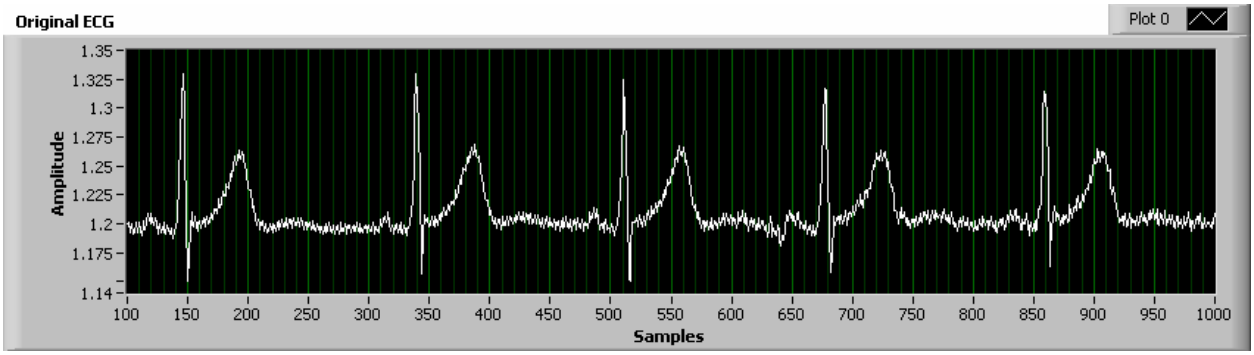

Figure 3-21: Original ECG signal

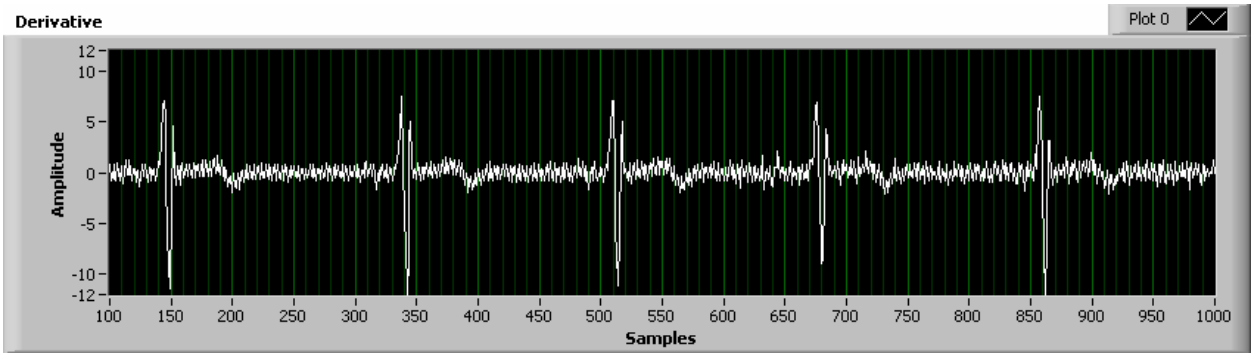

Figure 3-22: Derivative of ECG signal

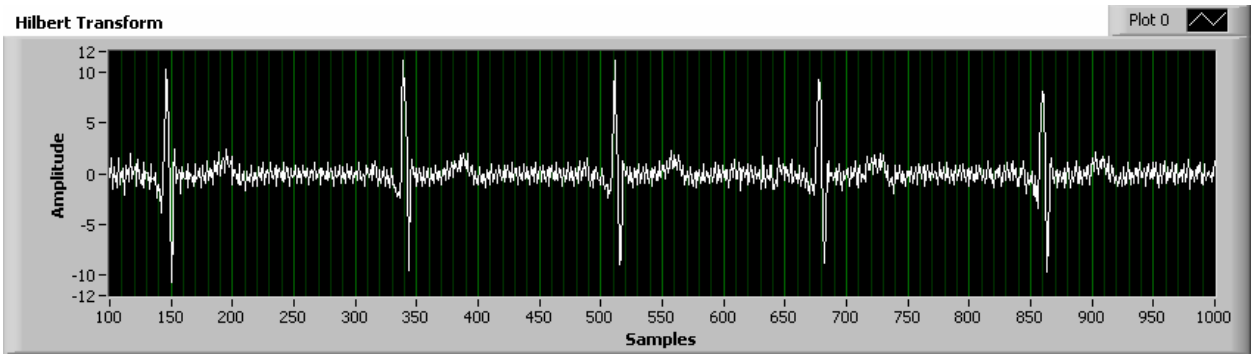

Figure 3-23: Hilbert Transform of Derivative

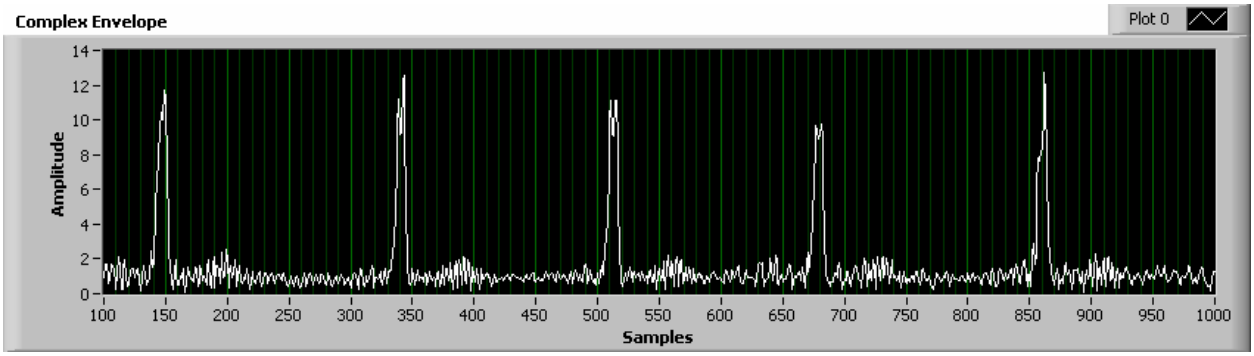

Figure 3-24: Complex envelope using hilbert transform

3.3.4 Data filtering & editing

The modified signals are then sent to an editing process. The editing process includes a digital low pass filter to eliminate high frequency components that the analog filters did not

remove as well as the distorting noise seen in the complex envelope. The cutoff frequency varies between 0.005 and 10 Hertz depending on the individual signals.

The second part of the editing process is the deleting of the beginning and ends of the data sets. The ends of the data set became corrupted after they were sent through the first derivative function. This was caused by initial and final conditions of the function. However, they were deleted from the series and this action did not affect the final HRV signal. The editing programming is displayed in Figure 3-25. Figures 3-26 and 3-27 show the before and after pictures of the signals when processed through the previously mentioned Hilbert algorithm and the filtering/editing functions.

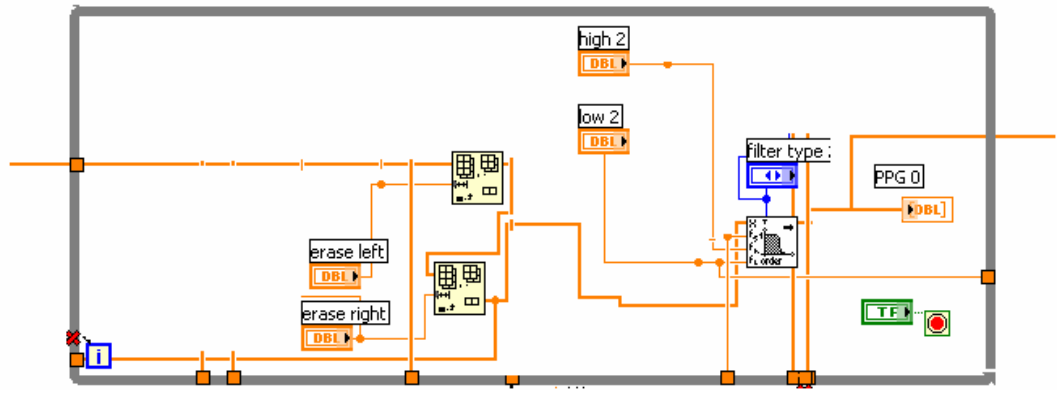

Figure 3-25: Data filtering and editing programming

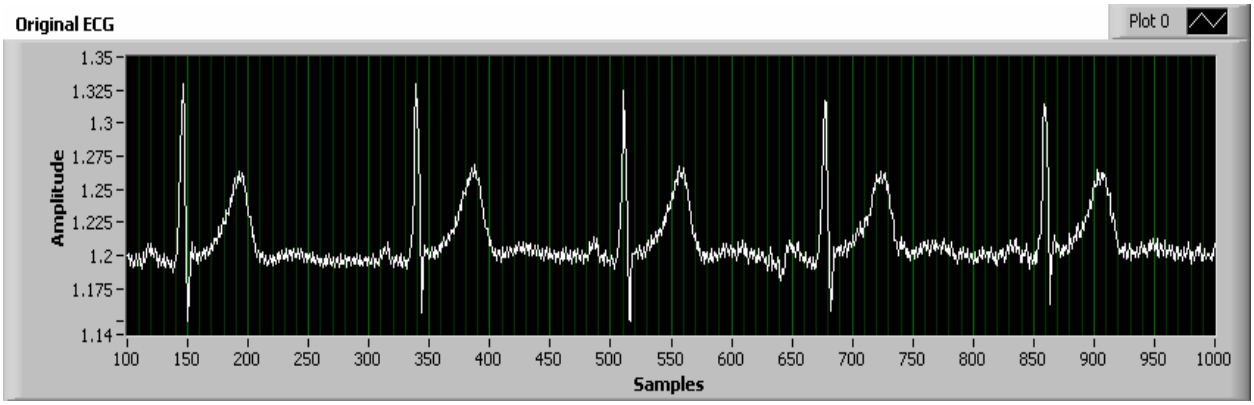

Figure 3-26: ECG before Hilbert and editing

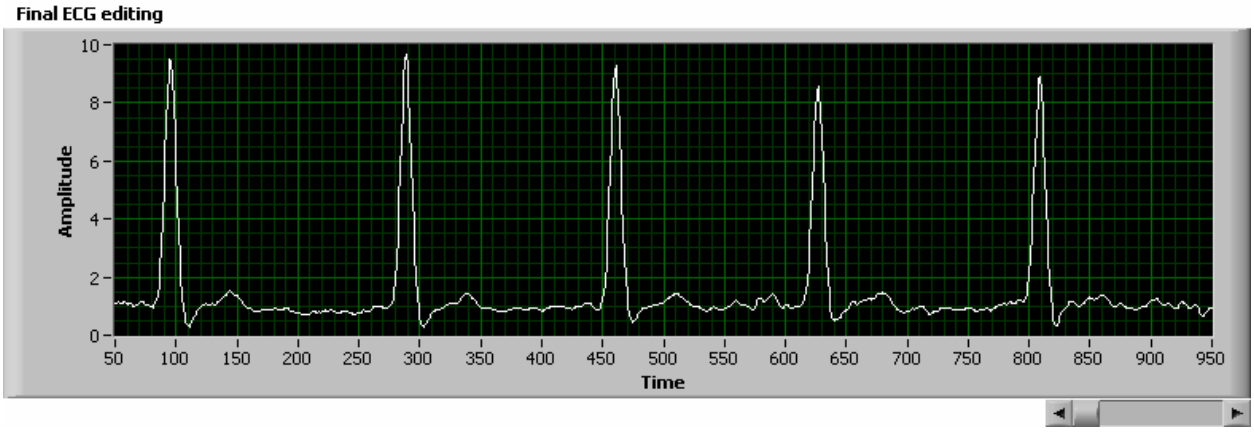

Figure 3-27: ECG after Hilbert and editing

3.3.5 Peak Detection Algorithm

The important part of the HRV derivation process is the detection of the individual peaks in the signal. A red line is adjusted so that the program would detect any peaks above it. A peak detection algorithm was used to detect all the major peaks (e.g. QRS complexes), determine their locations (sample in the array), convert the location into seconds, and send the converted locations into an array. Since the time values of the signals were in samples, they were easily converted into seconds by indicating the sampling rate (197 S/s) used to acquire the data in the first place. Figure 3-28 is the programming element used to perform the peak detection. Figures 3-29 is an example of a result of the peak detection algorithm.

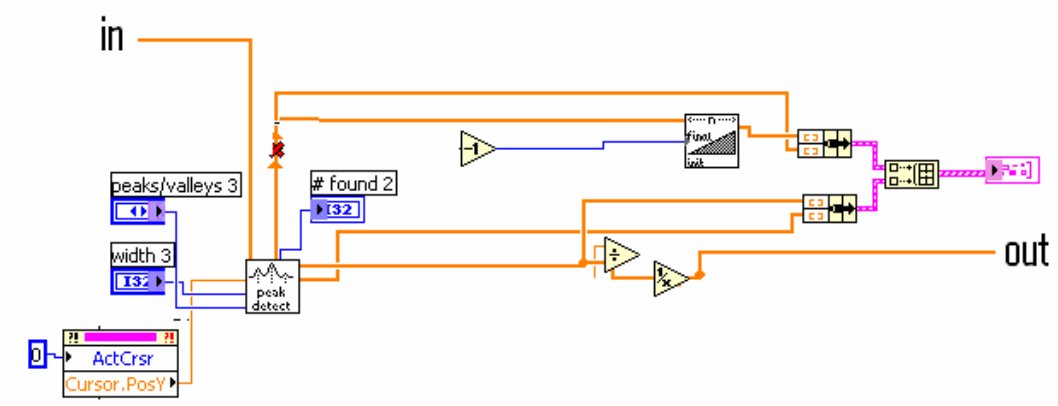

Figure 3-28: Peak detection algorithm

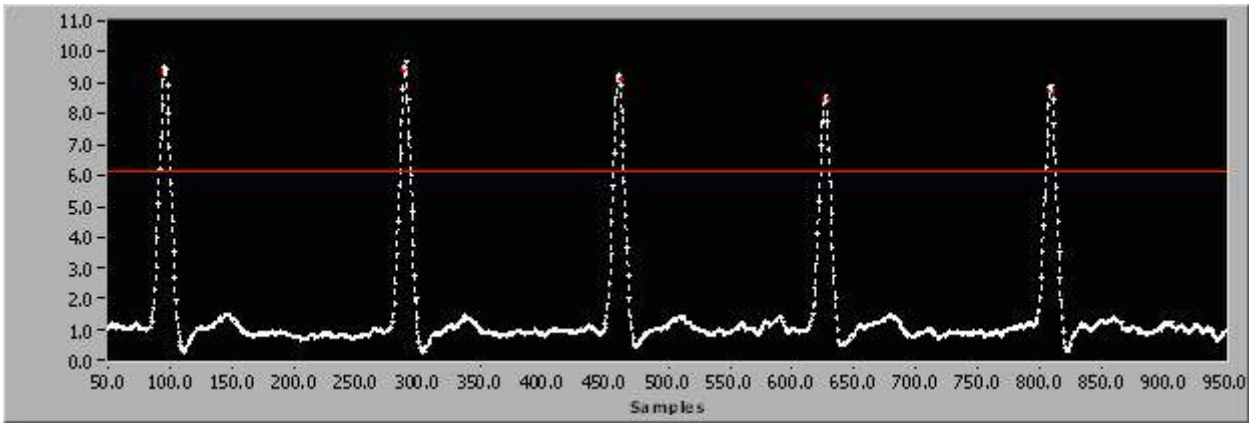

Figure 3-29: Peak detection performed on ECG signal

3.3.6 HRV tachogram

The time locations of every major peak in the signals were stored in an array. They were then subtracted from the proceeding time location in order to obtain the time differences. These would be the RR or DD intervals. The RR (DD) time differences were sent and stored into another array. The complete array is the final HRV data set. Figure 3-30 is the programming to

obtain the HRV tachogram. Figures 3-31 is an example of the HRV tachogram obtained from the ECG signal.

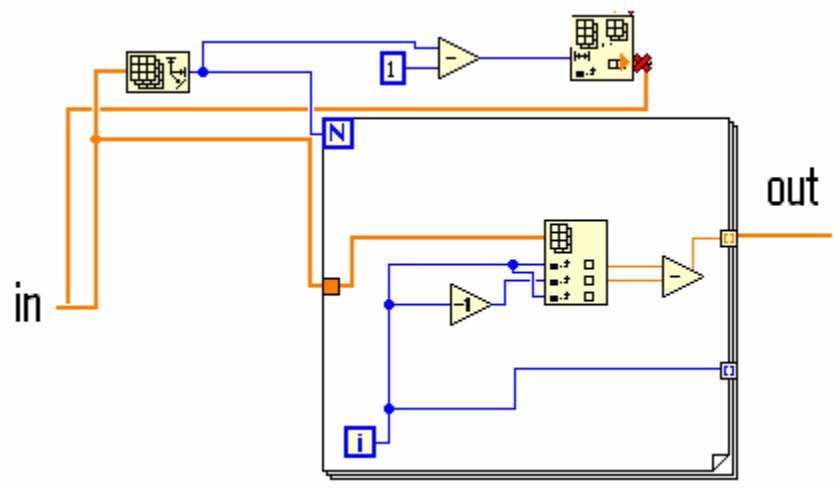

Figure 3-30: HRV derivation and tachogram programming

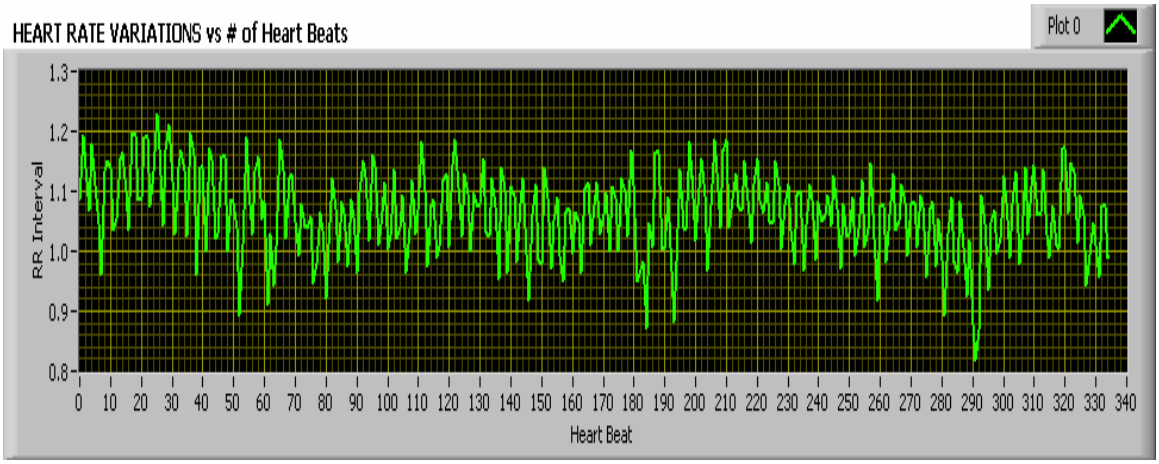

Figure 3-31: HRV tachogram from ECG signal

3.3.7 Saving HRV data to file

The derivation of the HRV data set required some manual changes made using controls on the front panel of the LabVIEW program such as the editing and filtering stage. To avoid the necessity of doing the same process again to obtain the same HRV, the final HRV data set is

simply saved into memory to be called upon anytime in the future for further analysis. The data is saved as a text file (.txt). For the purpose of this research, the HRV will be analyzed to compare to glucose changes, but the same HRV files can be opened and used for other purposes. The HRV gathered and saved will serve as a data base for any future HRV applications. Figure 3-32 shows the subroutine for saving HRV data to the database.

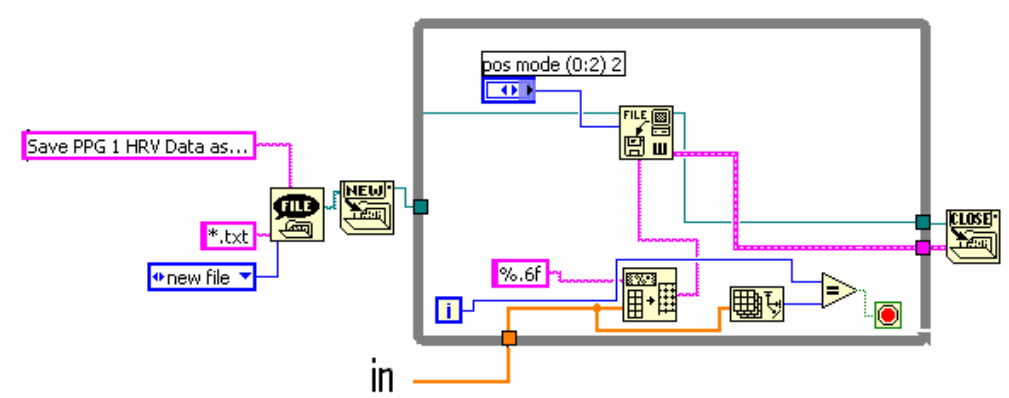

Figure 3-32: HRV "save to file" programming

3.4 HRV Analysis in a PC Environment

3.4.1 HRV Analysis Graphical User Interface

HRV data can be analyzed in a PC environment using the graphical user interface (Figure 3-33). The program displays HRV tachograms, histograms, power spectral densities using Fast Fourier Transform and autoregressive estimation. Statistical values and power calculations are also displayed. Poincare' plots and Approximate Entropy calculations provide nonlinear analysis of HRV data. A user manual describing the operation of the program can be found in the appendix.

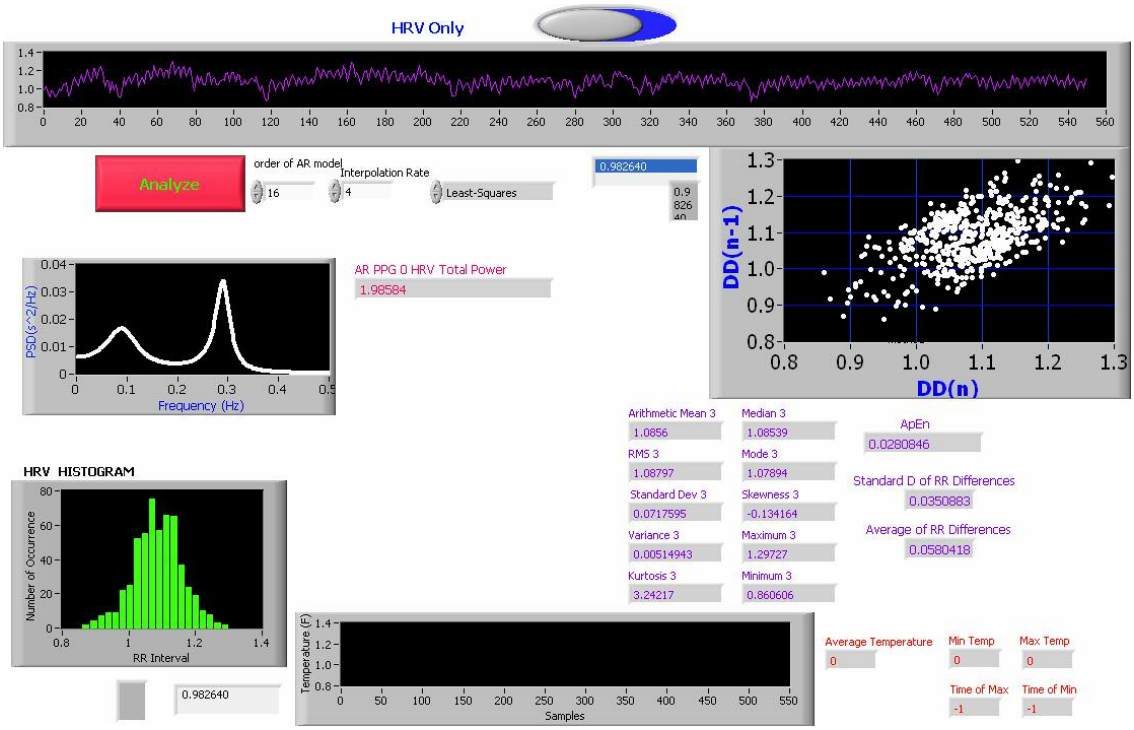

Figure 3-33: HRV Analysis GUI

3.4.2 HRV data upload

The HRV analysis program can be run at any time and analyze any HRV file stored in the collected data base. When the program is run, a prompt will ask which HRV data set is to be analyzed due to programming in Figure 3-34.

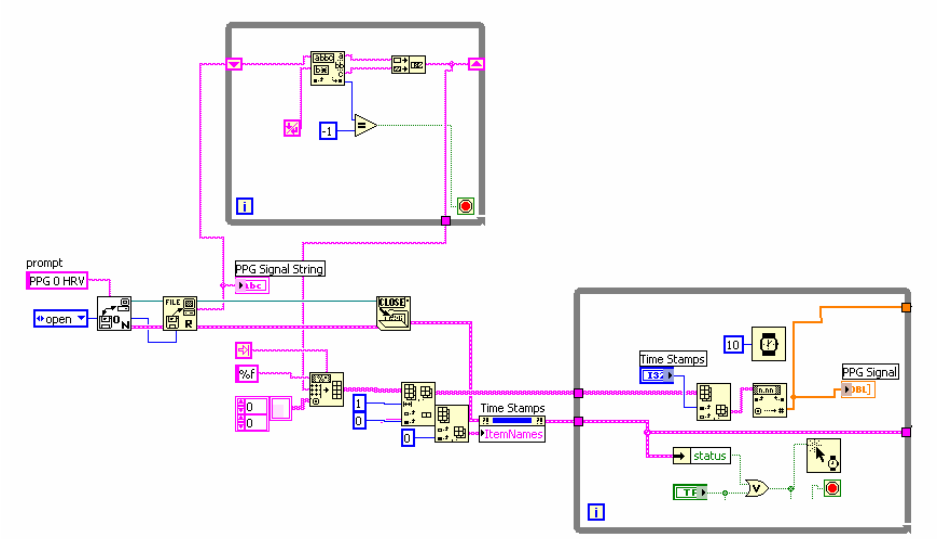

Figure 3-34: HRV uploading programming

3.4.3 Interpolation

Once the HRV data sets are opened and loaded into the program, the data sets need to be interpolated for purposes of frequency domain analysis. HRV sets are unevenly sampled and therefore require interpolation. The original time series, however, can be analyzed in time domain. The recommended value for interpolation is a factor of 4 which would determine four values between each RR interval. This value can be modified via the GUI if a lower or higher interpolation factor is desired. Figure 3-35 shows the programming written to perform the interpolation.

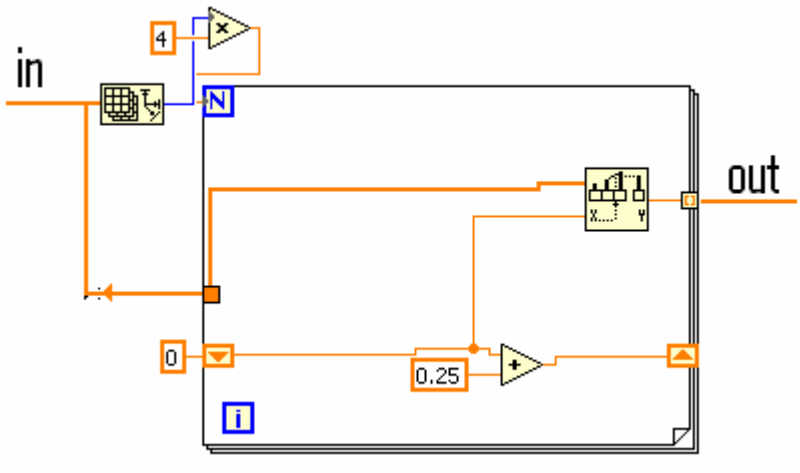

Figure 3-35: Interpolation program

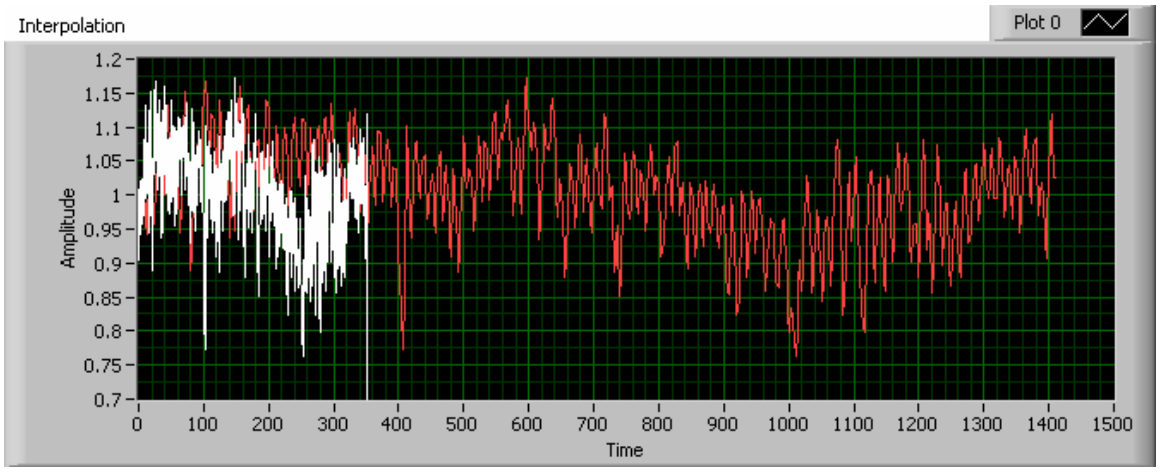

Figure 3-36: Previous HRV (white) and interpolated HRV (red)

3.4.4 Time Domain Analysis

RR(DD)Maximum and Minimum

The maximum and minimum RR or DD intervals were found by inputting the HRV array into the max/min function. Figure 3-37 is the programming used to perform this function.

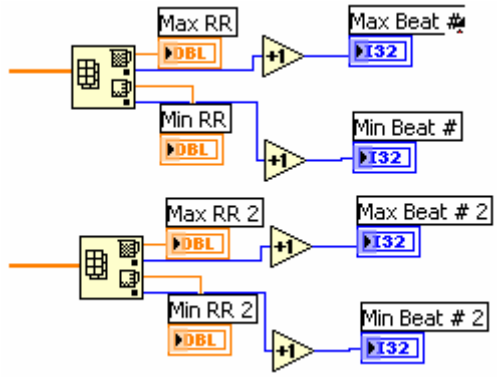

Figure 3-37: Max/Min programming

RR(DD)Standard Deviation

The standard deviation of the RR or DD intervals was found by inputting the HRV array into an original standard deviation program seen in Figure 3-38.

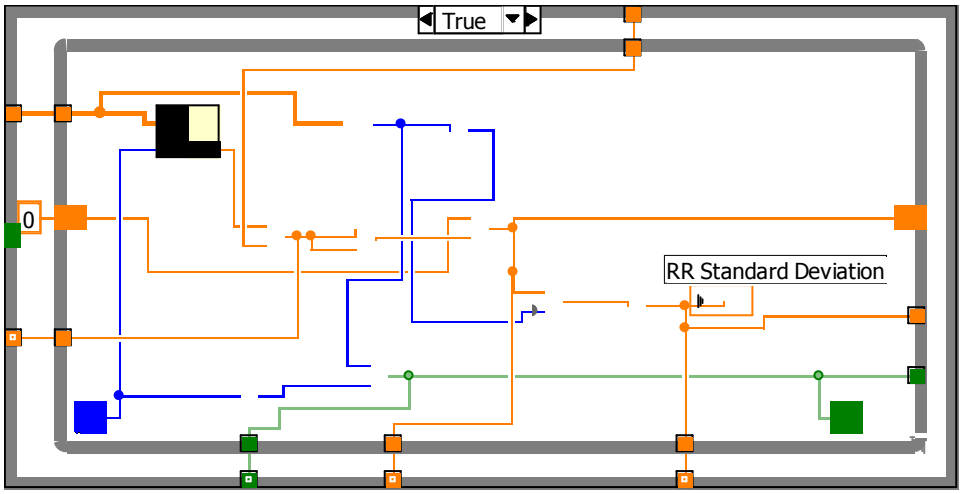

Figure 3-38: Standard Deviation programming

RR(DD)Mean

The average of the RR or DD intervals was found by inputting the HRV array into an original mean program seen in Figure 3-39.

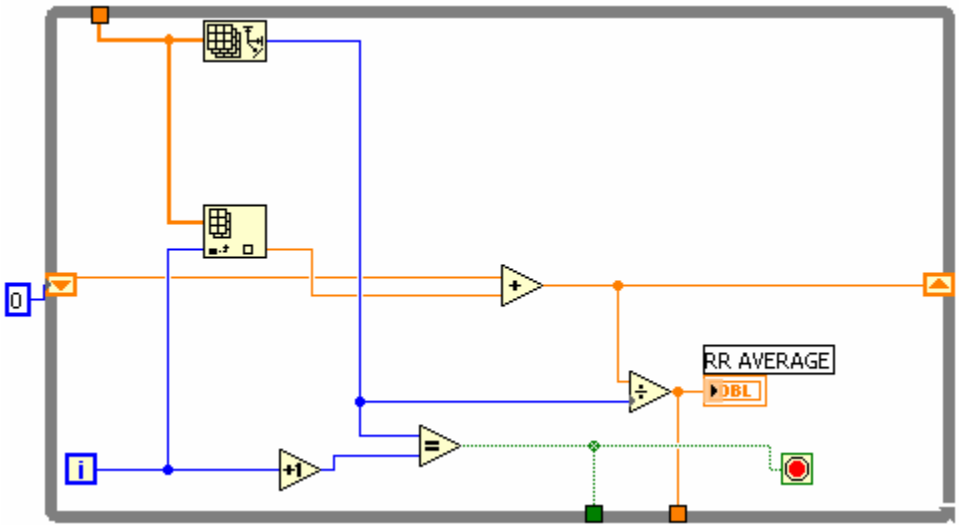

Figure 3-39: Mean programming

ΔRR(ΔDD) Standard Deviation

The standard deviation of the ΔRR or ΔDD was found by inputting the HRV array into an original standard deviation program seen in Figure 3-40.

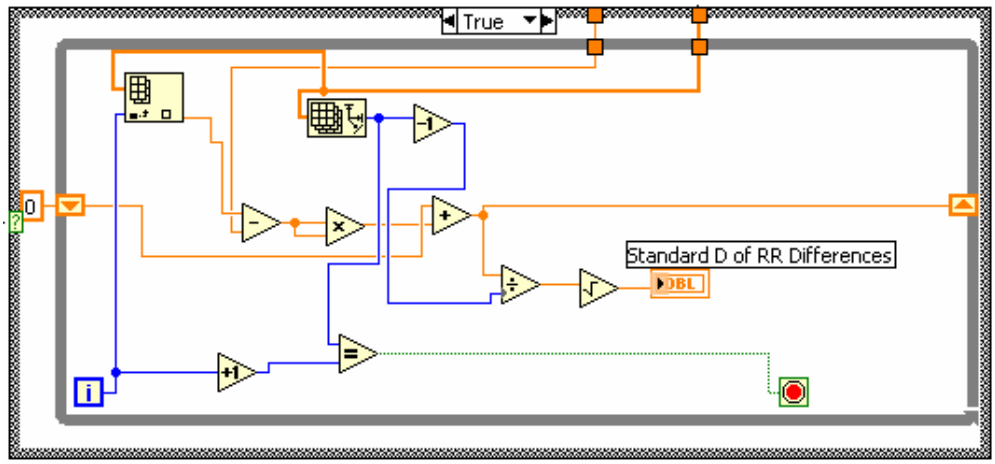

Figure 3-40: ΔRR (ΔDD) Standard Deviation programming

ΔRR(ΔDD) Mean

The average of the ΔRR or ΔDD intervals was found by inputting the HRV array into an original mean program seen in Figure 3-41.

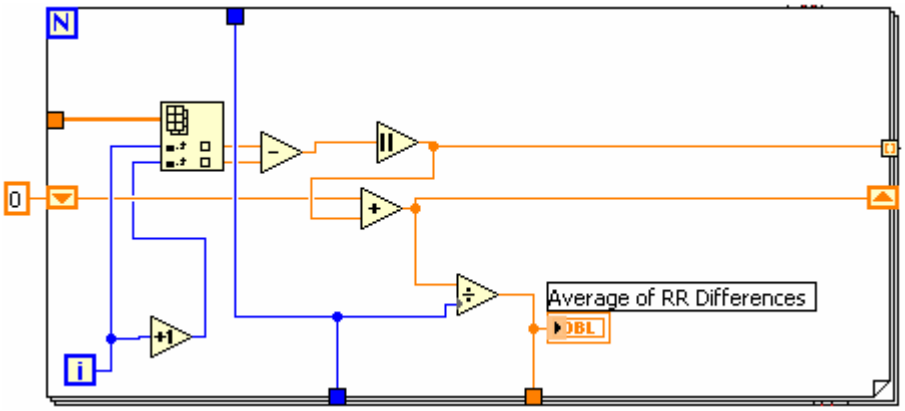

Figure 3-41: ΔRR (ΔDD) Mean programming

3.4.5 Frequency Domain Analysis

FFT Power Spectral Density

The Fast Fourier Transform could be used to determine the spectral density of the HRV data set now that the data set is evenly sampled. The HRV array was inputted into the FFT power spectral density function.

$$P_{FFT}(f) = \sum_{k=0}^{N-1} a_k e^{-j2\pi fk\Delta t}$$

The function used can be seen in Figure 3-42 and an example of its output in Figure 3-43.

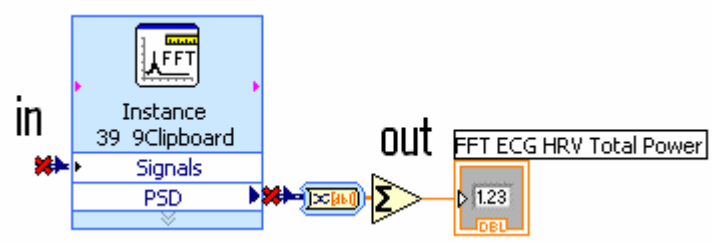

Figure 3-42: FFT PSD programming

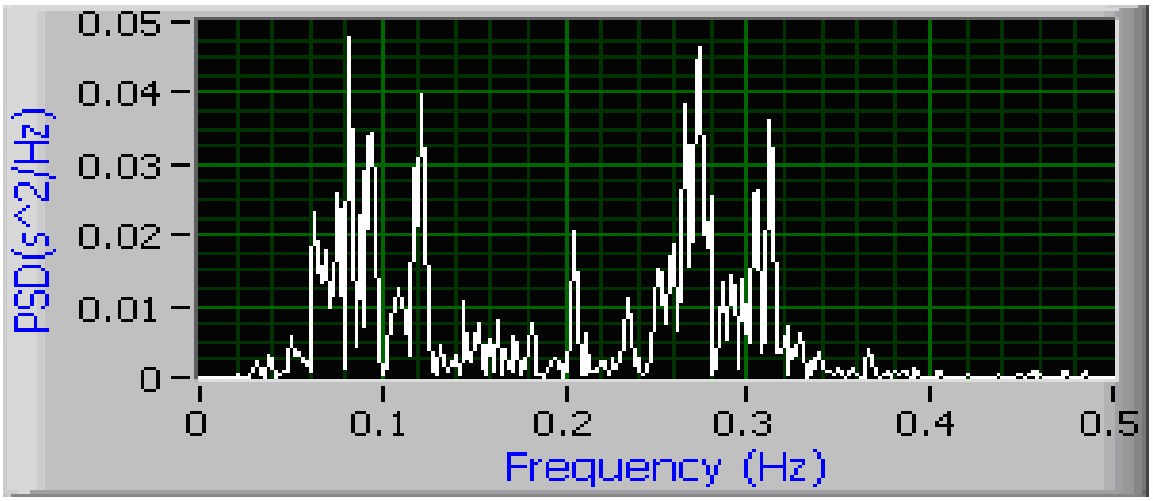

Figure 3-43: FFT PSD output

AR Modeling Power Spectral Density

The Autoregressive (AR) estimation method was used because compared to the traditional FFT method, AR modeling provides better resolution for short amounts of data[19]. The AR method also provides a representation of the HRV power spectral density through smooth curves which make the spectral components more distinguishable. An order of 12 was implemented in the model as suggested by previous AR methods used in HRV analysis. An AR process of order p can be written as $x_t = n_t + a_1 x_{n-1} + a_2 x_{n-2} + \ldots\ldots\ldots + a_p x_{n-p}$, where n_t is the white noise driving signal, which is the innovation of the AR process, and p is the order of the AR model. To estimate the AR power spectrum density function, the parameters of the filter,

$\{a_1, a_2, \ldots, a_p\}$, and the variance that characterizes the white noise, σ^2, must be found. The system of equations to find the AR parameters is linear and its solution is straightforward. Furthermore, it can be solved iteratively, using the Levinson–Durbin equations, thus reducing processing time (Kay and Marple 1981). The AR power spectrum density estimate is given by where σ^2 is the variance of the white noise driving function and Δt is the re-sampling interval.

$$P_{AR}(f) = \frac{\sigma^2 \Delta t}{\left| 1 + \sum_{k=1}^{p} a_k e^{-j 2\pi f k \Delta t} \right|^2}$$

The program created to implement AR modeling can be seen in Figure 3-44 and an example of its output can be seen in Figure 3-45.

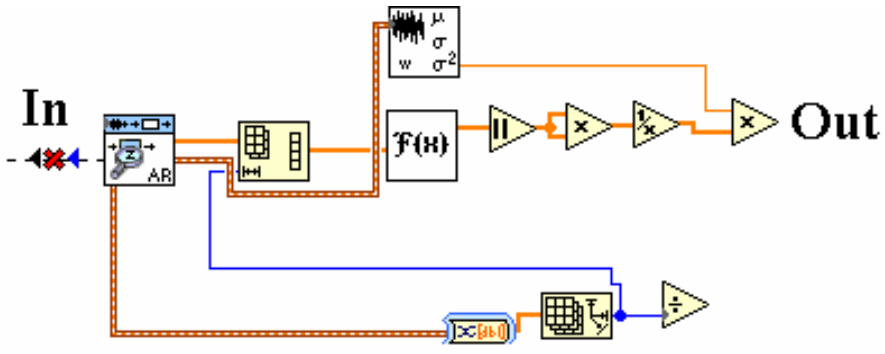

Figure 3-44: AR estimation programming

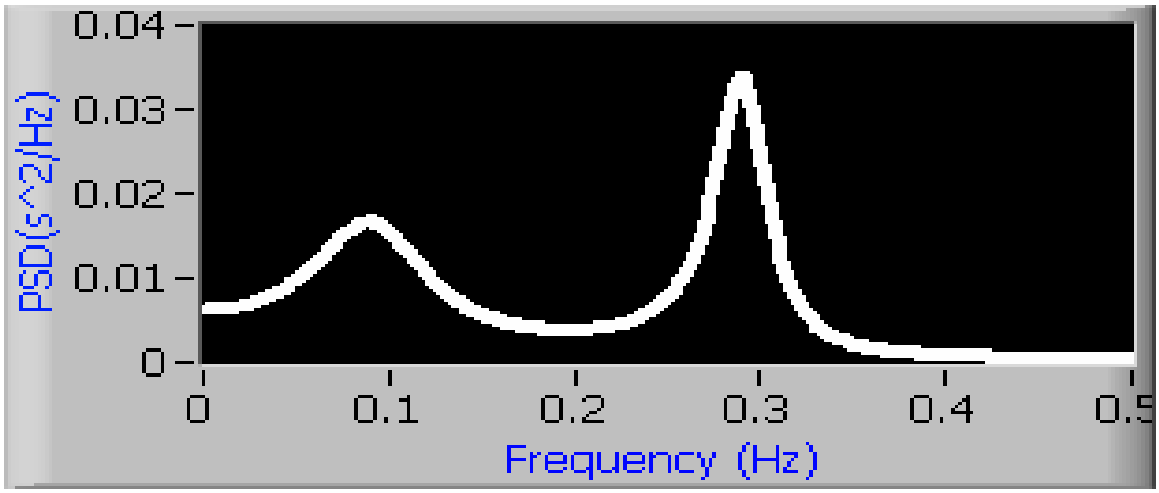

Figure 3-45: AR PSD output

3.4.6 Non Linear Analysis

Poincare' Plots

Poincare' plots are useful in monitoring the non linear properties of HRV and determining if the data sets are trustworthy. Poincare' plots plot the HRV data points against their previous data points (e.g. RR_n vs RR_{n-1}). A valuable datum set will have data points clustered together in one region of the Poincare' plot. The programming written to derive the Poincare' plots can be seen in Figure 3-46 and an example of the Poincare plot in Figure 3-47.

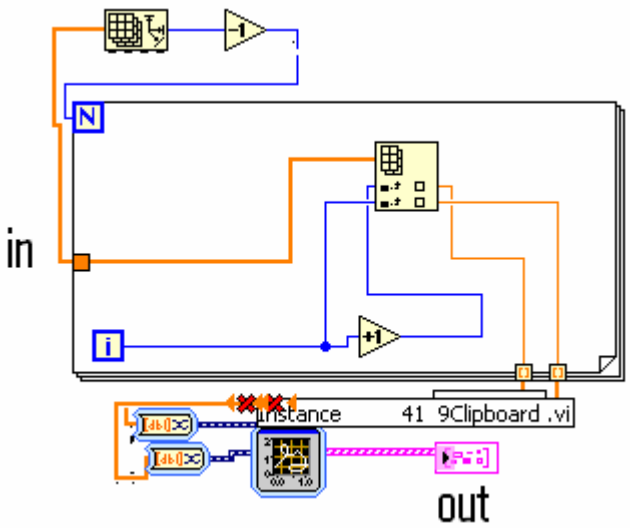

Figure 3-46: Poincare' plot programming

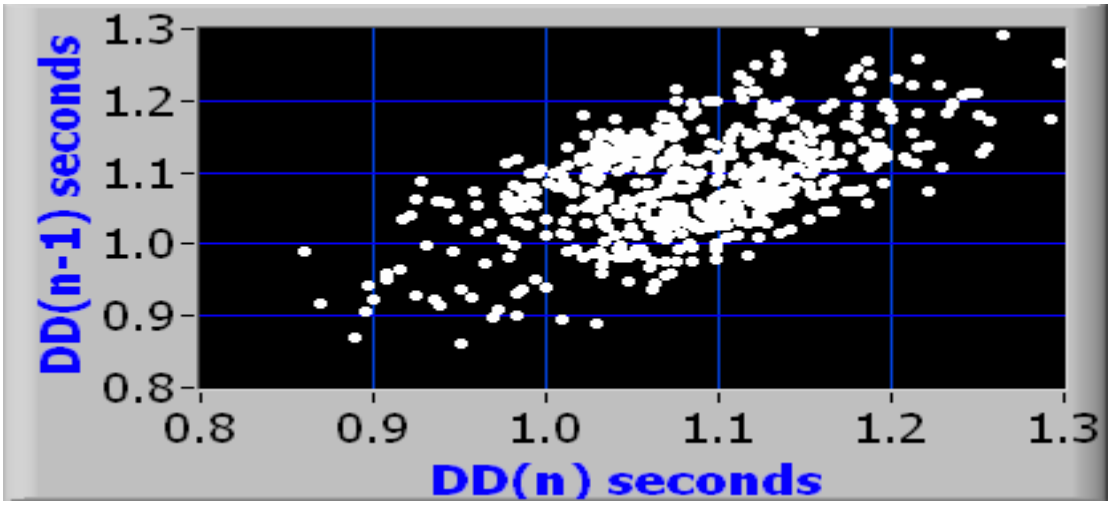

Figure 3-47: Poincare plot output

SD1 and SD2

A simple way of evaluating the Poincare' plot is to draw an ellipse around the scattered data at a line of identity positioned at a fourty-five degree angle with respect to the normal axis. The SD1 value is the standard deviation of the points perpendicular to the line of identity. This value represents short-term variability. The SD2 value is the standard deviation of the points

along the line of identity and represents long-term variability. The Matlab programming used to determine these values can be seen in Appendix C.3.

Approximate Entropy

Approximate Entropy (ApEn) is a regularity statistic that quantifies the unpredictability of fluctuations in HRV. A predictable HRV data set will result in low ApEn value and a very random and unpredictable HRV data set will result in a high ApEn value[20]. The program written to determine the ApEn values of HRV data sets can be seen in Appendix B.1.

3.4.7 Statistical Analysis

Skewness

The amount of asymmetry in a data set probability distribution can be estimated by the skewness value determined by:

$$Skew(X) = \frac{E\left[(X - \mu)^3\right]}{\sigma^3}$$

Equation 1: Skewness

where **X** represents the HRV data set, □ is the mean value, and□ represents the standard deviation. A positive skewness indicates that most of the data are located to the left of the mean and a negative value shows that most of the data are on the right side of the mean [15].

Kurtosis

The shapes of the probability distributions were analyzed using the Kurtosis coefficient. This coefficient was calculated by using:

$$Kurtosis(X) = \frac{E\left[\left(X-\mu\right)^4\right]}{\sigma^4}$$

Equation 2: Kurtosis

where **X** represents the HRV data set, □ is the mean value, and□ represents the standard deviation. This is an indication of how much the values peak around the mean of the data set. A kurtosis greater than 3 indicates a leptokurtic data set and a value less than 3 indicates a platykurtic data set [14].

Cross Correlation

Cross correlation was used to determine the relation between the HRV data sets derived from ECG and PPG methods. The data sets were numerically related through the correlation coefficient calculated by using:

$$R = \frac{m\Sigma x_m y_m - \Sigma x_m \Sigma y_m}{\sqrt{\left[m\Sigma {x_m}^2 - \left(\Sigma x_m\right)^2\right] * \left[m\Sigma {y_m}^2 - \left(\Sigma y_m\right)^2\right]}}$$

Equation 3: Cross Correlation

where **m** equals the number of intervals, **x** represents the RR intervals, and **y** represents the DD intervals. A correlation coefficient close to 1 indicates direct relation, whereas values close to -1 indicate inverse relation, while values close to 0 indicate little or no relation.

RMSSD

The square root of the mean of the squared differences between adjacent normal R-R intervals (RMSSD) is a another statistical approach at analyzing heart rate variations. RMSSSD was calculated by using:

$$RMSSD = \sqrt{\frac{\sum_{i=0}^{N-1} (RR_i - RR_{i-1})^2}{N-1}}$$

Equation 4: RMSSD

NN50

The number of R-R consecutive intervals that differ by more than fifty milliseconds results in the NN50 value. The NN stands for normal to normal intervals.

pNN50

The percentage value of the number of R-R consecutive intervals that differ by more than fifty milliseconds results in the pNN50 value. The NN stands for normal to normal intervals.

3.4.8 Geometric Analysis

RR triangular index

The total area of the HRV histogram divided by the maximum value in the histogram results in the RR triangular index.

TINN

The baseline width of the minimum square difference triangular interpolation of the maximum value of the HRV histogram is known as the TINN value of HRV.

Chapter 4 : Human Testing and Experimental Tools

4.1 Institutional Review Board

Experimentation involving human subjects requires permission from the university and is referred to as the Institutional Review Board (IRB). An IRB document answers the Who, What, Where, Why, and How aspects of the research experiment. After a thorough review by the board, the IRB is accepted or rejected. The IRB document also consists of a consent form for the volunteer test subjects to sign. The consent form provides an explanation to the subject about the procedure of the experiment as well as information on the risks and benefits of participating in the research. The IRB and consent forms developed and approved for this study can be seen in Appendix D. Two different versions of the consent form were written since different testing procedures were used on individuals with diabetes than those without diabetes.

4.2 Glucose Monitoring

Two different methods of glucose monitoring were used in this research project. The OneTouch Ultra glucose monitor was used to collect glucose samples from the volunteer subjects without diabetes. The Continuous Glucose Monitoring System (CGMS) Gold by Minimed was used to collect glucose samples from the volunteers diagnosed with Type 1 diabetes.

4.2.1 OneTouch Ultra Portable Glucose Monitor

The OneTouch® Ultra is a small, easy to use and very fast meter, producing results in five seconds. It's extremely light and portable and adequate for this research project's needs. The OneTouch Ultra and its components can be seen in Figure 4-1.

Figure 4-1: OneTouch Ultra glucose monitor

Lancets

The lancets are sharp short needles that penetrate the skin in order to cause a small amount of blood to form at the tip of the finger. The lancets are loaded into a lancing device also called a senserter (Figure 4-2) that quickly inserts and removes the lancet (Figure 4-3).

Figure 4-2: Lancet loading device

Figure 4-3: Lancets

Blood strips

The OneTouch Ultra uses FastDraw™ Design test strips (Figure 4-4), a new capillary action, end-fill test strip that takes only 1 micro liter of blood, is touchable, and is approved for alternative sites.

Figure 4-4: Blood strips

Blood Sampling Procedure

A new blood strip is inserted into the monitor for preparation of receiving a blood sample. The lancet device is loaded with a new sharp lancet. The device is adjusted to penetrate the skin at a particular depth. The device is placed firmly against the tip of the finger and the lancet quickly pokes the finger (Figure 4-5). When a drop of blood forms at the tip of the finger, the test strip is placed against the blood and filled with blood. Within five seconds, a reading of the current glucose levels in the blood is delivered.

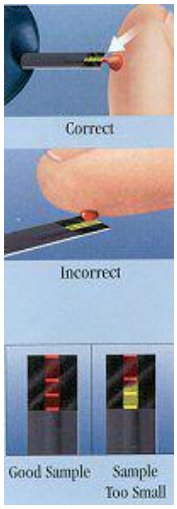

Figure 4-5: Glucose testing procedure

4.2.2 Continuous Glucose Monitoring System (CGMS) Gold

The Continuous Glucose Monitoring System (CGMS) Gold (Figure 4-6) is a system developed by MiniMed Medtronic for use of continuous glucose monitoring. This device is the alternative to the previously mentioned finger stick method. The system allows the user to acquire 288 glucose readings in a twenty-four hour period. The system can be worn around the waist and measures sugar levels between 40 -400 mg/dL. Up to fourteen days of data can be stored within the device. The continuously recorded data can then be transferred to a personal computer for analysis.

Figure 4-6: CGMS Gold by MiniMed

Glucose sensor

The CGMS Gold uses disposable glucose sensors (Figure 4-7) that are used to monitor the changing glucose levels of a subject. The sensors consist of a 16 millimeter electrode needle that inserts into the fatty layer of skin of the abdomen at a four-five degree angle. The sensor operates by using an enzyme known as glucose oxidase to convert glucose under the skin into electrical signals. The signals are sent to the CGMS monitor. An average of glucose readings are then recorded every five minutes. Each sensor is good for measuring glucose up to seventy-two hours.

Figure 4-7: Glucose sensor for CGMS Gold

Com-Station and CGMS solutions software

The glucose data stored onto the CGMS Gold can be transferred to a desktop computer for analysis by a doctor or researcher. The monitor is interfaced to the PC through the use of a docking comstation (Figure 4-8) that connects to the computer via a serial port. The software used to analyze the glucose data is the CGMS solutions software which reads the glucose information stored in the monitor. The software provides a complete visual recording (Figure 4-9) of a subject's glucose activity so that doctors can appropriately recommend a glucose management routine.

Figure 4-8: Com-Station interfacing CGMS to PC

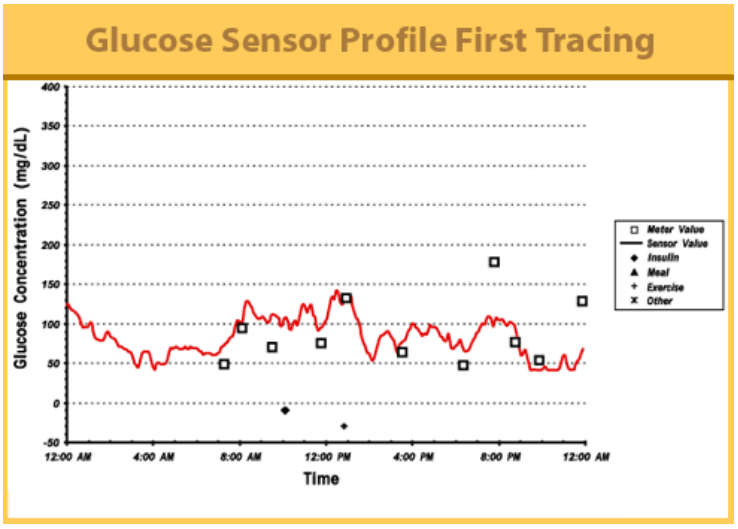

Figure 4-9: Example of analyzed glucose recording using Solutions software

4.3 ECG Monitoring

Two different methods of ECG monitoring were used in this research project in order to acquire HRV data. The PDA biosignal acquisition system was used to collect ECG data from the volunteers without diabetes. The holter monitor was used to collect twenty-four hours of ECG data from the volunteer subjects with Type 1 diabetes.

4.3.1 PDA Acquisition System

The electrocardiogram data for the volunteers without diabetes was collected using the PDA acquisition system developed and described in Chapter 3.

4.3.2 Holter Monitoring

The Nasiff Holter Monitoring system consists of a device for recording electrocardiogram measurements for up to seventy-two hours continuously. The device is designed to collect ECG during exercise, sleep, and any other activity during the course of a day.

The holter monitor (Figure 4-10) performs the same task as the PDA acquisition system developed for this study. A holter monitor was used instead of the PDA system because of its ability to withstand extraneous activities that a subject may experience during the day. The holter monitor's extensive use in the medical research world also made it a reputable tool for acquiring accurate ECG recordings.

Figure 4-10: Nasiff ECG Holter monitor

Nasiff Cardio Software

The Nasiff Holter monitor is made complete with the use of the Cardio Software (Figure 4-11) developed by the Nasiff Company. The software allows the ECG recordings to be analyzed by the doctor or researcher on a PC. The software allows the user to detect abnormalities in the entire recording and edit out artifacts such as arrhythmias or distorted ECG peaks. The edited ECG recordings can then be exported to text files so that they may be analyzed further by the HRV conversion and analysis programs developed for this study.

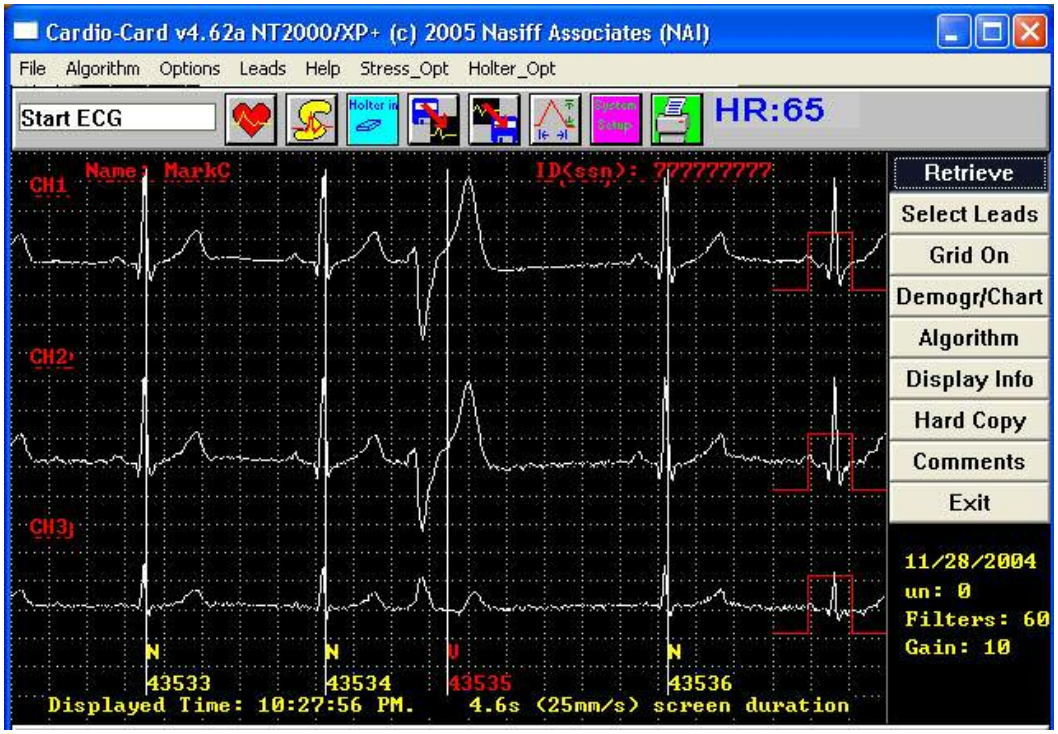

Figure 4-11: Nasiff Cardio Software

Electrode Placement

The holter monitor can record electrocardiogram data for up to seventy-two hours. To ensure accurate and clean signals, the electrode patches used to acquire the signal must be placed in clean, hair free and stable areas of the chest. The holter uses five electrodes to acquire three channels of ECG recordings. The type of electrodes used is Ag/AgCl (Silver/Silver Chloride) patches (Figure 4-12). The areas where the patches are attached need to be shaven to eliminate any hair, scrubbed with a small scrubbing pad to removed dead skin cells, and finally cleaned with an alcohol swab. The electrodes are first connected to snap-on electrode wires similar to those in Figure 4-13. The patches are then attached according to Figure 4-14. The areas designated by the picture are the most stable parts because the patches are located on bone where movement of the patches is less prone hence preventing distortion in the signals as they are being recorded.

Figure 4-12: ECG electrode patches

Figure 4-13: Snap-on electrode patch wires

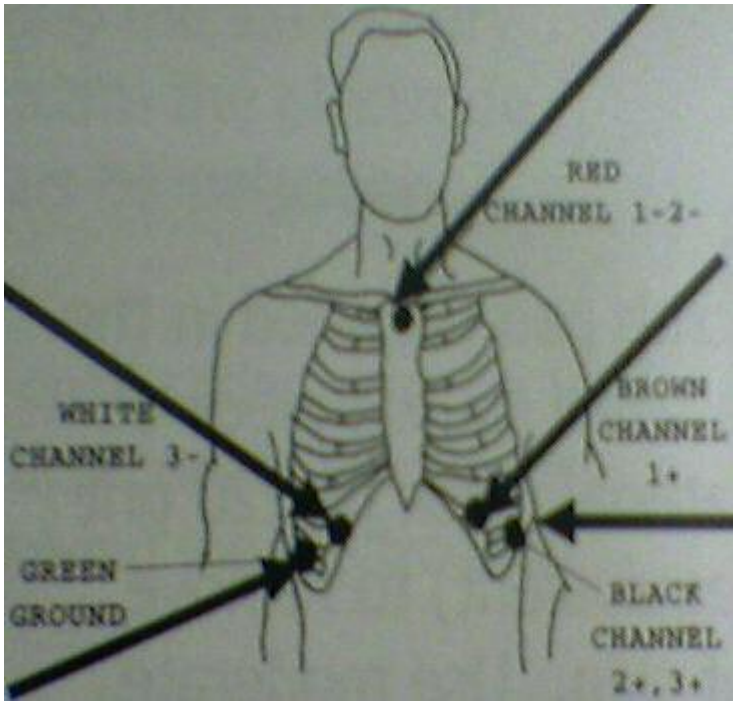

Figure 4-14: Electrode placement for Holter monitoring

Chapter 5 : Experimental Methodology

5.1 Comparing ECG derived HRV with PPG derived HRV in healthy subjects

The HRV acquisition and analysis system was initially tested by using it to record five minutes of ECG and PPG information from two individuals (one male and one female). The recording system recorded both signals simultaneously so that they both had the same starting and ending times. This would help provide trustworthy data to determine if the system was reliable at producing correct HRV information despite the method of derivation. Furthermore, repeatability of the system was determined by repeating the PPG and ECG recordings each three times and deriving three separate HRV data sets for each method.

The PDA based biosignal acquisition system was used to record electrocardiogram and photoplethysmographic data from the subject simultaneously. The ECG electrodes were properly attached to the subject's chest and the PPG finger probe was placed on the middle finger of the subject. The PDA GUI was used to initiate the recording process. The recording time was set to five minutes. The subject was asked to remain calm, relaxed, and abstain from moving. After the five minute recording concluded, the PDA was detached from the transducer part of the system and placed in its cradle. The cradle was connected to the desktop computer which allowed the transferring of the ECG and PPG data file from the PDA to the PC. The .txt files containing the ECG and PPG information could then be analyzed using the HRV conversion program to convert the ECG and PPG data into HRV data.

The HRV conversion program written in LabVIEW was used to convert the ECG and PPG data into HRV data. After pressing the run button, a prompt window asked to select the biosignals for conversion. After the proper files were selected, the signals were converted to

heart rate variability and the resulting data was saved as .txt files for the purpose of future analysis.

The newly acquired HRV data was analyzed using the HRV analysis program written in LabVIEW. When the program was run, a prompt asked to select the desired HRV file to analyze. After being selected, the GUI immediately provided time, frequency, and non linear information about the HRV data which was recorded onto an excel file. Time, frequency, and nonlinear parameters of the HRV data from the ECG and PPG sources were compared to determine if equivalent information could be acquired.

5.2 Comparing HRV to glucose in volunteers without diabetes

The data gathered from the volunteers without diabetes would serve as a baseline as to compare abnormal HRV parameters and unsafe glucose levels to. Since individual without diabetes are not accustomed to having an invasive glucose monitoring device implanted under their skin, their glucose levels were monitored by using the OneTouch Ultra glucose monitor. A population sample of ten volunteers not diagnosed with diabetes, described in Table 5.1, was subjected to glucose level measurements using the OneTouch Ultra device. They were asked to fast prior to being tested so that low glucose levels could be collected. Two more glucose measurements were obtained after giving the subjects a high sugar concentrated drink. Two last glucose measurements were obtained after the subject then ate a meal. PPG and ECG recordings were obtained before each blood test making a total of six ECG/PPG recordings per subject.

Table 5.1: Demographic of subjects without diabetes

Subject w/out Diabetes	Age	Sex	Race
Subject 1	25	Male	Caucasian (Hispanic)
Subject 2	25	Female	Caucasian (Hispanic)
Subject 3	21	Male	Caucasian (Hispanic)
Subject 4	22	Male	Caucasian (Hispanic)
Subject 5	25	Male	Caucasian (Hispanic)

Subject 6	27	Male	Caucasian (Hispanic)
Subject 7	22	Male	Caucasian (Hispanic)
Subject 8	27	Female	Caucasian (non Hispanic)
Subject 9	28	Female	Caucasian (Hispanic)
Subject 10	25	Female	Caucasian (Hispanic)

The OneTouch Ultra glucose monitor was used on the subjects not diagnosed with diabetes. The subject was asked to sit down comfortably in a chair with their arm laid out on the table at a level just above their heart. The tip of the middle finger of the subject was swabbed once with an alcohol pad. While the alcohol dried on the finger, a lancet was inserted into the spring loaded lancet device. The device was then pressed up against the tip of the disinfected finger during which the release button on the lancet device was pressed and the sharp lancet poked a small hole into the fingertip. The lancet was then removed from the lancet inserting device and disposed of into a sharps container. The finger tip was then massaged slightly to allow a bead of blood to form. Once the bead of blood was formed, a OneTouch Ultra blood strip was inserted into the glucose monitor. The strip was then touched up against the bead of blood after which the blood immediately would enter the strip's receptacle. In five seconds, the glucose monitor would provide a numerical value of the glucose concentration in the blood. The value was recorded into the log book and the biosignal acquisition portion took place immediately after.

The PDA based biosignal acquisition system was used to record electrocardiogram data from the subject. The electrodes were properly attached to the subject's chest and the PDA GUI was used to initiate the recording process. The recording time was set to ten minutes. The subject was asked to remain calm, relaxed, and abstain from moving. After the ten minute recording concluded, the PDA was detached from the transducer part of the system and placed in its cradle. The cradle was connected to the desktop computer which allowed the transferring of the ECG

data file from the PDA to the PC. The .txt file containing the ECG information could then be analyzed using the HRV conversion program to convert the ECG data to HRV data.

Unlike the ECG data collected from the subjects with diabetes, as will be discussed later, the data recorded from the subjects without diabetes were clean. All QRS complexes were present and distinguishable from the other waves in the ECG. This was due to the close control of the recording process. The volunteer remained in the room and the recording of the ECG was closely watched by the experimenter to make sure noise was minimal and all QRS complexes were detected and recorded. The subject remained relaxed and remained seated for the entire ten minute recording thus providing a high quality ECG recording. This high quality ECG recording was translated into a high quality and reliable HRV data set by the HRV conversion program.

The HRV conversion program written in LabVIEW was used to convert the ECG data into HRV data. After pressing the run button, a prompt window asked to select the biosignal for conversion. After the proper file was selected, the signal was converted to heart rate variability and the resulting data was saved as a .txt file for the purpose of future analysis.

The newly acquired HRV data was analyzed using the HRV analysis program written in LabVIEW. When the program was run, a prompt asked to select the desired HRV file to analyze. After being selected, the GUI immediately provided time, frequency, and non linear information about the HRV data. The information was recorded onto an excel file. Twenty-five various parameters of HRV were collected for determining relationships between the HRV and glucose measurements collected earlier.

The measurements included average, rms, standard deviation, variance, kurtosis, median, mode, skewness, maximum, minimum, RMSSD, NN50, pNN50, RR triangular index, TINN, SD1 and SD2 from the Poincare' plots, HF fft, LF fft, LF/HF fft, HF ar, LF ar, LF/HF ar, VLF

fft, and approximate entropy. The complete spreadsheet with all collected data values can be found in the Appendix A.1.

The next step was to determine if any patterns could be recognized in the data as sugar levels increased. Correlation analysis was performed to determine if glucose and the twenty-five HRV parameters varied together. The table of correlation coefficients can be found in Appendix A.2. Although extreme ranges of glucose levels below 70 mg/dL or above 200 mg/dL were not expected in the volunteers without diabetes, box plots (Appendix A.3) were utilized to determine if the twenty-five HRV parameters could be categorized based on glucose levels below 90 mg/dL, between 90 and 110 mg/dL, and above 110 mg/dL. Histograms and probability density functions (Appendix A.4) were also analyzed to determine if the probability distribution of the HRV tachograms could be related to changing glucose.

If a relationship between changing glucose and HRV in individuals without diabetes could not be found, an overall range of values expected during normal glucose measurements (as would be observed in healthy individual without diabetes) would be determined. The HRV parameters of each volunteer without diabetes were normalized and then pooled together into a column of data points under twenty-five different HRV parameter categories. The average and standard deviations of the overall HRV parameters were calculated and plotted side by side. The diagram would provide a visual representation of the degree of variation from greatest to least of each of the HRV parameters.

5.3 Comparing HRV to glucose in volunteers diagnosed with Type 1 diabetes

The volunteers diagnosed with diabetes are more prone to experiencing glucose levels that go below the normal acceptable levels of 70 mg/dL. Since levels below 70 mg/dL were not possible in healthy subjects without diabetes, further important information could be gathered

through the testing of individuals diagnosed with the disease. The glucose levels of the diabetes sufferers were acquired through the use of the CGMS Gold by having a registered nurse insert the glucose sensor into the interstitial layer of the abdomen. The holter monitor was also attached to the diabetes sufferer in order to collect continuous readings of the electrocardiogram. Both the holter monitor and CGMS gold were activated simultaneously to ensure accurate comparisons between biological signal recordings. This procedure was performed on a sample population of six volunteers, described in Table 5.2, diagnosed with Type 1 diabetes who each wore the devices for an entire twenty-four hour period.

Table 5.2: Demographics of subjects with Type 1 diabetes

Subjects w/ Diabetes	Age	Sex	Race
Subject 1	**47**	**Male**	**Caucasian (Hispanic)**
Subject 2	**24**	**Female**	**Caucasian (non Hispanic)**
Subject 3	**35**	**Female**	**Caucasian (non Hispanic)**
Subject 4	**56**	**Female**	**Caucasian (non Hispanic)**
Subject 5	**72**	**Male**	**Caucasian (Hispanic)**
Subject 6	**21**	**Male**	**Caucasian (Hispanic)**

The Continuous Glucose Monitoring System (CGMS) Gold by MiniMed was used to collect glucose concentration levels in the six volunteers diagnosed with Type 1 diabetes. The glucose monitor was designed for long term data collection and used a small sensor that inserted into the abdomen or around the fatty areas on the lower torso. A registered nurse and employee of the University of Texas at El Paso working at the student health center volunteered their time to perform the procedure of inserting the CGMS sensor into the subject. The insertion procedure required the use of a needle to position the flexible glucose sensor under the skin. The nurse used the Senserter device to inject the glucose sensor into the skin at a forty-five degree angle. After insertion, the needle portion was immediately removed leaving only the flexible and small sensor under the skin. The nurse placed tape specially designed for holding such types of catheters in

place. The nurse then connected the CGMS device to the sensor and placed the device on the belt of the subject.

After the CGMS was securely fastened against the subject, pressing the red power button turned on the device. The next step was to press the select button until the word CLEAR appeared on the screen. The Activate button was then pressed to clear any memory left in the device. Next, the Select button was pressed until the word INIT appeared on the screen. By pressing the Activate button, the device was initialized. A countdown from sixty minutes began. After the sixty minute countdown finished, it would be time to input the first calibration glucose value.

The OneTouch Ultra glucose monitor was used for the calibration process of the CGMS. The volunteers were accustomed to testing their blood every day and knew the procedure to acquiring glucose measurements using the glucose monitor. A basic demonstration on the use of the OneTouch Ultra device was provided to those not familiar with the use of the device. The subjects were instructed to swab the finger once with an alcohol pad. While the alcohol dried on the finger, a lancet was inserted into the spring loaded lancet device. The device was then pressed up against the tip of the disinfected finger during which the release button on the lancet device was pressed and the sharp lancet poked a small hole into the fingertip. The lancet was then removed from the lancet inserting device and disposed of into a sharps container. The finger tip was then massaged slightly to allow a bead of blood to form. Once the bead of blood was formed, a OneTouch Ultra blood strip was inserted into the glucose monitor. The strip was then touched up against the bead of blood after which the blood immediately would enter the strip's receptacle. In five seconds, the glucose monitor would provide a numerical value of the glucose concentration in the blood. The value was then manually inputted into the CGMS device.

The value appearing on the OneTouch Ultra glucose monitor was inputted into the CGMS by pressing the Select button followed by the Activate button. Using the up and down arrows, the glucose value was scrolled to. After the proper value was found, the Activate button was pressed to enter the value. This initial calibration started the recording process of the CGMS device. The subject was instructed to perform the blood test using the OneTouch Ultra and input the value into the CGMS every time before eating and before going to sleep at night. This was performed for a twenty-four hour period. It was crucial that the exact time during which the sixty minute countdown finished was recorded. This would be needed to match recording times with the holter monitor.

The second part of the experimental method for the subjects diagnosed with diabetes was to acquire the electrocardiogram. This was accomplished by using the holter monitor. The five electrodes were prepared by attaching them to the holter monitor wires first. The locations for the electrodes were shaven if any hair was present. The electrodes were placed as described in Figure 4-14. After placement of the electrodes, the batteries (two AA batteries) were inserted into the device to begin the calibration process. The holter turned on immediately after the batteries were inserted and three ECG tracings could be seen on the screen. The tracings were there to insure that the electrodes were properly attached to the subject's torso. Proper ECG tracings had high and distinctive QRS complexes. If the complexes were not there then the electrodes were replaced or moved around until proper tracings appeared on the screen. After fifteen minutes passed, the tracings on the screen would disappear and the word RECORDING would flash on the screen. This indicated that the holter was now recording the ECG data to the compact flash card located in the holter device. It was crucial that the exact time during which the holter monitor turned on was recorded in order to match the times with the CGMS.

After both devices were securely fastened to the subject, the subject was instructed not to take a shower, do perform the blood glucose tests as previously mentioned, and return the devices after a twenty-four hour period passed. The CGMS sensor could be removed by the subject or have the nurses at the student health center remove it. In most cases, the volunteer removed the sensor themselves with no pain. After the devices were acquired back from the volunteers, the data was inputted into the desktop computer.

The CGMS was turned on and placed onto the CGMS comstation which was connected to the computer via a serial port. The glucose data was then transferred to the desktop and saved under the subject's name. The holter monitor's batteries were removed and the compact flash card was then taken out. The card was inserted into the card reader attached to the desktop USB port. The Cardiocard software was then opened and the Holter acquisition button was clicked to read the ECG data on the compact flash card and save it to the PC memory. The ECG data would immediately appear on the computer screen and be saved as an ASCII file. The file was then opened using NOTEPAD. The glucose measurements acquired by the CGMS were then displayed on the computer screen by running the CGMS solutions software and opening the desired glucose file. The glucose record could be viewed on a graph or on a spreadsheet. The spreadsheet was used because it provided the exact times and levels of glucose concentrations in the blood. The spreadsheet was visually inspected and the times during which glucose levels were above 200 mg/dL, below 60 mg/dL, and between 90 and 110 mg/dL were written down. The times were evaluated in ten minute increments. The ten minute increments were then associated with the times of the ECG tracings. For example, the glucose levels between 2:00 am and 2:10 am were below 60 mg/dL. The next step would be to look at the ECG tracing recorded between 2:00 am and 2:10 am. The ASCII file possessed the time stamps for the ECG so it was a

method of searching for the time interval, copying the corresponding ECG data, and pasting the data onto a new notepad document and naming it ECG Hypo _1. This procedure was repeated for every ten minute interval that was desired for analyses. The final product of this procedure resulted in three categories of files (ECG Hypo_#, ECG Hyper_#, and ECG Normal_#) with a minimum of fifteen .txt files in each category. However, it should be noted that during the recording process of the ECG, wires that became disconnected or sudden movements by the subject may have caused undesirable amounts of noise and distorted ECG tracings. The ten minute interval ECG tracings selected were first visually scanned on the computer to make certain that major noise artifacts were not present or minimal and that QRS complexes were clearly distinguishable.

The HRV conversion program written in LabVIEW was used to convert the ECG data into HRV data. After pressing the run button, a prompt window asked to select the biosignal for conversion. After the proper file was selected, the signal was converted to heart rate variability and the resulting data was saved as a .txt file for the purpose of future analysis. The HRV data was then viewed in Notepad to make sure that errors in the data were minimal or absent. This was done by performing a search for any data points that were outside acceptable ranges for the particular HRV file. For example, if the beat to beat intervals in the file were ranging mostly from 0.6 to 1.4 seconds, it was desirable to eliminate any data points that were clearly beyond these limits. A data point of 0.2 seconds would be eliminated as well as a data point such as 1.9 seconds. This was performed manually using the FIND function in Notepad to assure quality HRV files were analyzed for this study. The manually edited HRV files were once again saved.

The newly acquired HRV data was analyzed using the HRV analysis program written in LabVIEW. When the program was run, a prompt asked to select the desired HRV file to analyze.

After being selected, the GUI immediately provided time, frequency, and non linear information about the HRV data. The information was recorded onto an excel file. Twenty-five various parameters of HRV were collected for determining relationships between the HRV and glucose measurements collected earlier. The measurements include average, rms, standard deviation, variance, kurtosis, median, mode, skewness, maximum, minimum, RMSSD, NN50, pNN50, RR triangular index, TINN, SD1 and SD2 from the Poincare' plots, HF fft, LF fft, LF/HF fft, HF ar, LF ar, LF/HF ar, VLF fft, and approximate entropy.

The next step was to determine if any patterns could be recognized in the HRV data as sugar levels changed. Each diabetes sufferer's data was separated into three categories: hypoglycemic (glucose less than 70 mg/dL, normal (glucose between 70 and 180 mg/dL), and hyperglycemic (glucose above 180 mg/dL). These parameter measurements can be viewed in Appendix A.5. Boxplots evaluating the range of data during each level of glucose would also be constructed. This would result in twenty-five box plots for each diabetes sufferer. These plots can be viewed in Appendix A.6. Three plots would also be generated to visually examine the variances of all twenty-five HRV parameters within the entire sample population of volunteers with diabetes just as was done for those without the disease. However in this case, a hypoglycemic plot and hyperglycemic plot would be added along with the normal plot. Each plot would visually compare variances of HRV parameter values in each glucose category for the subjects with diabetes.

Chapter 6 : Results

6.1 Comparisons between ECG and PPG derived HRV

The analysis of ECG and PPG derived HRV from the two healthy test subjects resulted in various measurements, Poincare' plots, and power spectral density plots. The plots and measurements provided enough information to determine that ECG and PPG provided similar HRV data in healthy individuals.

6.1.1 Healthy Subject 1 HRV Analysis

The analysis of all three electrocardiogram and photoplethysmograph recordings of the subject 1 are explored within Table 6-1. Table 6-2 reveals the correlation coefficients of the HRV power spectral densities within PPG and ECG sources. Table 6-2 reveals the correlation coefficients of the HRV power spectral densities and tachograms between PPG and ECG derived HRV. Comparisons among power spectral density plots can be viewed in Figures 6-1 through 6-5. A comparison between ECG HRV and PPG HRV poincare' plots can be viewed in Figures 6-6 and 6-7. The table values and overlapping plots reveal indisputable similarities in time, frequency, and non linear properties of ECG and PPG derived HRV in healthy individual 1.

Table 6.1: Subject 1 ECG and PPG HRV comparisons

Subject		**Sex**	**Age**			
1		Male	24			
			ECG HRV 0	**ECG HRV 1**	**ECG HRV 2**	**Avg**
TIME	**Min RR (s)**		0.81	0.82	0.76	.80
	Max RR (s)		1.22	1.16	1.17	1.18
	Mean RR (s)		1.06	1.01	1.00	1.02
	Mode RR (s)		1.08	1.02	1.00	1.03
	Stand Dev (s)		0.061	0.057	0.070	0.063
STAT	**Variance**		0.00	0.00	0.00	0.00
	Skewness		-0.32	-0.41	-0.52	-0.42
	Kurtosis		3.45	2.94	3.21	3.20
	ApEn		1.052	1.055	1.040	1.049
FREQ	**Total Pwr (s^2/Hz)**		1.08	1.03	1.10	1.07
	HF Power (n.u.)		0.44	0.41	0.41	0.42
	LF Power (n.u.)		0.62	0.64	0.64	0.63
	LF/HF		1.41	1.56	1.56	1.51

		PPG HRV 0	**PPG HRV 1**	**PPG HRV 2**	**Avg**
TIME	**Min DD (s)**	0.82	0.82	0.76	.80
	Max DD (s)	1.22	1.17	1.17	1.19
	Mean DD (s)	1.06	1.01	1.00	1.02
	Mode DD (s)	1.08	1.02	1.00	1.03
	Stand Dev (s)	0.062	0.058	0.071	0.064

S T A T	**Variance**	0.00	0.00	0.01	0.00
	Skewness	-0.30	-0.39	-0.50	-0.40
	Kurtosis	3.32	2.93	3.18	3.14
	ApEn	1.053	1.055	1.040	1.049
F R E Q	**Total Pwr (s^2/Hz)**	1.13	1.05	1.07	1.08
	HF Power (n.u.)	0.44	0.39	0.42	1.25
	LF Power (n.u.)	0.61	0.64	0.64	0.63
	LF/HF	1.38	1.64	1.52	1.51

Table 6.2: Subject 1 ECG (PPG) vs ECG (PPG) HRV cross correlations

		Total Power	**HF**	**LF**
ECG	**HRV 0 vs HRV 1**	0.95	0.94	0.94
	HRV 1 vs HRV 2	0.98	0.92	0.97
	HRV 2 vs HRV 0	0.95	0.90	0.99
PPG	**HRV 0 vs HRV 1**	0.96	1.00	0.91
	HRV 1 vs HRV 2	0.95	0.94	0.94
	HRV 2 vs HRV 0	0.93	0.90	0.96

Table 6.3: Subject 1 ECG vs PPG HRV cross correlations

	Tachogram	**Total Power**	**HF**	**LF**
PPG HRV 0 vs ECG HRV 0	0.99	0.99	0.99	0.99
PPG HRV 1 vs ECG HRV 1	0.99	0.99	0.99	0.99

PPG HRV 2 vs ECG HRV 2	0.99	0.99	0.99	0.99

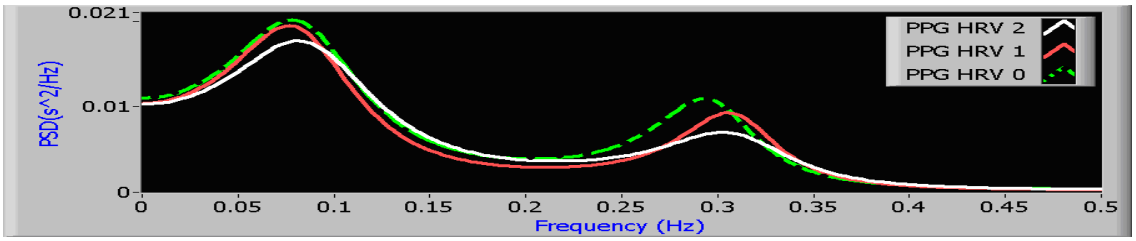

Figure 6-1: Subject 1 comparison of HRV Power Spectral Densities (PPG0, PPG1, PPG2)

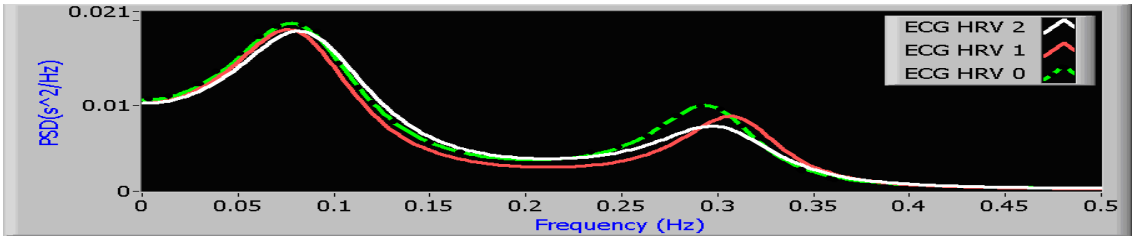

Figure 6-2: Subject 1 comparison of HRV Power Spectral Densities (ECG0, ECG1, ECG2)

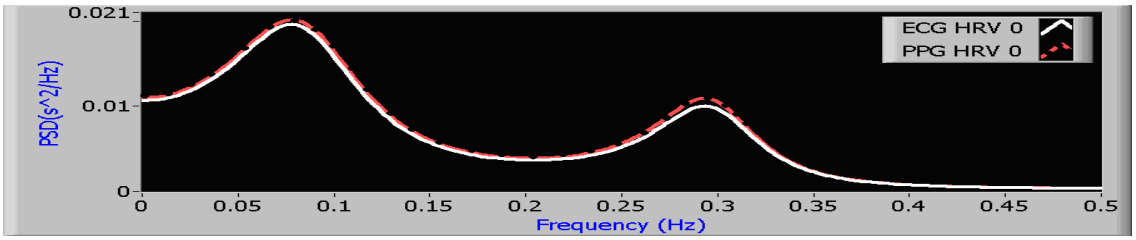

Figure 6-3: Subject 1 comparison of HRV Power Spectral Densities (ECG0 & PPG0)

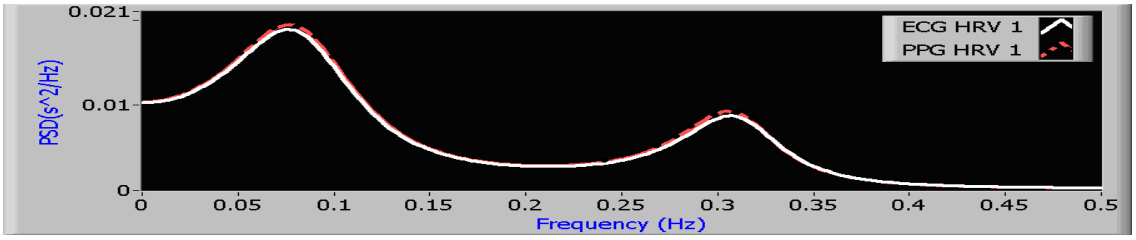

Figure 6-4: Subject 1 comparison of HRV Power Spectral Densities (ECG1 & PPG1)

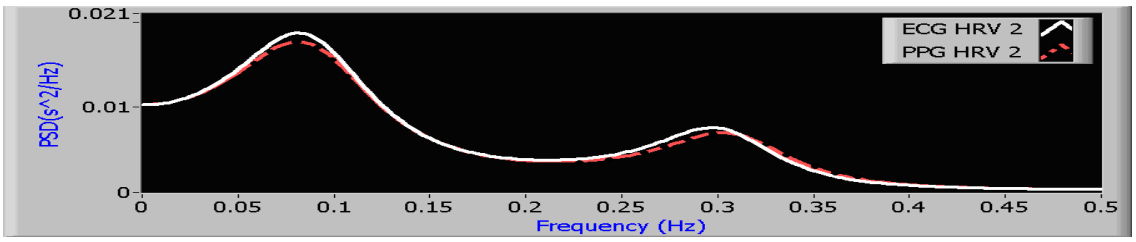

Figure 6-5: Subject 1 comparison of HRV Power Spectral Densities (ECG2 & PPG2)

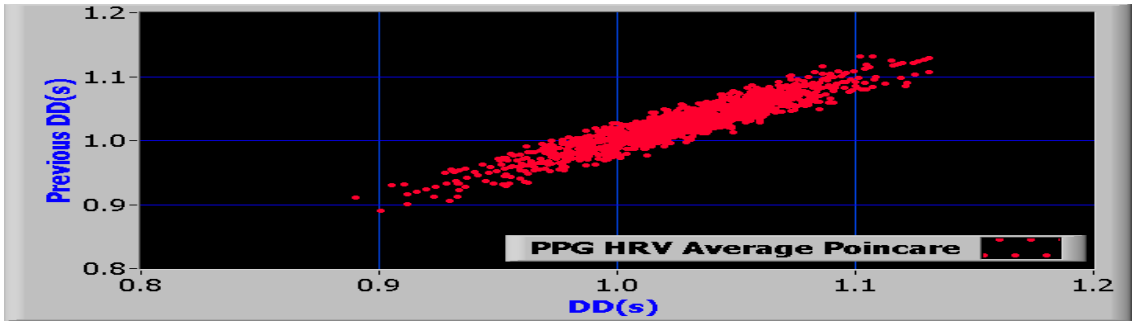

Figure 6-6: Subject 1 Average Poincare' plot of all three PPG HRV

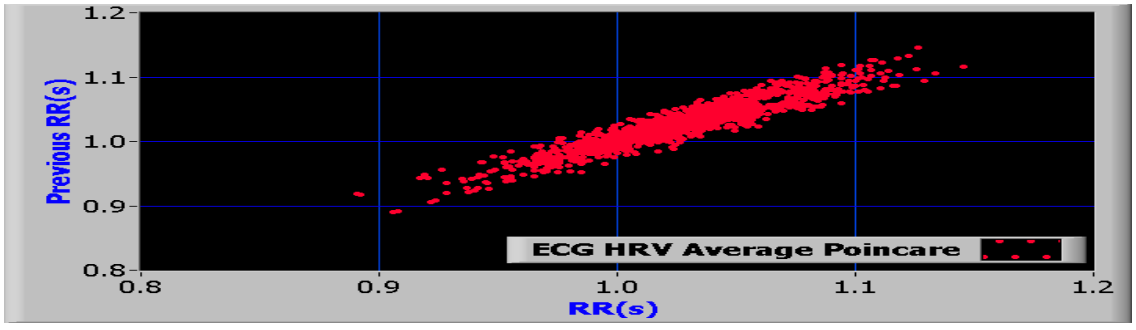

Figure 6-7: Subject 1 Average Poincare' plot of all three ECG HRV

6.1.2 Healthy Subject 2 HRV Analysis

The analysis of all three electrocardiogram and photoplethysmograph recordings of the subject 2 are explored within Table 6-4. Table 6-5 reveals the correlation coefficients of the

HRV power spectral densities within PPG and ECG sources. Table 6-6 reveals the correlation coefficients of the HRV power spectral densities and tachograms between PPG and ECG derived HRV. Comparisons among power spectral density plots can be viewed in Figures 6-8 through 6-12. A comparison between ECG HRV and PPG HRV poincare' plots can be viewed in Figures 6-13 and 6-14. The table values and overlapping plots reveal indisputable similarities in time, frequency, and non linear properties of ECG and PPG derived HRV in healthy individual 2.

Table 6.4: Subject 2 ECG and PPG HRV comparisons

Subject	**Sex**	**Age**			
2	Female	25			
		ECG HRV 0	**ECG HRV 1**	**ECG HRV 2**	**Avg**
TIME	**Min RR (s)**	0.82	0.73	0.78	0.78
	Max RR (s)	1.22	1.20	1.23	1.22
	Mean RR (s)	1.06	1.03	1.02	1.04
	Mode RR (s)	1.11	1.07	1.04	1.07
	Stand Dev(s)	0.07	0.07	0.07	0.07
STAT	**Variance**	0.01	0.01	0.01	0.01
	Skewness	-0.96	-1.52	-0.73	1.07
	Kurtosis	3.93	5.88	4.42	4.74
	ApEn	1.03	1.02	1.02	1.02
FREQ	**Total Pwr (s^2/Hz)**	2.01	1.97	1.27	1.75
	HF Power (n.u.)	0.52	0.41	0.49	.47
	LF Power (n.u.)	0.53	0.63	0.59	0.58
	LF/HF	1.01	1.54	1.20	1.25

		PPG HRV 0	PPG HRV 1	PPG HRV 2	Avg
TIME	**Min DD (s)**	0.83	0.72	0.71	0.75
	Max DD (s)	1.22	1.19	1.23	1.21
	Mean DD (s)	1.06	1.03	1.02	1.04
	Mode DD (s)	1.10	1.06	1.03	1.06
	Stand Dev (s)	0.07	0.08	0.07	0.07
STAT	**Variance**	0.01	0.01	0.01	0.01
	Skewness	-0.91	-1.46	-0.75	-1.04
	Kurtosis	3.73	5.59	4.80	4.71
	ApEn	1.03	1.02	1.03	1.03
FREQ	**Total Pwr (s^2/Hz)**	2.14	2.13	1.49	1.92
	HF Power (n.u.)	0.55	0.45	0.55	0.52
	LF Power (n.u.)	0.51	0.61	0.54	0.55
	LF/HF	0.93	1.35	0.98	1.09

Table 6.5: Subject 2 ECG (PPG) vs ECG (PPG) HRV cross correlations

		Total Power	HF	LF
ECG	**HRV 0 vs HRV 1**	0.99	0.99	0.99
	HRV 1 vs HRV 2	0.98	0.97	0.98
	HRV 2 vs HRV 0	0.99	1.00	0.98
PPG	**HRV 0 vs HRV 1**	0.99	0.98	0.99
	HRV 1 vs HRV 2	0.97	0.95	0.99
	HRV 2 vs HRV 0	0.98	1.00	0.98

Table 6.6: Subject 2 ECG vs PPG HRV cross correlations

	Tachogram	Total Power	HF	LF
PPG HRV 0 vs ECG HRV 0	0.99	0.99	0.99	0.99
PPG HRV 1 vs ECG HRV 1	0.99	0.99	0.99	0.99
PPG HRV 2 vs ECG HRV 2	0.99	1.00	1.00	1.00

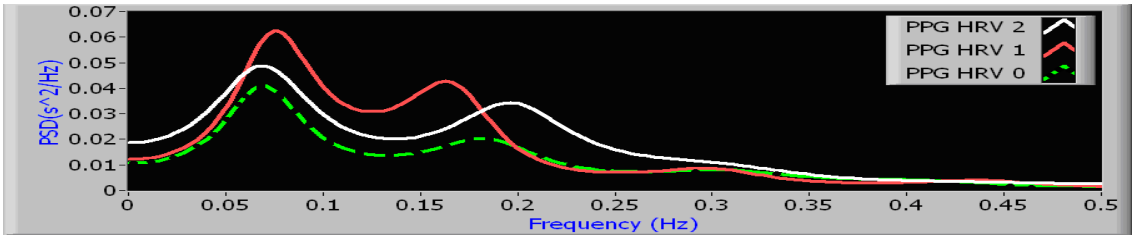

Figure 6-8: Subject 2 comparison of HRV Power Spectral Densities (PPG0, PPG1, PPG2)

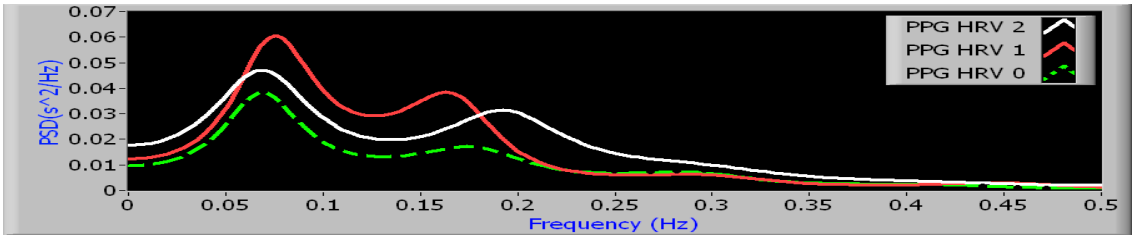

Figure 6-9: Subject 2 comparison of HRV Power Spectral Densities (ECG0, ECG1, ECG2)

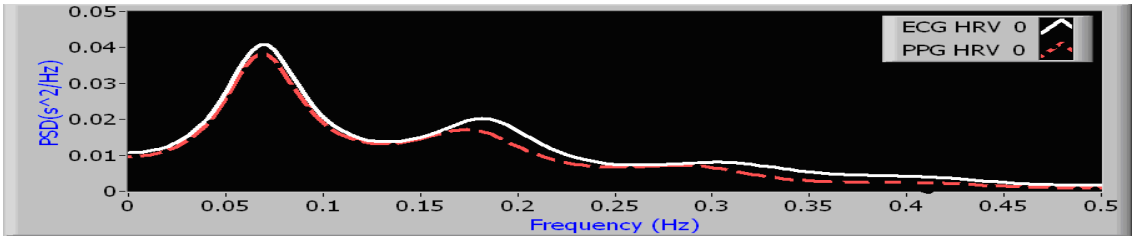

Figure 6-10: Subject 2 comparison of HRV Power Spectral Densities (ECG0 & PPG0)

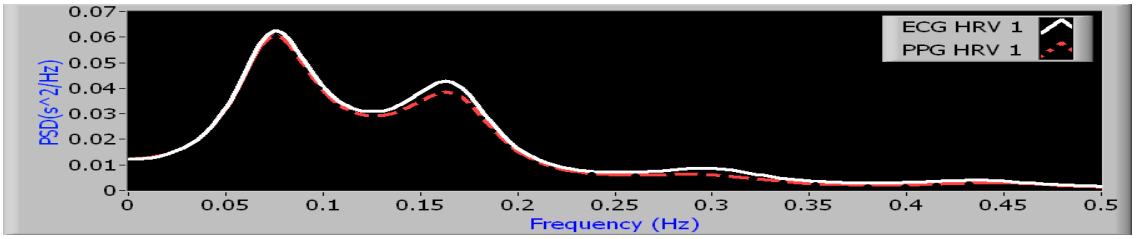

Figure 6-11: Subject 2 comparison of HRV Power Spectral Densities (ECG1 & PPG1)

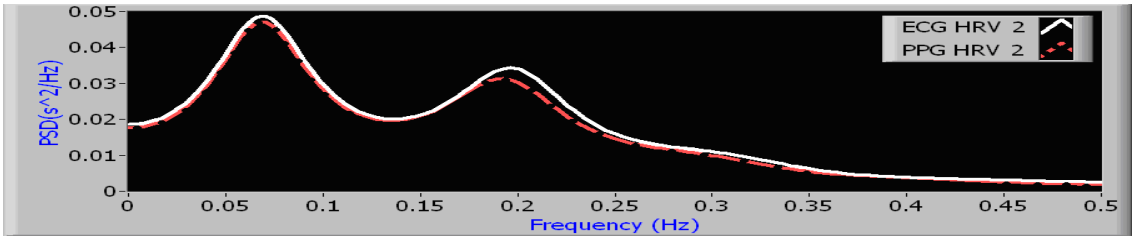

Figure 6-12: Subject 2 comparison of HRV Power Spectral Densities (ECG2 & PPG2)

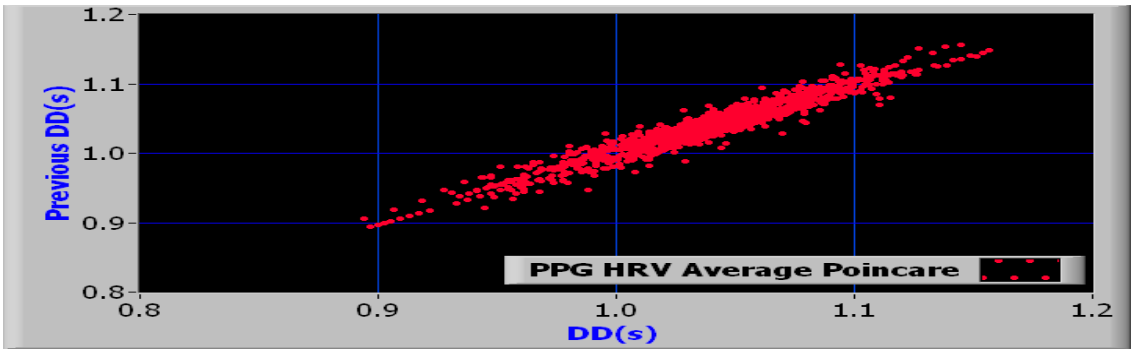

Figure 6-13: Subject 2 Average Poincare' plot of all three PPG HRV

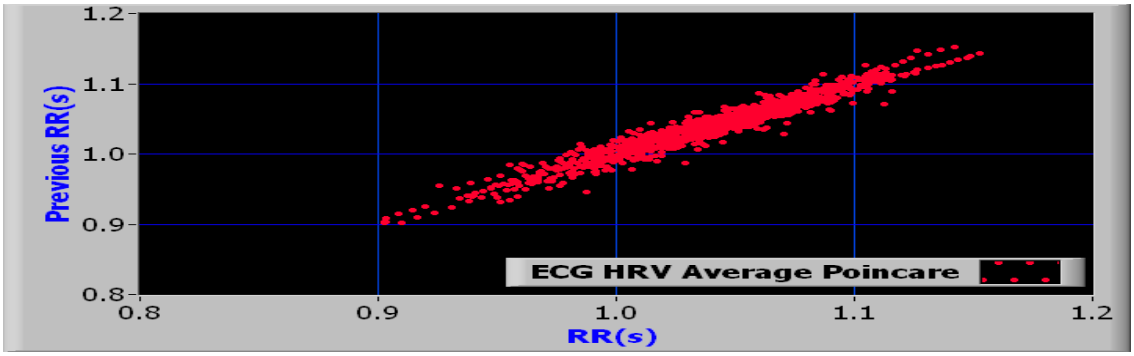

Figure 6-14: Subject 2 Average Poincare' plot of all three ECG HRV

6.2 Comparing between HRV and glucose levels in volunteers without diabetes

The population sample average and standard deviation of the various HRV parameters collected from the subjects without diabetes were evaluated and graphed (Figure 6-15) to determine levels of variance during normal glucose levels ranging from 70 to 150 mg/dL. Coefficients of variance were calculated to numerically determine the parameters with lowest variance during normal glucose levels (Figure 6-16) in those without diabetes.

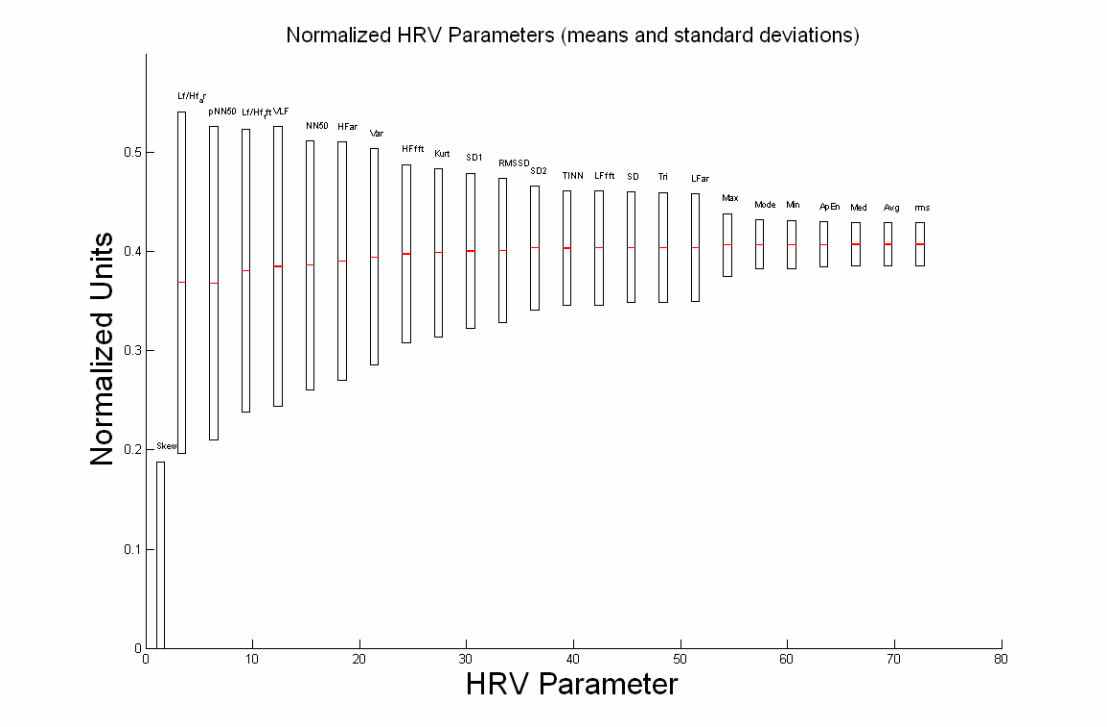

Figure 6-15: Normalized HRV parameters (means and standard deviations)

Table 6.7: HRV parameter coefficients of variance

HRV Parameter	Coefficient of Variance (%)
Skewness	260
LF_HF_ar	46.6
pNN50	42.9
LF_HF_fft	37.5
VLF_fft	36.6
NN50	32.4
HF_ar	30.7
Variance	27.5
HF_fft	22.6
Kurtosis	21.2
SD1	19.5
RMSSD	18.0
SD2	15.4
TINN	14.3
LF_fft	14.2
SD	13.7
Triangular	13.7
LF_ar	13.3
Maximum	7.7
Mode	6.0
Minimum	5.9
ApEn	5.6
Median	5.3
Average	5.2
RMS	5.2

6.3 Comparing HRV and glucose levels in volunteers diagnosed with Type 1 Diabetes

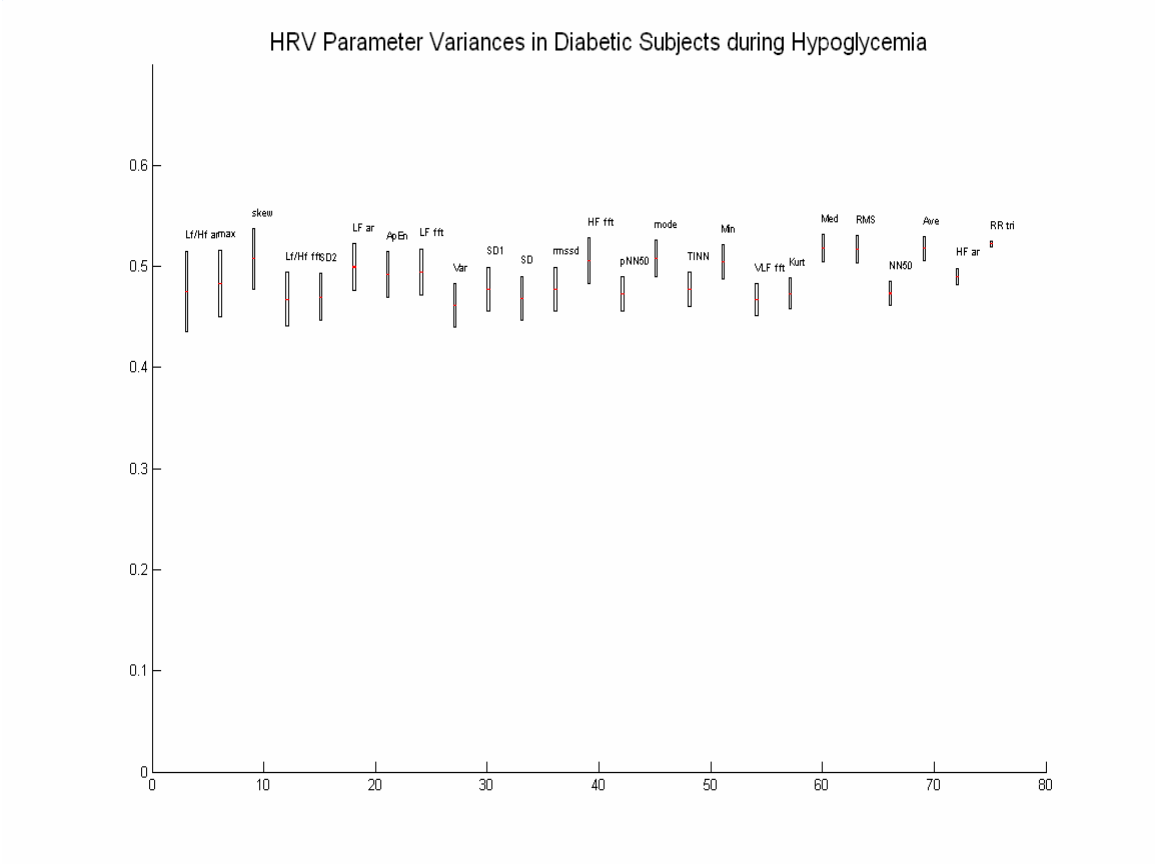

Figure 6-16: HRV Parameter Variances in Diabetics during Hypoglycemia

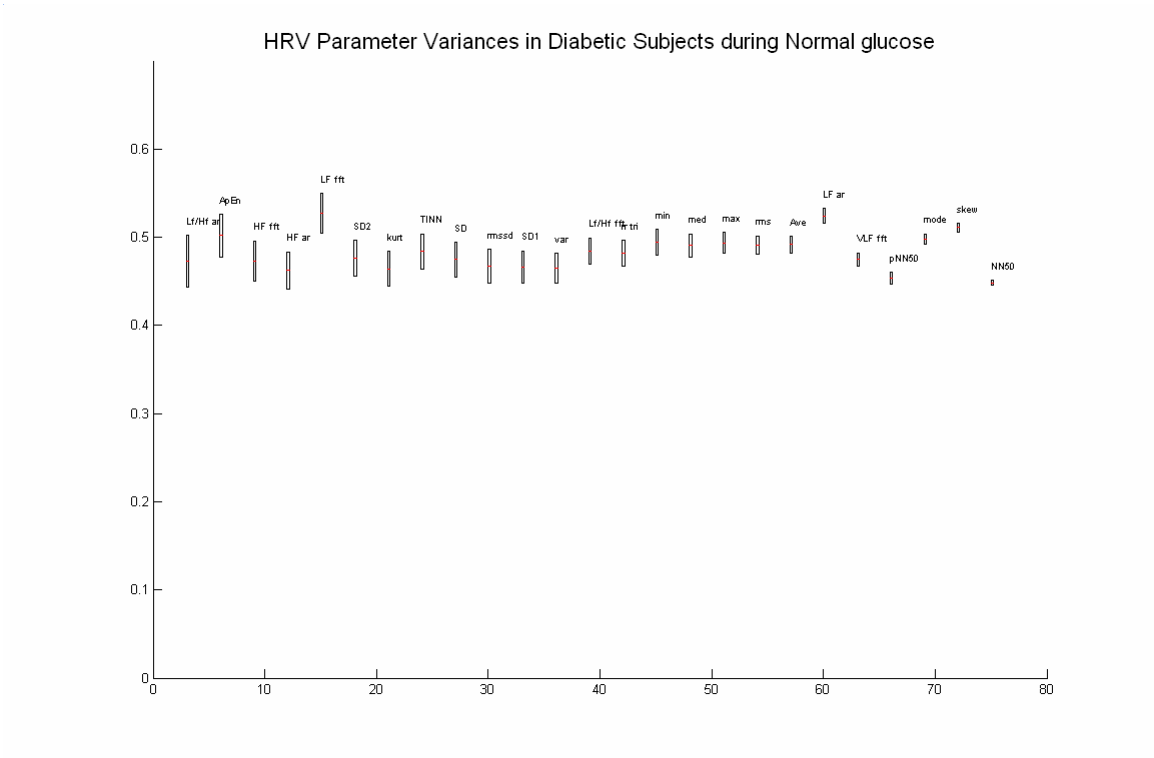

Figure 6-17: HRV Parameter Variances in Diabetics during Normal Glucose levels

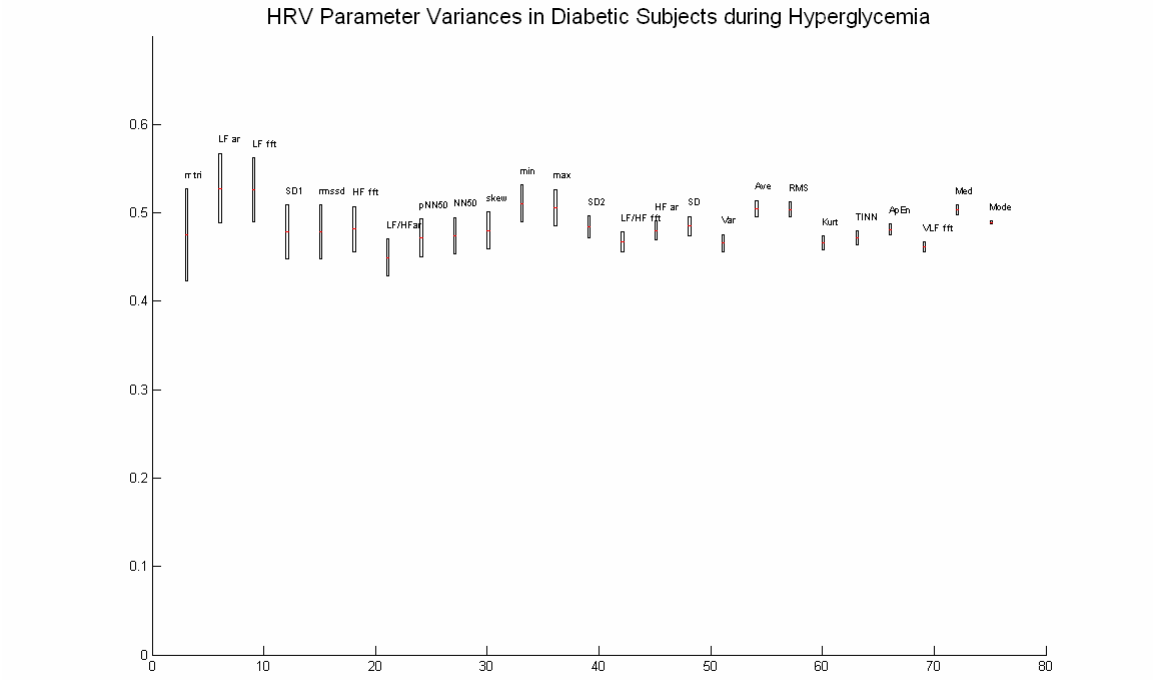

Figure 6-18: HRV Parameter Variances in Diabetics during Hyperglycemia

Table 6.8: Coefficients of Variance during Hypoglycemia

Coefficients of Variance (%) during Hypoglycemia	
Power(AR) LF/HF	8.4
maximum	6.8
skewness	5.8
Power(FFT) LF/HF	5.6
SD2(poincare')	5.0
Power(AR) LF	4.6
ApEn	4.6
Power(FFT) LF	4.6
Var	4.6
SD1(poincare')	4.5
SD	4.5
RMSSD	4.5
Power(FFT) HF	4.5
pNN50	3.6
mode	3.5
TINN	3.4
min	3.3
Power(FFT) VLF	3.3
Kurtosis	3.1
Median	2.6
RMS	2.5
NN50	2.4
Average	2.2
Power(AR) HF	1.6
RR tri indx	0.5

Table 6.9: Coefficients of Variance during Normal Glucose levels

Coefficients of Variance (%) during Normal Glucose	
Power(AR) LF/HF	6.2
ApEn	4.8
Power(FFT) HF	4.8
Power(AR) HF	4.5
Power(FFT) LF	4.3
SD2(poincare')	4.3
Kurtosis	4.2
TINN	4.1
SD	4.1
RMSSD	4.0
SD1(poincare')	3.8
Var	3.5
Power(FFT) LF/HF	3.0
RR tri indx	3.0
min	2.9
Median	2.6
maximum	2.4
RMS	2.0
Average	1.9
Power(AR) LF	1.6
Power(FFT) VLF	1.6
pNN50	1.5
mode	1.1
skewness	1.0
NN50	0.5

Table 6.10: Coefficients of Variance during Hyperglycemia

Coefficients of Variance (%) during Hyperglycemia	
RR tri indx	10.9
Power(AR) LF	7.4
Power(FFT) LF	6.9
SD1(poincare')	6.4
RMSSD	6.4
Power(FFT) HF	5.2
Power(AR) LF/HF	4.6
pNN50	4.5
NN50	4.3
skewness	4.2
min	4.0
maximum	4.0
SD2(poincare')	2.5
Power(FFT) LF/HF	2.3
Power(AR) HF	2.3
SD	2.2
Var	2.1
Average	1.8
RMS	1.7
Kurtosis	1.6
TINN	1.6
ApEn	1.2
Power(FFT) VLF	1.1
Median	1.1
mode	0.4

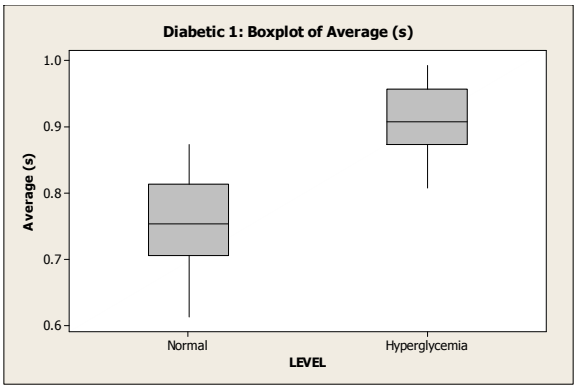

Figure 6-19: Diabetic 1 Average Boxplot

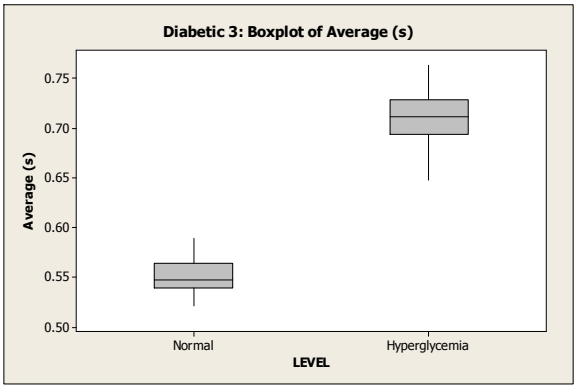

Figure 6-20: Diabetic 3 Average Boxplot

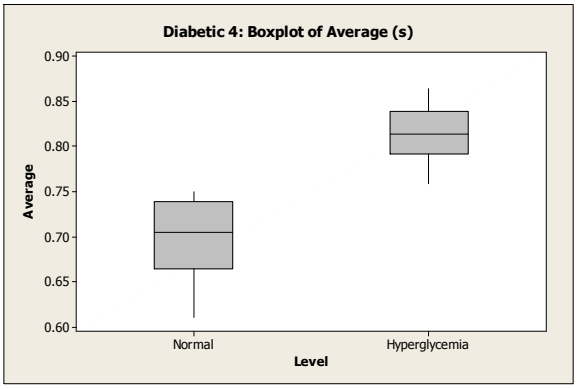

Figure 6-21: Diabetic 4 Average Boxplot

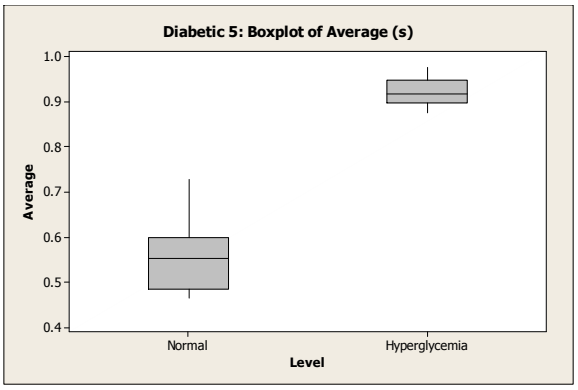

Figure 6-22: Diabetic 5 Average Boxplot

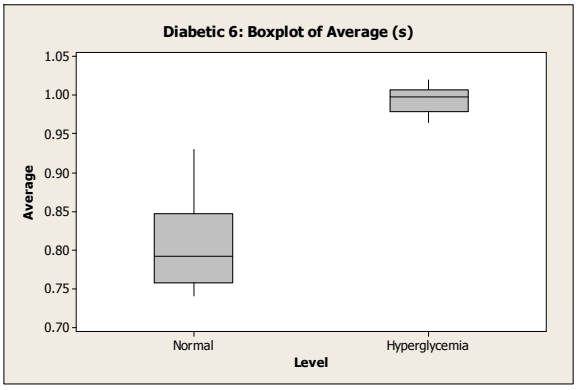

Figure 6-23: Diabetic 6 Average Boxplot

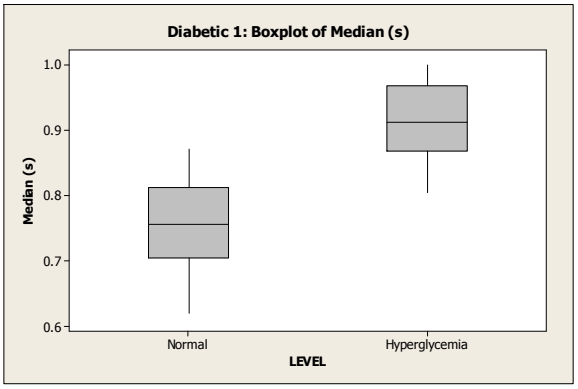

Figure 6-24: Diabetic 1 Median Boxplot

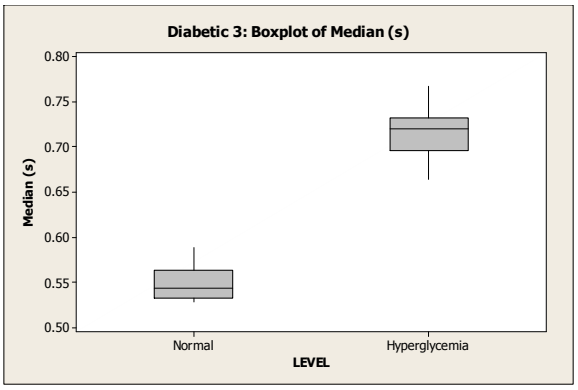

Figure 6-25: Diabetic 3 Median Boxplot

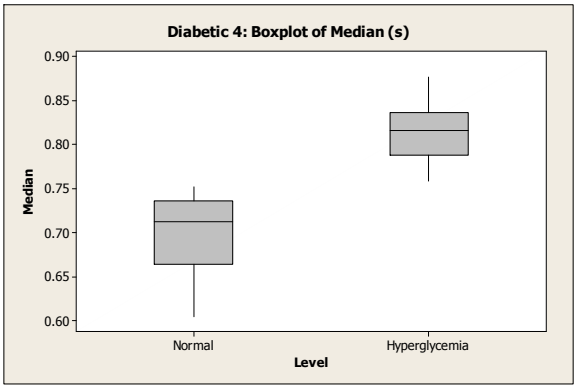

Figure 6-26: Diabetic 4 Median Boxplot

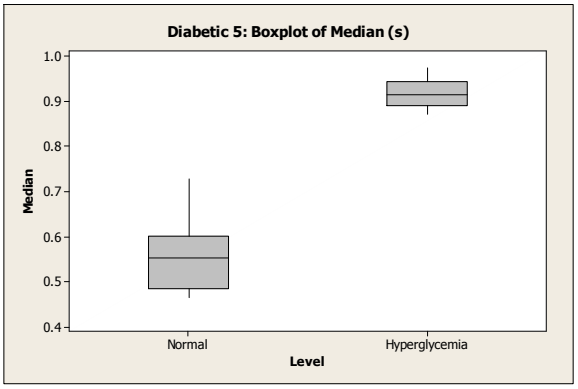

Figure 6-27: Diabetic 5 Median Boxplot

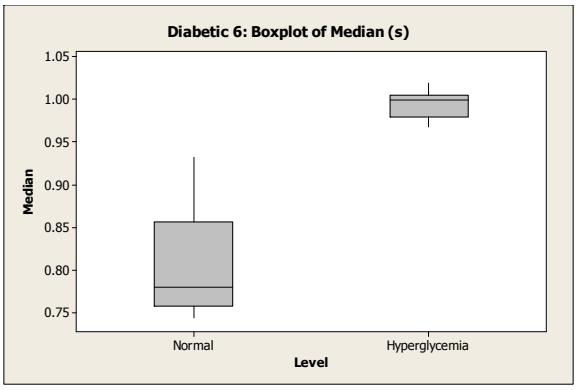

Figure 6-28: Diabetic 6 Median Boxplot

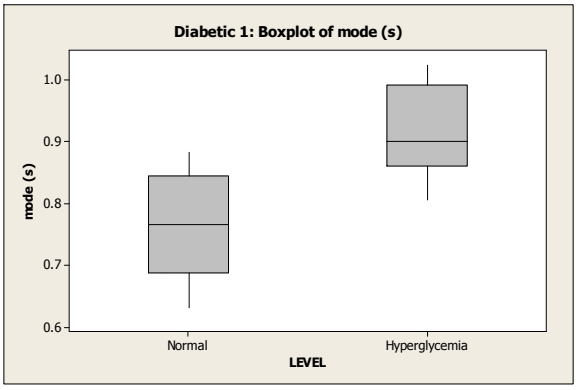

Figure 6-29: Diabetic 1 Mode Boxplot

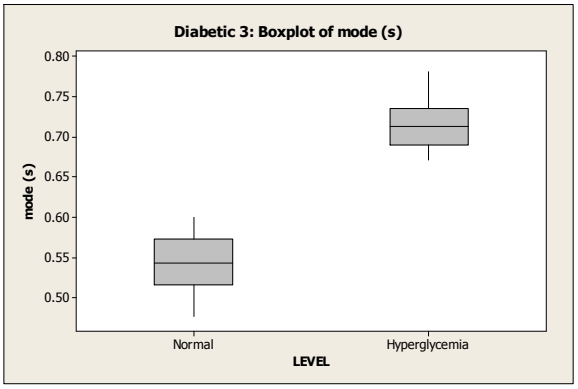

Figure 6-30: Diabetic 3 Mode Boxplot

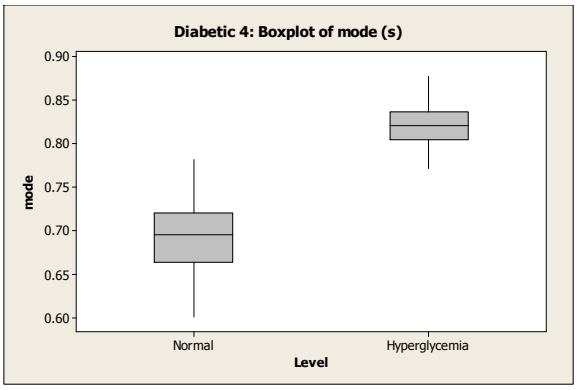

Figure 6-31: Diabetic 4 Mode Boxplot

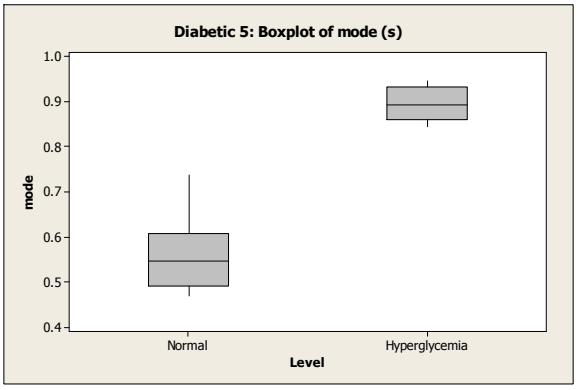

Figure 6-32: Diabetic 5 Mode Boxplot

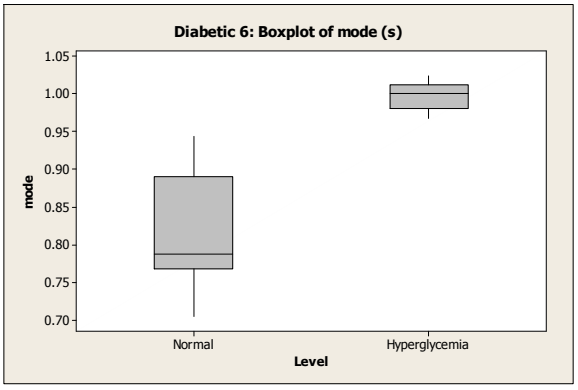

Figure 6-33: Diabetic 6 Mode Boxplot

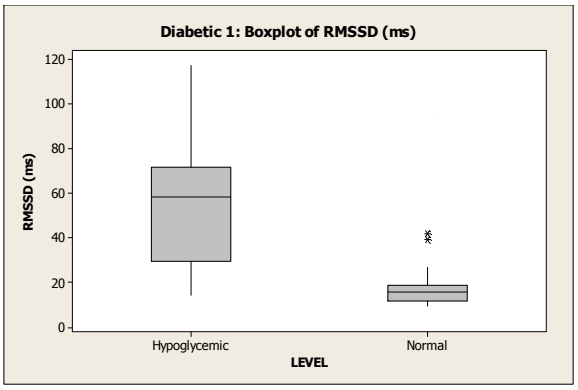

Figure 6-34: Diabetic 1 RMSSD Boxplot

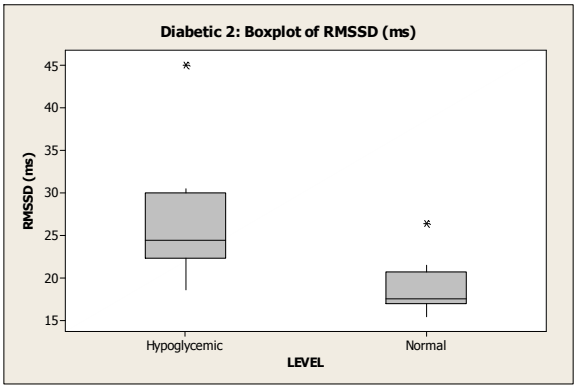

Figure 6-35: Diabetic 2 RMSSD Boxplot

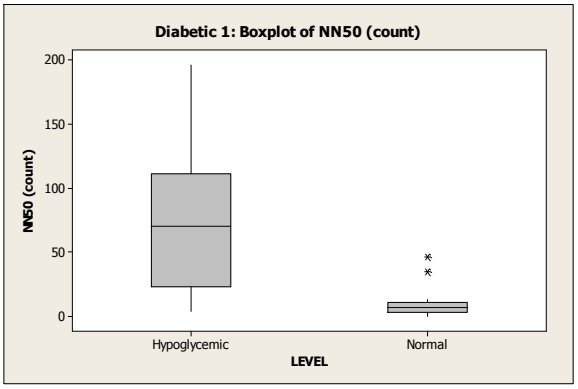

Figure 6-36: Diabetic 1 NN50 Boxplot

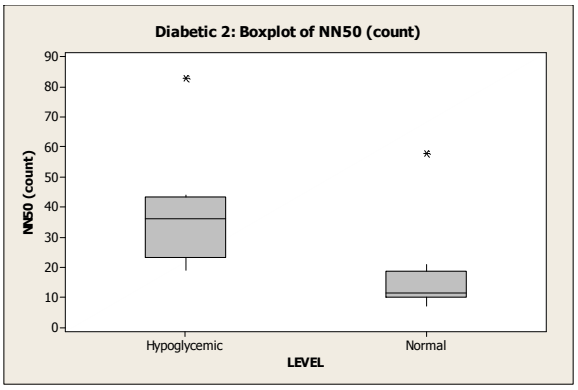

Figure 6-37: Diabetic 2 NN50 Boxplot

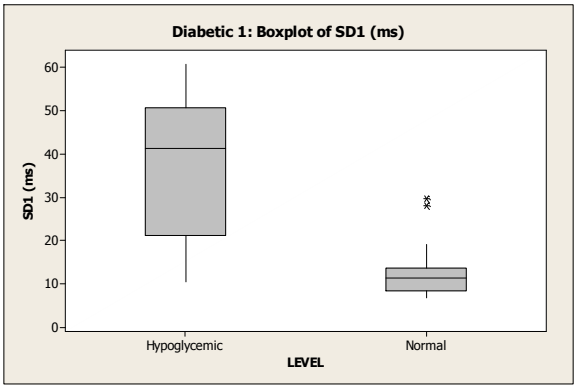

Figure 6-38: Diabetic 1 SD1 Boxplot

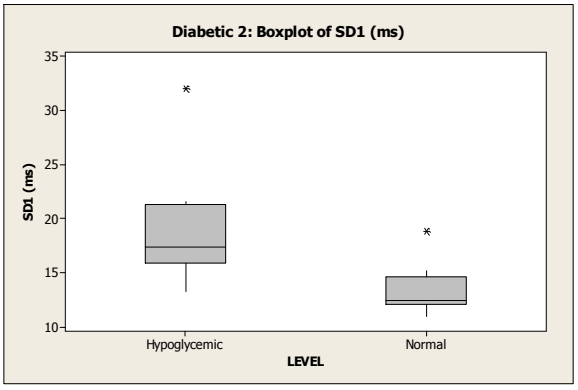

Figure 6-39: Diabetic 2 NN50 Boxplot

Chapter 7 : Discussion

7.1 Comparisons between ECG and PPG derived HRV

7.1.1 Healthy Subject 1 HRV Analysis

Looking at Subject 1, a 24-year old male, the HF and LF peaks in Figure 6-1 to Figure 6-5 are clearly distinguishable. The repeated tests showed similar results. The probability distribution of the HRV data from subject 1 showed a kurtosis above 3, classifying it as leptokurtic. Accompanied by a negative skewness near zero, it is observed that the probability distribution is clustered to the right of the mean and peaks about the mean. The repeated data sets from the ECG data produced similar results. The similarity in the repeated tests is observed in Table 6-1 where the correlation coefficients between each of the ECG HRVs are very close to 1, indicating almost perfect matches between the repeated tests. This can be observed in Figures 6-1 and 6-2 where the PSD of each of the repeated signals overlap. These results are indicative of excellent measurement repeatability and dependability for the system. Time, statistical, and frequency values in Table 6-1 show that the PPG method is a reliable means in derivation of the HRV signal. The HRV data derived from the PPG method are very similar to those derived from the ECG method. This similarity can be clearly viewed in detail in Table 6-3 where the correlation coefficients are used to compare PPG HRV with corresponding ECG HRV. The coefficients are only 1% away from 1 indicating that the HRV data acquired from both methods are practically perfect matches. Figures 6-3 to 6-5 show the similarities in power spectra of both HRVs. In Figures 6-6 and 6-7, the same similarities can be observed through common Poincare' plots. The average Poincare' of all three PPG HRV and the average of all ECG HRV cluster within the same region. The dots, indicating the heart rate intervals, cluster together in a common

region also indicate that the peak detection algorithm was accurate at detecting every peak in the ECG and PPG signals. For subject 1, the PPG method provided the equivalent HRV data as the ECG method.

7.1.2 Healthy Subject 2 HRV Analysis

The HRV analysis for subject 2, a 25 year old female, resulted in a power spectral density slightly different from subject 1. Both HF and LF peak are clearly distinguishable, however the HF peak in the power spectrum is closer to the LF peak than in this subject. The probability distribution (Table 6-4) is similar for both subjects. This is concentrated to the right of the mean and highly peaked about the mean (leptokurtic). Approximate entropy indicates that subject 2's HRV is more predictable than subject 1's HRV as can be seen in the low ApEn values. Figures 6-8 and 6-9 show the repeatability of the system by displaying the common characteristics in the HRV power spectra derived from both signals. Table 6-5 shows that all three HRV signals derived from the ECG method provide similar results. This similarity is obvious with a 5% maximum difference away from a correlation coefficient of 1. The numerical and graphical results clearly demonstrate the dependability and repeatability of the PDA-based system. Also, the similarity of PPG-derived HRV with ECG-derived HRV (seen in Table 6-6) is apparent with a correlation coefficient only 1% away from 1. Once again, the common Poincare' plots in Figures 6-13 and 6-14 visually demonstrate the matching HRVs derived from both PPG and ECG. PPG and ECG prove once more that they provide equivalent HRV data.

7.2 Comparing between HRV and glucose levels in volunteers without diabetes

The normal blood sugar range of the subjects was 70 mg/dL –150 mg/dL. These were the expected values for normal individuals with no history of diabetes or other glycemic ailments.

After evaluating the population means and standard deviations (Figure 6-15), it was concluded that there were very little variations (coefficients of variation less than 7%) in the maximum, mode, minimum, median, average, and approximate entropy when compared to the rest of the HRV parameters (Table 6-7).

The various HRV parameters for normal individuals were classified according to variation within the entire sample population of 10 subjects. It was concluded that approximate entropy was the favorable parameter because of its low coefficient of variance and its nonlinear properties. The data ranges for ApEn reflect the normal sugar levels. Tests involving volunteers diagnosed with Type 1 diabetes would allow the exploration of how the data ranges of ApEn will change when heart rate variations are recorded during abnormal sugar levels such as those observed during cases of hyperglycemia and hypoglycemia.

A direct correlation between HRV parameters and changing glucose levels could not be determined from the ten subjects without diabetes. HRV parameters measured in the lower end of the normal glucose ranges could not be distinguished from the HRV parameters measured in the upper end of the normal glucose ranges. Since no abnormal ranges were measured in the subjects without diabetes, an attempt was made to separate the normal range into upper, mid, and lower categories. However, this strategy lead to no conclusions, possibly because all the normal ranged glucose values shared common HRV parameters. The three categories of HRV parameters explored during normal glucose levels can be viewed in the boxplots of Appendix A.3. All boxplots overlapped thus demonstrating that lower end normal glucose could not be distinguished from upper end normal glucose levels through the evaluation of all twenty-five explored HRV parameters.

7.3 Comparing between HRV and glucose levels in volunteers with Type 1 diabetes

The three plots of the HRV parameter variances within the population of diabetes sufferers demonstrate the fluctuation of variance during the different levels of glucose balance in the body. Compared to the data of the subjects without diabetes, all three plots showed significantly lower variances throughout the entire spectrum of HRV parameters. According to previously mentioned research articles, this observation in decreased variance is expected in people with diabetes. However, it can also be noted that the average of the HRV parameters during all three glucose levels increased slightly compared to the normal glucose levels in those without diabetes. Revisiting the ApEn parameter from the data of the non-diabetes sufferers, it can be determined that ApEn significantly decreased in variability during hyperglycemia when compared to its higher coefficients of variation during normal and hypoglycemia levels. Another observation is the NN50 parameter which decreased significantly in variability during normal glucose levels compared to hypo and hyperglycemic levels. Further analysis demonstrates that many other parameters fluctuated significantly in variability during each levels of glucose balance.

Through the analysis of the twenty-five parameters using the box plot method, it was observed that subjects 1 and 2 with diabetes shared common characteristics in the distribution of values for NN50, SD1, and RMSSD. The range of values during hypoglycemia was significantly higher than the range of values during normal glucose levels. Parametric analysis of using Student T-tests was performed and the HRV parameters demonstrated a 95% confidence level that the hypoglycemic and normal glucose levels do not share common averages. A p value less than 0.005 was observed for each t-test performed between the pairs of hypoglycemic and normal glucose data. Assuming non-normality, a non parametric test known as the Mann-

Whitney rejected the null hypothesis of equal medians at 95% confidence with a p value less than 0.004.

It was also observed that diabetes subjects 1, 3, 4, 5 and 6 shared common qualities in the distribution of values for mode, average, and median when comparing normal to hyperglycemic levels. By observing the data in all five diabetes sufferers, the range of values during hyperglycemia was significantly higher than the range of values during normal glucose levels. Parametric analysis of using Student T-tests was performed and the HRV parameters demonstrated a 95% confidence level that the hyperglycemic and normal glucose levels do not share common averages. A p value less than 0.005 was observed for each t-test performed between the pairs of hyperglycemic and normal glucose data. Assuming non-normality once again, Mann-Whitney rejected the null hypothesis of equal medians at 95% confidence with a p value less than 0.001

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Chapter 8 : Conclusion

8.1 Comparisons between ECG and PPG derived HRV

The HRV data sets derived from ECG and PPG signals for each of the two volunteer subjects were closely matched. This demonstrated that the PDA-based system was reliable in recording the same information for the same state of relaxation and health in each subject.

The tachograms and power spectra of the HRV data sets associated with each pair of corresponding PPG and ECG signals resulted in correlation coefficients very close to 1. Statistical analysis of the probability distributions demonstrated that the majority of the HRV data points collected from both PPG and ECG signals were located to the right side of the mean and mainly characterized as leptokurtic. This demonstrates that the PPG signal could be as dependable as the popular ECG in the derivation of the HRV signal.

Advantages of the PPG method over the ECG method (in addition to its ease of data acquisition and a high correlation between the HRV signals derived from both signals) may provide justification that PPG signals are not only a useful supplement but may be potentially a practical replacement for ECG-derived HRV signals in physiological monitoring. This point requires further investigation in a larger number of subjects. This study demonstrated that the PDA-based system is a useful and reliable tool in HRV studies that require ease of application to the subject to record the data and the possibility to replace ECG by PPG signals when the number of electrodes and wires could complicate the measurements and interfere with long term data acquisition and monitoring. An improvement in the PPG acquisition would be in the sensor itself since motion artifacts can prevent the dichrotic peaks from being properly detected by the peak detection algorithm. A new design of the sensor would need to incorporate a solution to

minimizing motion artifact interference and making wearing of the device more practical for everyday use.

8.2 Comparing between HRV and glucose levels in volunteers without diabetes

The HRV and glucose information gathered from the ten volunteers without diabetes proved useful to providing a baseline of normal HRV parameter values. This would prove useful in determining if any abnormalities were present in an individual if their corresponding HRV parameters were well beyond the normal range documented in this research. The favorable parameter was approximate entropy because of its nonlinear properties. This research concludes that any future studied HRV parameters observed within the given ranges of ApEn would indicate normal and safe glucose levels in an individual without diabetes. It would be desirable to test a larger population of subjects without diabetes to strengthen the conclusions obtained through the testing of only ten subjects without the disease. A larger population sample would strengthen the statistical analysis and determine if the observations derived from this study would apply to a wider subject population. A larger sample is necessary if a final product is to be introduced to the market since similar diabetes products go through hundreds of testing with various subjects in order to obtain FDA approval. It would also be very desirable to use the continuous glucose monitor for acquiring glucose measurements from subjects without diabetes since the finger lancing method using the OneTouch Ultra monitor only provided a small amount of samples. It would be quite expensive and painful to test each subject without diabetes more than six times using the finger lancing method in future research.

8.3 Comparing between HRV and glucose levels in volunteers with Type 1 diabetes

The HRV parameters measured during hypoglycemia, normal, and hyperglycemia demonstrated various key characteristics as described by the variance plots and the box plots. The variance plots strengthened the study by agreeing with other published articles that HRV parameters decreased in variability in those with diabetes as compared to those without the disease. Parameters such as ApEn which decreased during hyperglycemia can be further explored with more Type 1 diabetes diagnosed subjects to determine if dangerously high levels of sugar in the blood can be detected by monitoring the variability of the HRV parameter.

The side by side box plot comparisons demonstrated that the HRV parameters mean, median, mode increased significantly during hyperglycemia when compared to normal glucose levels. The parameters NN50, RMSSD, and SD1 increased significantly during hypoglycemia when compared to normal glucose levels. T-tests demonstrated significantly different averages between normal glucose and hyperglycemia and between normal glucose and hypoglycemia. Further investigation using more subjects suffering from diabetes is necessary in order to clearly define the measured HRV parameter boundaries between safe and unsafe glucose levels in a person. Ultimately, once a clear distinction between safe and unsafe glucose levels are determined through HRV parameters, a non-invasive glucose monitor could be developed.

Chapter 9 : System Specifications

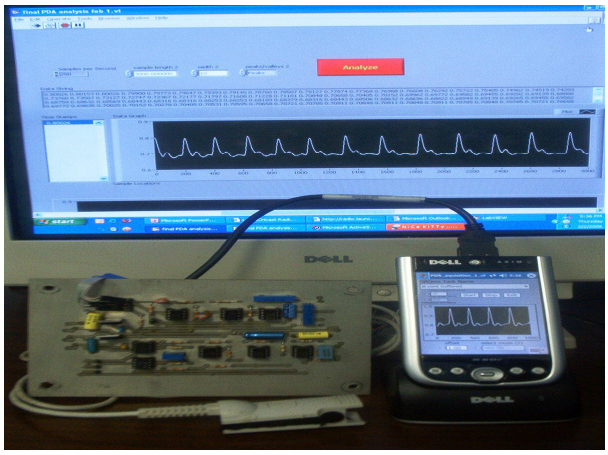

Figure 9-1: HRV acquisition/analyses system

Table 9.1: System specifications

ECG/PPG Circuit		
	Length	**5.5”**
	Width	**3”**
	Weight	**15oz**
	DC power input	**+9 volts**
	AC signal output	**0 – 1 Volts**
CF 6004 DAQ		
	Sampling Rate	**18kS/s total**
	Channels	**4**
Dell PDA	**Battery life**	**24 hrs(constantly on)**

	Operating System	**Windows Pocket PC**
	Speed	**624 MHz**
	Memory	**512 Mb SD card**

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Glossary

Heart Rate Variations (HRV): The beat to beat changes of the heart rate of an individual usually acquired through the analysis of an electrocardiogram.

Electrocardiogram (ECG): The complex signal acquired through the use of at least 3 electrodes placed accordingly on the body to capture the heart's electrical activity.

Photoplethysmograph (PPG): A pressure signal obtained through the use of infrared light being passed through an artery and the amount of light reflected back to a optical receiver.

Appendix A : Data and Graphs

A.1 Non-Diabetic HRV parameter measurements (10 subjects)

A.1.1 Healthy Subject 1

Subject 1	Sugar (mg/dL)	70	80	103	125	135	95
Subject 1	Average (s)	1.08	1.07	1.07	1.03	0.95	0.87
Subject 1	RMS (s)	1.08	1.00	1.08	1.00	0.95	0.88
Subject 1	SD (s)	0.07	0.06	0.07	0.08	0.07	0.05
Subject 1	Var (s)	0.00	0.00	0.01	0.01	0.01	0.00
Subject 1	Kurtosis	3.44	3.95	5.79	3.32	3.26	3.18
Subject 1	Median	1.09	1.08	1.09	1.05	0.96	0.88
Subject 1	mode (s)	1.08	1.06	0.98	0.97	0.91	0.85
Subject 1	skewness (s)	-0.16	-0.53	-1.17	-0.67	-0.60	-0.44
Subject 1	maximum (s)	1.30	1.26	1.27	1.20	1.14	1.00
Subject 1	min (s)	0.86	0.86	0.69	0.74	0.69	0.71
Subject 1	RMSSD (ms)	67.50	62.40	76.70	83.30	63.00	44.80
Subject 1	NN50 (count)	302.00	305.00	333.00	377.00	296.00	211.00
Subject 1	pNN50 (%)	54.80	55.00	60.10	65.60	47.20	30.80
Subject 1	RR tri indx	0.12	0.11	0.12	0.15	0.12	0.10
Subject 1	TINN (ms)	275.00	255.00	315.00	335.00	295.00	225.00
Subject 1	VLF Power(FFT)	189.00	66.00	190.00	187.00	178.00	92.00
Subject 1	LF Power(FFT)	485.00	281.00	408.00	726.00	750.00	353.00
Subject 1	HF Power(FFT)	816.00	748.00	1264.00	1485.00	710.00	498.00
Subject 1	LF/HF Power(FFT)	0.60	0.38	0.32	0.49	1.06	0.71

Subject 1	VLF Power(AR)	0.00	0.00	0.00	0.00	0.00	0.00
Subject 1	LF Power(AR)	365.00	203.00	432.00	474.00	547.00	247.00
Subject 1	HF Power(AR)	357.00	348.00	577.00	672.00	320.00	199.00
Subject 1	LF/HF Power(AR)	1.03	0.58	0.75	0.71	1.71	1.24
Subject 1	SD1(poincare') (ms)	47.90	44.20	54.40	59.10	44.70	31.80
Subject 1	SD2(poincare') (ms)	89.50	76.70	104.10	109.80	97.90	71.00
Subject 1	ApEn	1.36	1.35	1.31	1.38	1.43	1.31
Subject 1	HF fft n.u	0.55	0.68	0.68	0.62	0.43	0.53
Subject 1	LF fft n.u	0.33	0.26	0.22	0.30	0.46	0.37
Subject 1	LF/HF fft n.u.	0.59	0.38	0.32	0.49	1.06	0.71
Subject 1	HF ar n.u	0.49	0.63	0.57	0.59	0.37	0.45
Subject 1	LF ar n.u	0.51	0.37	0.43	0.41	0.63	0.55
Subject 1	LF/HF ar n.u.	1.02	0.58	0.75	0.71	1.71	1.24
Subject 1	Sugar (mg/dL)	70	80	103	125	135	95
Subject 1	Average (s)	1.08	1.07	1.07	1.03	0.95	0.87
Subject 1	RMS (s)	1.08	1.00	1.08	1.00	0.95	0.88
Subject 1	SD (s)	0.07	0.06	0.07	0.08	0.07	0.05
Subject 1	Var (s)	0.00	0.00	0.01	0.01	0.01	0.00
Subject 1	Kurtosis	3.44	3.95	5.79	3.32	3.26	3.18
Subject 1	Median	1.09	1.08	1.09	1.05	0.96	0.88
Subject 1	mode (s)	1.08	1.06	0.98	0.97	0.91	0.85
Subject 1	skewness (s)	-0.16	-0.53	-1.17	-0.67	-0.60	-0.44
Subject 1	maximum (s)	1.30	1.26	1.27	1.20	1.14	1.00

Subject 1	min (s)	0.86	0.86	0.69	0.74	0.69	0.71
Subject 1	RMSSD (ms)	67.50	62.40	76.70	83.30	63.00	44.80
Subject 1	NN50 (count)	302.00	305.00	333.00	377.00	296.00	211.00
Subject 1	pNN50 (%)	54.80	55.00	60.10	65.60	47.20	30.80
Subject 1	RR tri indx	0.12	0.11	0.12	0.15	0.12	0.10
Subject 1	TINN (ms)	275.00	255.00	315.00	335.00	295.00	225.00
Subject 1	VLF Power(FFT)	189.00	66.00	190.00	187.00	178.00	92.00
Subject 1	LF Power(FFT)	485.00	281.00	408.00	726.00	750.00	353.00
Subject 1	HF Power(FFT)	816.00	748.00	1264.00	1485.00	710.00	498.00
Subject 1	LF/HF Power(FFT)	0.60	0.38	0.32	0.49	1.06	0.71
Subject 1	VLF Power(AR)	0.00	0.00	0.00	0.00	0.00	0.00
Subject 1	LF Power(AR)	365.00	203.00	432.00	474.00	547.00	247.00
Subject 1	HF Power(AR)	357.00	348.00	577.00	672.00	320.00	199.00
Subject 1	LF/HF Power(AR)	1.03	0.58	0.75	0.71	1.71	1.24
Subject 1	SD1(poincare') (ms)	47.90	44.20	54.40	59.10	44.70	31.80
Subject 1	SD2(poincare') (ms)	89.50	76.70	104.10	109.80	97.90	71.00
Subject 1	ApEn	1.36	1.35	1.31	1.38	1.43	1.31
Subject 1	HF fft n.u	0.55	0.68	0.68	0.62	0.43	0.53
Subject 1	LF fft n.u	0.33	0.26	0.22	0.30	0.46	0.37
Subject 1	LF/HF fft n.u.	0.59	0.38	0.32	0.49	1.06	0.71
Subject 1	HF ar n.u	0.49	0.63	0.57	0.59	0.37	0.45
Subject 1	LF ar n.u	0.51	0.37	0.43	0.41	0.63	0.55
Subject 1	LF/HF ar n.u.	1.02	0.58	0.75	0.71	1.71	1.24

A.1.2 Healthy Subject 2

Subject 2	Sugar (mg/dL)	99	97	130	177	168	130
Subject 2	Average (s)	0.96	0.88	0.92	0.86	0.84	0.83
Subject 2	RMS (s)	0.96	0.88	0.92	0.87	0.85	0.83
Subject 2	SD (s)	0.07	0.08	0.07	0.06	0.06	0.06
Subject 2	Var (s)	0.01	0.01	0.01	0.00	0.00	0.00
Subject 2	Kurtosis	3.23	2.98	0.07	2.71	2.83	2.43
Subject 2	Median	0.98	0.87	0.92	0.87	0.85	0.83
Subject 2	mode (s)	0.92	0.91	0.91	0.84	0.83	0.83
Subject 2	skewness (s)	-0.82	0.51	-0.20	-0.45	-0.19	0.03
Subject 2	maximum (s)	1.14	1.11	1.08	1.01	0.99	0.99
Subject 2	min (s)	0.71	0.70	0.74	0.66	0.68	0.67
Subject 2	RMSSD (ms)	51.40	45.90	60.70	55.00	52.70	46.30
Subject 2	NN50 (count)	212.00	178.00	280.00	270.00	315.00	235.00
Subject 2	pNN50 (%)	34.10	26.10	42.90	39.10	44.50	32.70
Subject 2	RR tri indx	0.10	0.10	0.13	0.11	0.11	0.11
Subject 2	TINN (ms)	255.00	225.00	275.00	240.00	240.00	240.00
Subject 2	VLF Power(FFT)	270.00	127.00	200.00	200.00	162.00	145.00
Subject 2	LF Power(FFT)	387.00	473.00	719.00	551.00	339.00	452.00
Subject 2	HF Power(FFT)	402.00	344.00	689.00	530.00	533.00	442.00
Subject 2	LF/HF Power(FFT)	0.96	1.38	1.05	1.04	0.64	1.02
Subject 2	VLF Power(AR)	302.00	0.00	0.00	0.00	0.00	0.00
Subject 2	LF Power(AR)	171.00	366.00	488.00	441.00	328.00	386.00

Subject 2	HF Power(AR)	161.00	144.00	244.00	127.00	278.00	174.00
Subject 2	LF/HF Power(AR)	1.07	2.54	2.00	3.48	1.18	2.22
Subject 2	SD1(poincare') (ms)	36.60	32.60	43.10	39.10	37.40	32.90
Subject 2	SD2(poincare') (ms)	102.70	105.40	90.80	87.70	75.80	84.50
Subject 2	ApEn	1.25	1.34	1.47	1.44	1.46	1.39
Subject 2	HF fft n.u	0.38	0.36	0.43	0.41	0.52	0.43
Subject 2	LF fft n.u	0.37	0.50	0.45	0.43	0.33	0.44
Subject 2	LF/HF fft n.u.	0.96	1.38	1.04	1.04	0.64	1.02
Subject 2	HF ar n.u	0.48	0.28	0.33	0.22	0.46	0.31
Subject 2	LF ar n.u	0.52	0.72	0.67	0.78	0.54	0.69
Subject 2	LF/HF ar n.u.	1.06	2.54	2.00	3.47	1.18	2.22

A.1.3 Healthy Subject 3

Subject 3	Sugar (mg/dL)	88	82	153	174	96	92
Subject 3	Average (s)	0.79	0.79	0.84	0.82	0.69	0.72
Subject 3	RMS (s)	0.79	0.79	0.84	0.82	0.69	0.72
Subject 3	SD (s)	0.04	0.05	0.05	0.04	0.04	0.04
Subject 3	Var (s)	0.00	0.00	0.00	0.00	0.00	0.00
Subject 3	Kurtosis	4.52	4.74	4.16	3.43	2.87	3.31
Subject 3	Median	0.79	0.79	0.84	0.82	0.68	0.72
Subject 3	mode (s)	0.84	0.84	0.89	0.80	0.69	0.71
Subject 3	skewness (s)	0.23	0.81	0.51	-0.15	0.27	-0.45
Subject 3	maximum (s)	1.01	1.01	1.09	0.95	0.81	0.83

Subject 3	min (s)	0.67	0.68	0.68	0.65	0.58	0.58
Subject 3	RMSSD (ms)	34.00	30.40	42.10	32.00	17.10	16.60
Subject 3	NN50 (count)	111.00	63.00	175.00	92.00	10.00	3.00
Subject 3	pNN50 (%)	14.60	8.30	24.50	12.60	1.10	0.40
Subject 3	RR tri indx	0.08	0.07	0.10	0.08	0.06	0.05
Subject 3	TINN (ms)	215.00	195.00	220.00	185.00	170.00	135.00
Subject 3	VLF Power(FFT)	73.00	34.00	114.00	101.00	91.00	32.00
Subject 3	LF Power(FFT)	363.00	168.00	298.00	300.00	393.00	239.00
Subject 3	HF Power(FFT)	263.00	132.00	276.00	173.00	61.00	53.00
Subject 3	LF/HF Power(FFT)	1.38	1.27	1.08	1.73	6.47	4.53
Subject 3	VLF Power(AR)	0.00	0.00	0.00	0.00	3.00	0.00
Subject 3	LF Power(AR)	226.00	214.00	278.00	228.00	230.00	154.00
Subject 3	HF Power(AR)	100.00	80.00	142.00	77.00	16.00	26.00
Subject 3	LF/HF Power(AR)	2.25	2.68	1.96	2.96	14.54	6.01
Subject 3	SD1(poincare') (ms)	24.10	21.60	29.90	22.80	12.20	11.80
Subject 3	SD2(poincare') (ms)	56.50	63.10	75.00	59.30	58.70	53.10
Subject 3	ApEn	1.48	1.37	1.46	1.44	1.04	1.22
Subject 3	HF fft n.u	0.38	0.40	0.40	0.30	0.11	0.16
Subject 3	LF fft n.u	0.52	0.50	0.43	0.52	0.72	0.74
Subject 3	LF/HF fft n.u.	1.38	1.27	1.08	1.73	6.44	4.51
Subject 3	HF ar n.u	0.31	0.27	0.34	0.25	0.07	0.14
Subject 3	LF ar n.u	0.69	0.73	0.66	0.75	0.93	0.86
Subject 3	LF/HF ar n.u.	2.26	2.68	1.96	2.96	14.38	5.92

A.1.4 Healthy Subject 4

Subject 4	Sugar (mg/dL)	88	85	133	172	110	101
Subject 4	Average (s)	0.97	0.97	0.93	0.90	0.87	0.87
Subject 4	RMS (s)	0.97	0.98	0.93	0.91	0.87	0.87
Subject 4	SD (s)	0.05	0.06	0.09	0.07	0.06	0.08
Subject 4	Var (s)	0.00	0.00	0.01	0.01	0.00	0.01
Subject 4	Kurtosis	3.77	4.01	4.85	2.49	2.34	3.06
Subject 4	Median	0.98	0.98	0.93	0.90	0.87	0.88
Subject 4	mode (s)	0.94	0.94	1.07	0.93	0.88	0.89
Subject 4	skewness (s)	-0.62	-0.75	0.27	0.06	-0.10	-0.38
Subject 4	maximum (s)	1.10	1.16	1.46	1.13	1.04	1.12
Subject 4	min (s)	0.78	0.73	0.69	0.73	0.72	0.66
Subject 4	RMSSD (ms)	45.80	57.40	69.70	63.30	36.90	42.00
Subject 4	NN50 (count)	176.00	256.00	272.00	295.00	125.00	139.00
Subject 4	pNN50 (%)	28.60	41.70	42.20	44.60	18.10	20.20
Subject 4	RR tri indx	0.09	0.12	0.14	0.13	0.10	0.13
Subject 4	TINN (ms)	220.00	310.00	495.00	310.00	255.00	345.00
Subject 4	VLF Power(FFT)	140.00	144.00	354.00	333.00	262.00	322.00
Subject 4	LF Power(FFT)	435.00	1024.00	1222.00	852.00	763.00	1870.00
Subject 4	HF Power(FFT)	294.00	513.00	777.00	799.00	237.00	279.00
Subject 4	LF/HF Power(FFT)	1.48	2.00	1.57	1.07	3.21	6.71
Subject 4	VLF Power(AR)	0.00	0.00	0.00	0.00	10.00	0.00
Subject 4	LF Power(AR)	312.00	510.00	926.00	588.00	526.00	1088.00
Subject	HF Power(AR)	155.00	219.00	335.00	326.00	76.00	80.00

Subject 4	LF/HF Power(AR)	2.02	2.33	2.76	1.80	6.97	13.67
Subject 4	SD1(poincare') (ms)	32.60	40.70	49.50	45.00	26.30	29.90
Subject 4	SD2(poincare') (ms)	73.60	87.30	118.50	101.00	85.30	108.00
Subject 4	ApEn	1.46	1.40	1.34	1.35	1.36	1.23
Subject 4	HF fft n.u	0.34	0.31	0.33	0.40	0.19	0.11
Subject 4	LF fft n.u	0.50	0.61	0.52	0.43	0.60	0.76
Subject 4	LF/HF fft n.u.	1.48	2.00	1.57	1.07	3.22	6.70
Subject 4	HF ar n.u	0.33	0.30	0.27	0.36	0.13	0.07
Subject 4	LF ar n.u	0.67	0.70	0.73	0.64	0.87	0.93
Subject 4	LF/HF ar n.u.	2.01	2.33	2.76	1.80	6.92	13.60

A.1.5 Healthy Subject 5

Subject 5	Sugar (mg/dL)	80	83	161	121	80	85
Subject 5	Average (s)	0.68	0.73	0.69	0.69	0.69	0.68
Subject 5	RMS (s)	0.68	0.73	0.69	0.69	0.69	0.68
Subject 5	SD (s)	0.04	0.06	0.06	0.06	0.05	0.06
Subject 5	Var (s)	0.00	0.00	0.00	0.00	0.00	0.00
Subject 5	Kurtosis	3.17	2.49	2.47	3.42	2.42	2.48
Subject 5	Median	0.68	0.73	0.69	0.69	0.69	0.67
Subject 5	mode (s)	0.69	0.74	0.71	0.71	0.71	0.68
Subject 5	skewness (s)	-0.06	-0.19	0.22	0.40	0.00	0.06
Subject 5	maximum (s)	0.82	0.90	0.87	0.87	0.85	0.84
Subject 5	min (s)	0.56	0.58	0.56	0.55	0.57	0.53

Subject 5	RMSSD (ms)	23.60	32.90	29.30	32.40	31.70	31.70
Subject 5	NN50 (count)	36.00	95.00	83.00	82.00	87.00	97.00
Subject 5	pNN50 (%)	4.10	11.60	9.60	9.40	10.00	11.00
Subject 5	RR tri indx	0.08	0.11	0.10	0.10	0.10	0.11
Subject 5	TINN (ms)	195.00	230.00	205.00	235.00	220.00	240.00
Subject 5	VLF Power(FFT)	101.00	151.00	157.00	207.00	100.00	175.00
Subject 5	LF Power(FFT)	477.00	752.00	338.00	610.00	420.00	822.00
Subject 5	HF Power(FFT)	193.00	228.00	214.00	235.00	303.00	315.00
Subject 5	LF/HF Power(FFT)	2.47	3.30	1.58	2.60	1.39	2.61
Subject 5	VLF Power(AR)	0.00	0.00	76.00	0.00	0.00	0.00
Subject 5	LF Power(AR)	304.00	474.00	230.00	455.00	369.00	469.00
Subject 5	HF Power(AR)	49.00	67.00	72.00	80.00	108.00	116.00
Subject 5	LF/HF Power(AR)	6.15	7.04	3.20	5.71	3.42	4.03
Subject 5	SD1(poincare') (ms)	16.80	23.40	20.90	23.00	22.50	22.60
Subject 5	SD2(poincare') (ms)	62.40	80.90	80.10	76.70	74.90	86.00
Subject 5	ApEn	1.21	1.28	1.21	1.22	1.25	1.16
Subject 5	HF fft n.u	0.25	0.20	0.30	0.22	0.37	0.24
Subject 5	LF fft n.u	0.62	0.66	0.48	0.58	0.51	0.63
Subject 5	LF/HF fft n.u.	2.47	3.30	1.58	2.60	1.39	2.61
Subject 5	HF ar n.u	0.14	0.12	0.24	0.15	0.23	0.20
Subject 5	LF ar n.u	0.86	0.88	0.76	0.85	0.77	0.80
Subject 5	LF/HF ar n.u.	6.20	7.07	3.19	5.69	3.42	4.04

A.1.6 Healthy Subject 6

Subject 6	Sugar (mg/dL)	87	90	148	131	91	92
Subject 6	Average (s)	0.99	0.99	0.97	0.93	0.85	0.91
Subject 6	RMS (s)	0.99	0.99	0.97	0.94	0.85	0.91
Subject 6	SD (s)	0.07	0.09	0.09	0.08	0.07	0.07
Subject 6	Var (s)	0.00	0.01	0.01	0.01	0.00	0.01
Subject 6	Kurtosis	3.35	3.36	2.85	3.00	2.64	3.12
Subject 6	Median	0.99	1.00	0.98	0.94	0.85	0.91
Subject 6	mode (s)	0.98	0.99	0.96	0.95	0.88	0.93
Subject 6	skewness (s)	-0.05	-0.58	-0.38	0.02	0.01	-0.04
Subject 6	maximum (s)	1.20	1.25	1.21	1.18	1.07	1.13
Subject 6	min (s)	0.77	0.74	0.71	0.72	0.69	0.73
Subject 6	RMSSD (ms)	43.20	47.40	53.00	53.90	38.60	48.80
Subject 6	NN50 (count)	133.00	159.00	231.00	224.00	137.00	217.00
Subject 6	pNN50 (%)	22.10	26.30	300.00	34.90	19.40	33.10
Subject 6	RR tri indx	0.11	0.13	0.13	0.13	0.12	0.13
Subject 6	TINN (ms)	275.00	305.00	300.00	330.00	300.00	300.00
Subject 6	VLF Power(FFT)	293.00	328.00	344.00	432.00	348.00	250.00
Subject 6	LF Power(FFT)	1031.00	1260.00	1387.00	1265.00	1145.00	1063.00
Subject 6	HF Power(FFT)	218.00	291.00	460.00	414.00	214.00	349.00
Subject 6	LF/HF Power(FFT)	4.73	4.33	3.01	3.05	5.34	3.04
Subject 6	VLF Power(AR)	0.00	0.00	0.00	0.00	25.00	0.00
Subject 6	LF Power(AR)	626.00	800.00	788.00	868.00	745.00	835.00
Subject	HF Power(AR)	62.00	65.00	104.00	133.00	68.00	166.00

Subject 6	LF/HF Power(AR)	10.14	12.37	7.58	6.54	10.94	5.05
Subject 6	SD1(poincare') (ms)	30.80	33.80	37.70	38.40	27.50	34.70
Subject 6	SD2(poincare') (ms)	96.30	119.10	121.50	105.50	94.60	98.30
Subject 6	ApEn	1.36	1.28	1.37	1.35	1.25	1.37
Subject 6	HF fft n.u	0.14	0.15	0.21	0.20	0.13	0.21
Subject 6	LF fft n.u	0.67	0.67	0.63	0.60	0.67	0.64
Subject 6	LF/HF fft n.u.	4.73	4.33	3.02	3.06	5.35	3.05
Subject 6	HF ar n.u	0.09	0.08	0.12	0.13	0.08	0.17
Subject 6	LF ar n.u	0.91	0.92	0.88	0.87	0.92	0.83
Subject 6	LF/HF ar n.u.	10.10	12.31	7.58	6.53	10.96	5.03

A.1.7 Healthy Subject 7

Subject 7	Sugar (mg/dL)	79	71	128	160	76	74
Subject 7	Average (s)	0.86	0.85	0.83	0.88	0.73	0.76
Subject 7	RMS (s)	0.86	0.85	0.83	0.88	0.73	0.76
Subject 7	SD (s)	0.07	0.07	0.07	0.07	0.04	0.04
Subject 7	Var (s)	0.01	0.00	0.01	0.00	0.00	0.00
Subject 7	Kurtosis	3.59	3.11	3.29	4.23	3.82	3.40
Subject 7	Median	0.86	0.86	0.83	0.88	0.73	0.76
Subject 7	mode (s)	0.92	0.85	0.81	0.85	0.73	0.77
Subject 7	skewness (s)	-0.08	-0.45	-0.26	-0.55	-0.21	-0.04
Subject 7	maximum (s)	1.21	1.03	1.05	1.11	0.89	0.94
Subject 7	min (s)	0.63	0.66	0.58	0.59	0.57	0.60

Subject 7	RMSSD (ms)	68.70	49.30	57.80	68.40	32.50	32.00
Subject 7	NN50 (count)	280.00	221.00	273.00	319.00	88.00	107.00
Subject 7	pNN50 (%)	40.40	31.40	37.80	46.80	10.70	13.60
Subject 7	RR tri indx	0.14	0.10	0.13	0.13	0.08	0.08
Subject 7	TINN (ms)	415.00	250.00	310.00	365.00	225.00	225.00
Subject 7	VLF Power(FFT)	71.00	95.00	166.00	66.00	37.00	70.00
Subject 7	LF Power(FFT)	1395.00	760.00	924.00	928.00	334.00	373.00
Subject 7	HF Power(FFT)	1135.00	506.00	726.00	960.00	252.00	252.00
Subject 7	LF/HF Power(FFT)	1.23	1.50	1.27	0.97	1.33	1.48
Subject 7	VLF Power(AR)	0.00	68.00	9.00	0.00	0.00	0.00
Subject 7	LF Power(AR)	831.00	455.00	615.00	539.00	225.00	218.00
Subject 7	HF Power(AR)	364.00	178.00	293.00	420.00	113.00	114.00
Subject 7	LF/HF Power(AR)	2.28	2.56	2.10	1.28	1.99	1.91
Subject 7	SD1(poincare') (ms)	48.70	35.00	41.10	48.60	23.10	22.70
Subject 7	SD2(poincare') (ms)	97.50	90.30	99.20	90.90	59.40	61.70
Subject 7	ApEn	1.44	1.44	1.37	1.45	1.34	1.38
Subject 7	HF fft n.u	0.44	0.37	0.40	0.49	0.40	0.36
Subject 7	LF fft n.u	0.54	0.56	0.51	0.47	0.54	0.54
Subject 7	LF/HF fft n.u.	1.23	1.50	1.27	0.97	1.33	1.48
Subject 7	HF ar n.u	0.30	0.28	0.32	0.44	0.33	0.34
Subject 7	LF ar n.u	0.70	0.72	0.68	0.56	0.67	0.66
Subject 7	LF/HF ar n.u.	2.28	2.56	2.10	1.28	1.99	1.91

A.1.8 Healthy Subject 8

Subject 8	Sugar (mg/dL)	97	81	140	130	121	111
Subject 8	Average (s)	0.78	0.81	0.81	0.81	0.79	0.75
Subject 8	RMS (s)	0.78	0.81	0.82	0.81	0.79	0.75
Subject 8	SD (s)	0.07	0.05	0.06	0.07	0.05	0.06
Subject 8	Var (s)	0.00	0.00	0.00	0.01	0.00	0.00
Subject 8	Kurtosis	4.05	4.21	3.77	5.49	3.70	5.23
Subject 8	Median	0.77	0.80	0.81	0.81	0.79	0.75
Subject 8	mode (s)	0.81	0.82	0.86	0.96	0.85	0.82
Subject 8	skewness (s)	0.44	0.37	0.44	0.73	0.31	0.74
Subject 8	maximum (s)	1.03	1.02	1.07	1.31	1.06	1.07
Subject 8	min (s)	0.58	0.61	0.65	0.62	0.64	0.58
Subject 8	RMSSD (ms)	40.20	38.70	45.30	56.10	36.70	37.90
Subject 8	NN50 (count)	119.00	109.00	135.00	138.00	96.00	84.00
Subject 8	pNN50 (%)	15.50	14.70	18.40	18.80	12.70	10.50
Subject 8	RR tri indx	0.12	0.11	0.11	0.11	0.09	0.09
Subject 8	TINN (ms)	305.00	275.00	320.00	440.00	285.00	330.00
Subject 8	VLF Power(FFT)	199.00	86.00	172.00	216.00	132.00	164.00
Subject 8	LF Power(FFT)	1491.00	1191.00	1161.00	1628.00	844.00	946.00
Subject 8	HF Power(FFT)	320.00	295.00	449.00	652.00	235.00	198.00
Subject 8	LF/HF Power(FFT)	4.66	4.04	2.59	2.50	3.59	4.79
Subject 8	VLF Power(AR)	7.00	1.00	1.00	0.00	3.00	1.00
Subject 8	LF Power(AR)	838.00	633.00	709.00	842.00	530.00	719.00
Subject	HF Power(AR)	65.00	61.00	95.00	183.00	70.00	63.00

Subject 8	LF/HF Power(AR)	12.93	10.34	7.50	4.59	7.54	11.46
Subject 8	SD1(poincare') (ms)	28.60	27.50	32.20	39.90	26.00	26.90
Subject 8	SD2(poincare') (ms)	90.50	75.20	89.10	99.20	76.30	87.90
Subject 8	ApEn	1.19	1.31	1.21	1.21	1.25	1.06
Subject 8	HF fft n.u	0.16	0.19	0.25	0.26	0.19	0.15
Subject 8	LF fft n.u	0.74	0.76	0.65	0.65	0.70	0.72
Subject 8	LF/HF fft n.u.	4.66	4.04	2.59	2.50	3.59	4.78
Subject 8	HF ar n.u	0.07	0.09	0.12	0.18	0.12	0.08
Subject 8	LF ar n.u	0.93	0.91	0.88	0.82	0.88	0.92
Subject 8	LF/HF ar n.u.	12.89	10.38	7.46	4.60	7.57	11.41

A.1.9 Healthy Subject 9

Subject 9	Sugar (mg/dL)	86	93	132	149	123	119
Subject 9	Average (s)	0.92	0.92	0.92	0.88	0.89	0.88
Subject 9	RMS (s)	0.92	0.92	0.92	0.88	0.89	0.88
Subject 9	SD (s)	0.04	0.04	0.04	0.05	0.05	0.05
Subject 9	Var (s)	0.00	0.00	0.00	0.00	0.00	0.00
Subject 9	Kurtosis	5.09	5.75	4.21	4.03	4.03	4.03
Subject 9	Median	0.92	0.93	0.92	0.89	0.89	0.88
Subject 9	mode (s)	0.90	0.88	0.89	0.85	0.85	0.85
Subject 9	skewness (s)	-0.86	-1.21	-0.76	-0.87	-0.90	-0.87
Subject 9	maximum (s)	1.06	1.04	1.03	1.01	1.01	1.11
Subject 9	min (s)	0.73	0.72	0.75	0.69	0.68	0.59

Subject 9	RMSSD (ms)	47.40	48.60	49.70	46.20	47.10	48.70
Subject 9	NN50 (count)	214.00	233.00	226.00	189.00	178.00	193.00
Subject 9	pNN50 (%)	32.80	36.00	34.60	27.80	27.60	29.30
Subject 9	RR tri indx	0.09	0.08	0.08	0.08	0.08	0.08
Subject 9	TINN (ms)	240.00	195.00	210.00	215.00	218.00	219.00
Subject 9	VLF Power(FFT)	27.00	84.00	60.00	48.00	52.00	66.00
Subject 9	LF Power(FFT)	249.00	231.00	249.00	301.00	340.00	928.00
Subject 9	HF Power(FFT)	362.00	406.00	474.00	398.00	406.00	960.00
Subject 9	LF/HF Power(FFT)	0.69	0.57	0.52	0.76	0.84	0.97
Subject 9	VLF Power(AR)	0.00	0.00	0.00	0.00	0.00	0.00
Subject 9	LF Power(AR)	175.00	146.00	163.00	201.00	205.00	539.00
Subject 9	HF Power(AR)	188.00	200.00	215.00	182.00	163.00	420.00
Subject 9	LF/HF Power(AR)	0.93	0.73	0.76	1.10	1.26	1.28
Subject 9	SD1(poincare') (ms)	33.60	34.50	35.30	32.80	31.70	48.60
Subject 9	SD2(poincare') (ms)	55.30	58.60	56.50	63.00	63.70	90.90
Subject 9	ApEn	1.40	1.39	1.47	1.41		
Subject 9	HF fft n.u	0.57	0.56	0.61	0.53	0.51	0.49
Subject 9	LF fft n.u	0.39	0.32	0.32	0.40	0.43	0.47
Subject 9	LF/HF fft n.u.	0.69	0.57	0.53	0.76	0.84	0.97
Subject 9	HF ar n.u	0.52	0.58	0.57	0.48	0.44	0.44
Subject 9	LF ar n.u	0.48	0.42	0.43	0.52	0.56	0.56
Subject 9	LF/HF ar n.u.	0.93	0.73	0.76	1.10	1.26	1.28

A.1.10 Healthy Subject 10

Subject 10	Sugar (mg/dL)	147	122	118	123	130	145
Subject 10	Average (s)	0.79	0.78	0.73	0.82	0.80	0.84
Subject 10	RMS (s)	0.79	0.78	0.73	0.82	0.80	0.84
Subject 10	SD (s)	0.06	0.06	0.05	0.04	0.04	0.05
Subject 10	Var (s)	0.00	0.00	0.00	0.00	0.00	0.00
Subject 10	Kurtosis	2.94	2.98	2.57	3.32	4.69	3.23
Subject 10	Median	0.79	0.78	0.73	0.82	0.80	0.83
Subject 10	mode (s)	0.77	0.80	0.73	0.80	0.77	0.84
Subject 10	skewness (s)	-0.36	0.32	-0.27	-0.22	-0.46	0.35
Subject 10	maximum (s)	0.95	0.97	0.88	0.94	0.90	1.00
Subject 10	min (s)	0.59	0.63	0.58	0.67	0.64	0.68
Subject 10	RMSSD (ms)	34.40	32.40	25.70	30.30	25.60	37.80
Subject 10	NN50 (count)	99.00	96.00	40.00	68.00	22.00	124.00
Subject 10	pNN50 (%)	13.10	12.60	4.90	9.30	2.90	17.40
Subject 10	RR tri indx	0.11	0.09	0.09	0.07	0.07	0.07
Subject 10	TINN (ms)	235.00	220.00	210.00	195.00	170.00	195.00
Subject 10	VLF Power(FFT)	252.00	134.00	124.00	53.00	58.00	111.00
Subject 10	LF Power(FFT)	542.00	639.00	542.00	428.00	185.00	309.00
Subject 10	HF Power(FFT)	193.00	237.00	134.00	177.00	110.00	271.00
Subject 10	LF/HF Power(FFT)	2.81	2.70	4.03	2.42	1.68	1.14
Subject 10	VLF Power(AR)	0.00	0.00	0.00	0.00	0.00	22.00
Subject 10	LF Power(AR)	486.00	446.00	367.00	235.00	180.00	189.00
Subject	HF Power(AR)	78.00	91.00	29.00	70.00	49.00	122.00

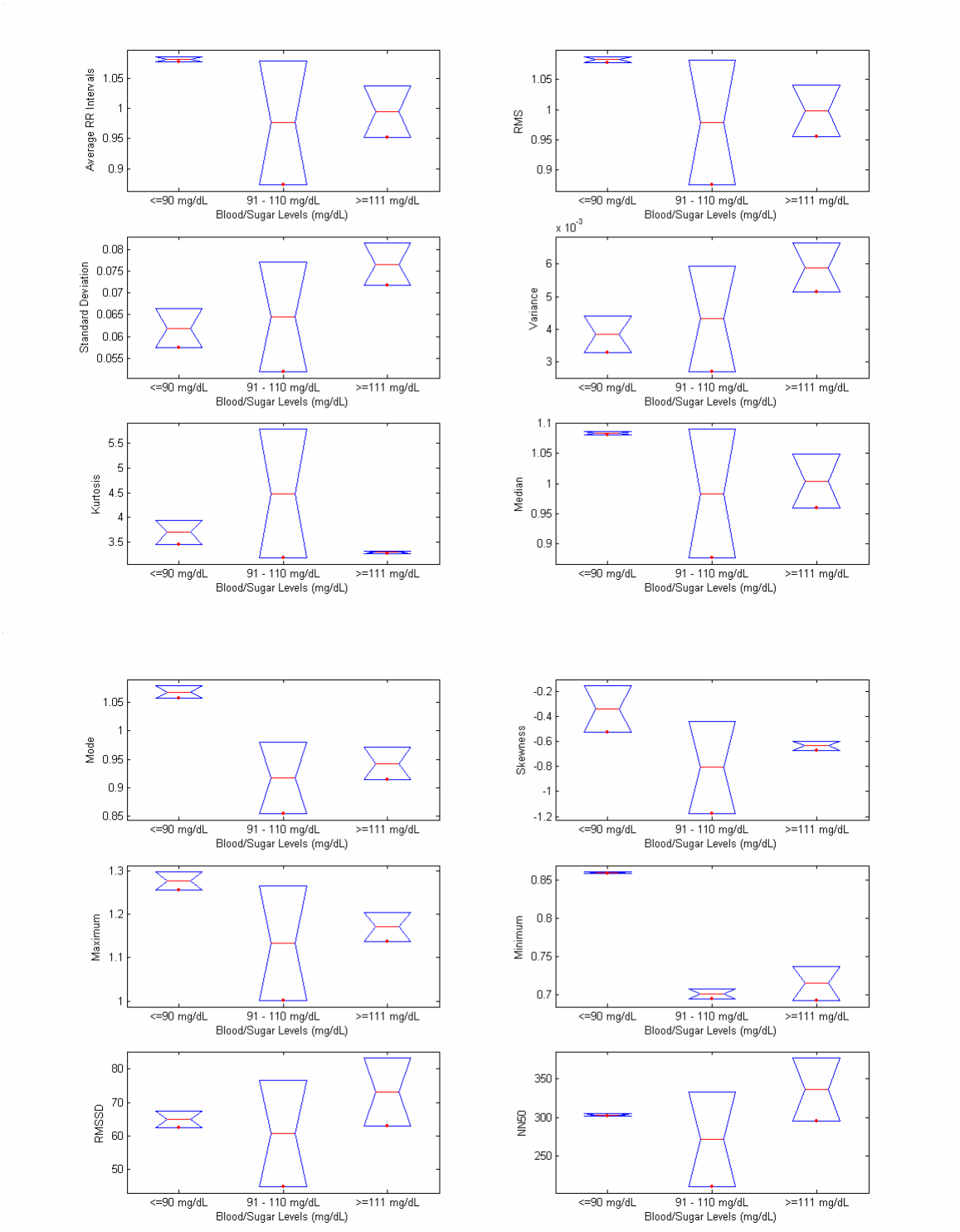
10 Subject	LF/HF						
10	Power(AR)	6.23	4.92	12.57	3.34	3.63	1.55
Subject	SD1(poincare')						
10	(ms)	24.50	23.10	18.30	21.50	18.20	26.90
Subject	SD2(poincare')						
10	(ms)	87.90	78.90	74.80	55.90	48.60	65.30
Subject							
10	ApEn	1.31	1.33	1.18	1.40	1.40	1.39
Subject							
10	HF fft n.u	0.20	0.23	0.17	0.27	0.31	0.39
Subject							
10	LF fft n.u	0.55	0.63	0.68	0.65	0.52	0.45
Subject							
10	LF/HF fft n.u.	2.81	2.70	4.04	2.42	1.68	1.14
Subject							
10	HF ar n.u	0.14	0.17	0.07	0.23	0.21	0.39
Subject							
10	LF ar n.u	0.86	0.83	0.93	0.77	0.79	0.61
Subject							
10	LF/HF ar n.u.	6.23	4.90	12.66	3.36	3.67	1.55

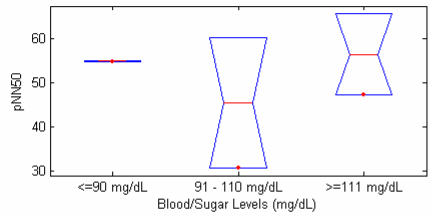
A.2 Non-Diabetic Glucose/HRV parameter correlation coefficients

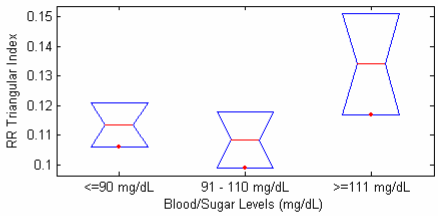
	Sugar(mg/dL)
Average	-0.00
RMS	0.00
SD	0.29
Var	0.29
Kurtosis	-0.08
Median	0.00
mode	-0.01
skewness	0.05
maximum	0.07
min	-0.18
RMSSD	0.37
NN50	0.41
pNN50	0.37
RR tri	0.23
TINN	0.21
Power VLF fft	0.38
Power HF fft	0.32
Power LF fft	-0.44
Power LF/HF fft	-0.35
Power HF ar	0.24
Power LF ar	-0.22
Power LF/HF ar	-0.20
SD1	0.39
SD2	0.26
ApEn	0.23

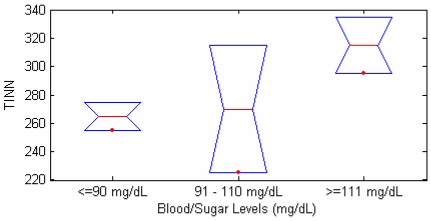
A.3 Non-Diabetic HRV parameter box plots

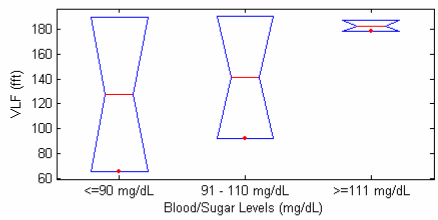
A.3.1 Healthy Subject 1

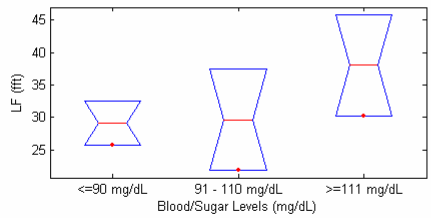


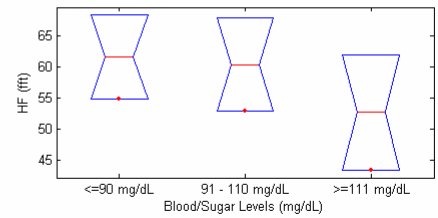

pNN50
60
50
40
30
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

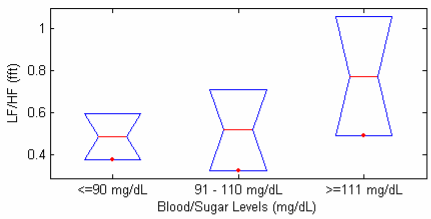

RR Triangular Index
0.15
0.14
0.13
0.12
0.11
0.1
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

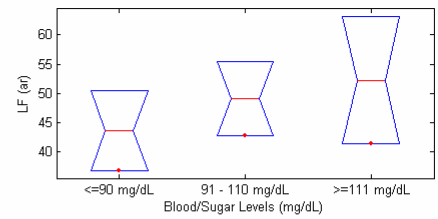

TINN
340
320
300
280
260
240
220
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

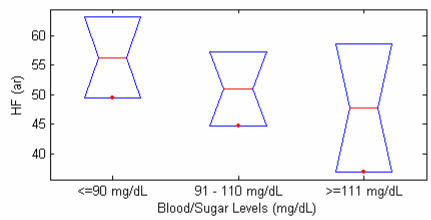

VLF (fft)
180
160
140
120
100
80
60
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

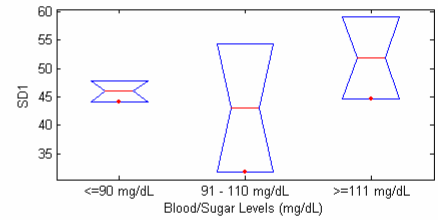

LF (fft)
45
40
35
30
25
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

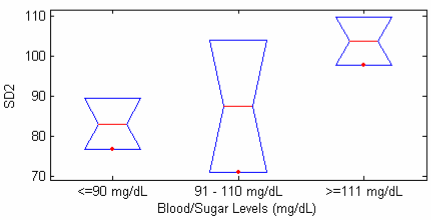

HF (fft)
65
60
55
50
45
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

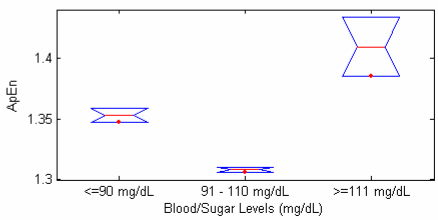

LF/HF (fft)
1
0.8
0.6
0.4
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)


LF (ar)
60
55
50
45
40
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

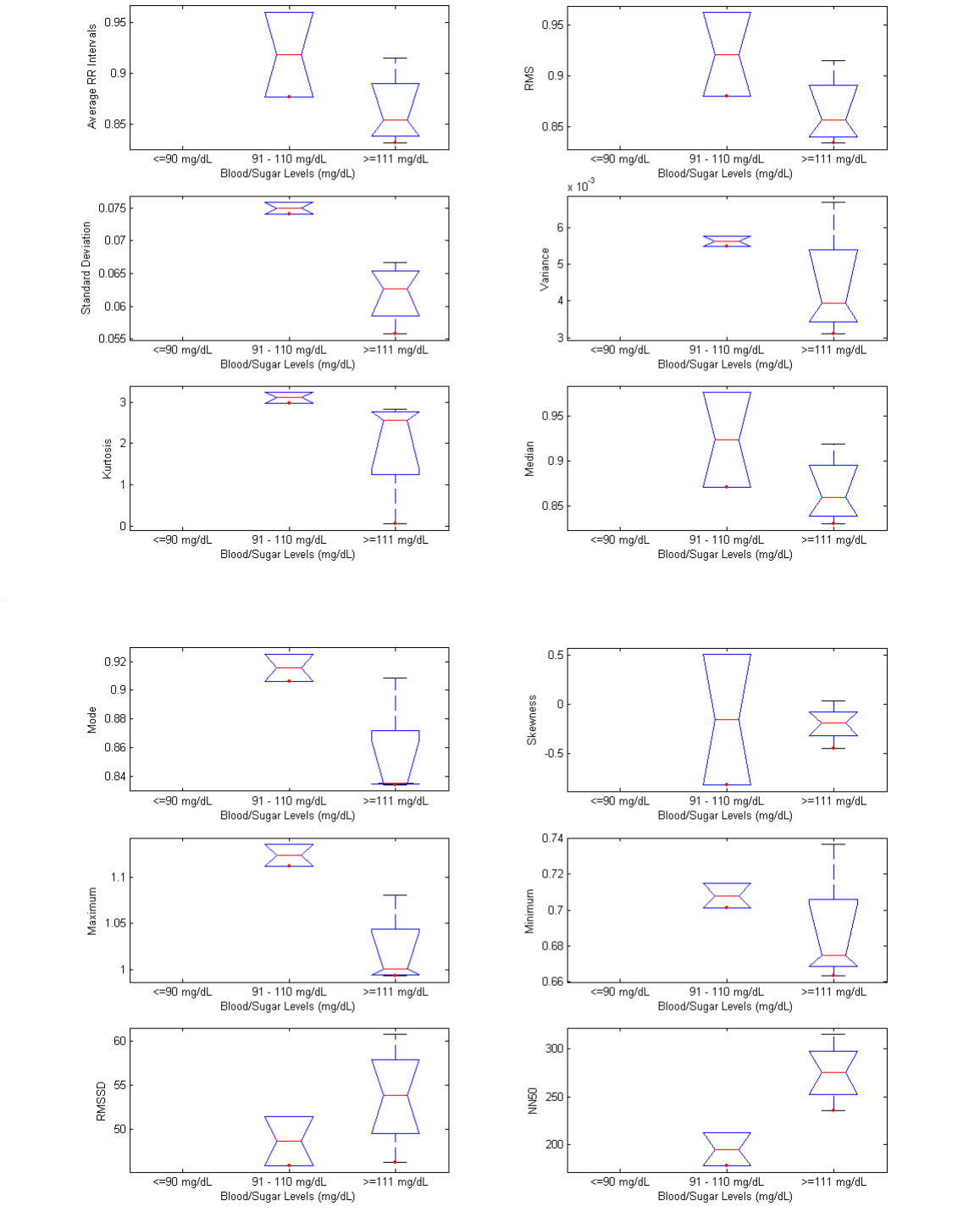

HF (ar)
60
55
50
45
40
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

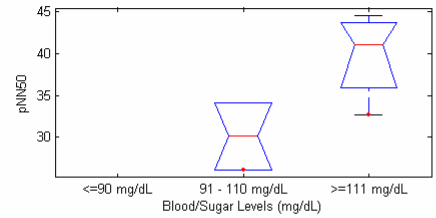

SD1
60
55
50
45
40
35
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

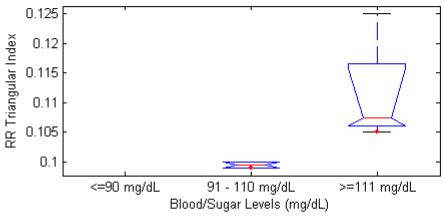

SD2
110
100
90
80
70
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

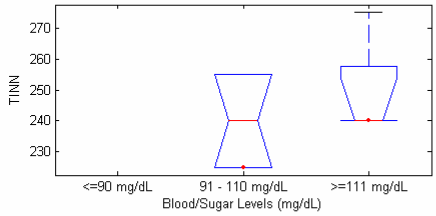

ApEn
1.4
1.35
1.3
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

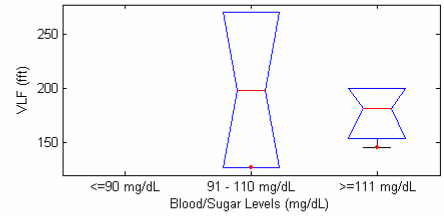
A.3.2 Healthy Subject 2

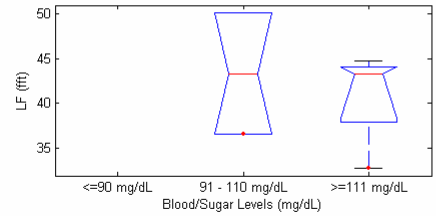


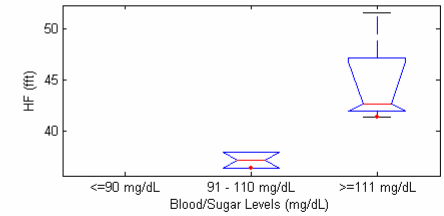

pNN50
45
40
35
30
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

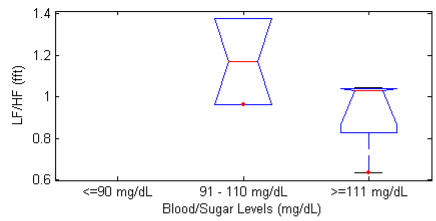

RR Triangular Index
0.125
0.12
0.115
0.11
0.105
0.1
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

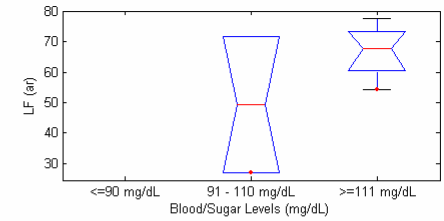

TINN
270
260
250
240
230
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

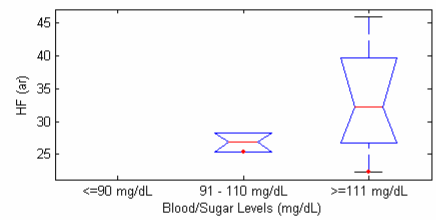

VLF (fft)
250
200
150
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

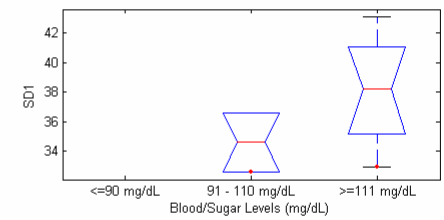

LF (fft)
50
45
40
35
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

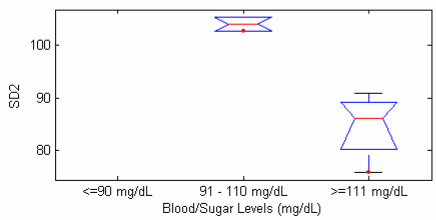

HF (fft)
50
45
40
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

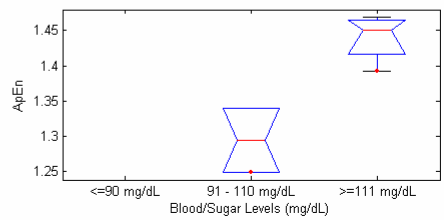

LF/HF (fft)
1.4
1.2
1
0.8
0.6
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)


LF (ar)
80
70
60
50
40
30
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

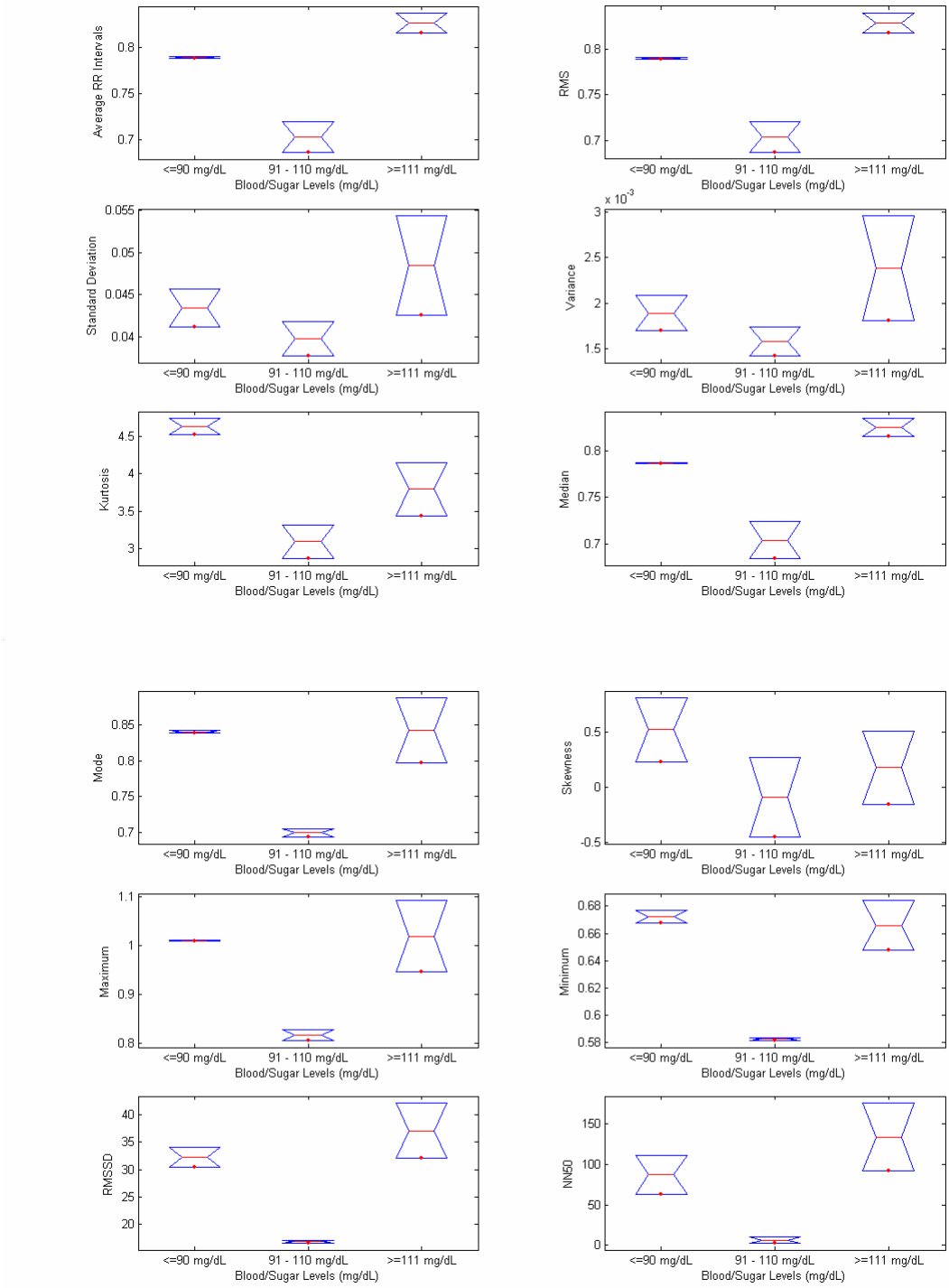

HF (ar)
45
40
35
30
25
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

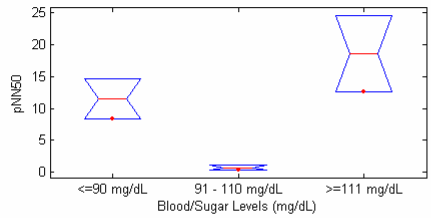

SD1
42
40
38
36
34
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

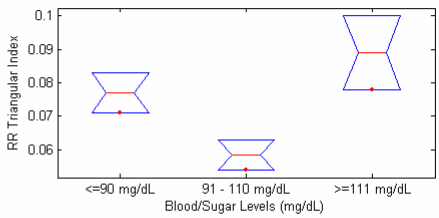

SD2
100
90
80
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

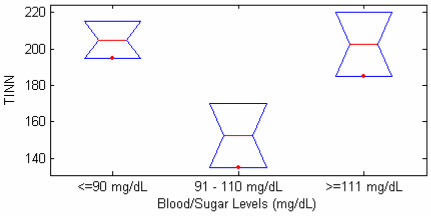

ApEn
1.45
1.4
1.35
1.3
1.25
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

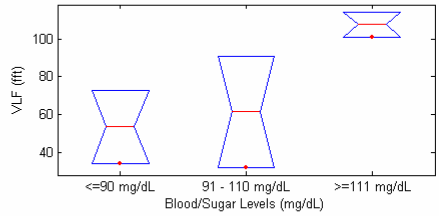
A.3.3 Healthy Subject 3

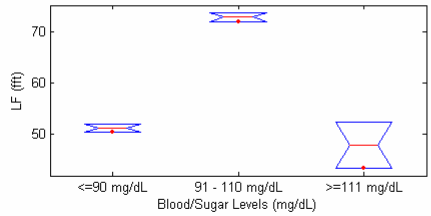


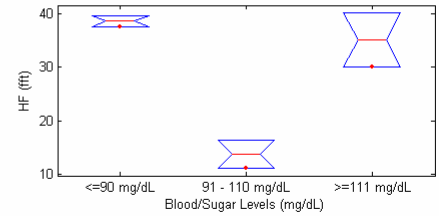

pNN50
25
20
15
10
5
0
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

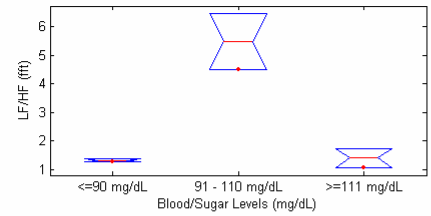

RR Triangular Index
0.1
0.09
0.08
0.07
0.06
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

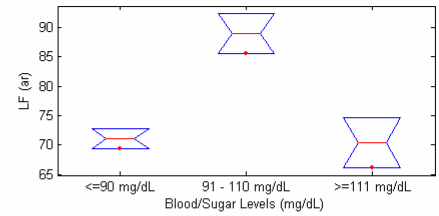

TINN
220
200
180
160
140
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

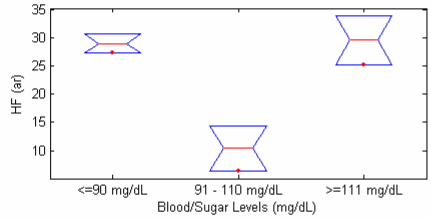

VLF (fft)
100
80
60
40
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

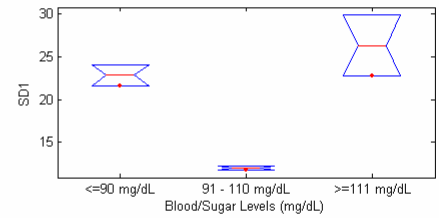

LF (fft)
70
60
50
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

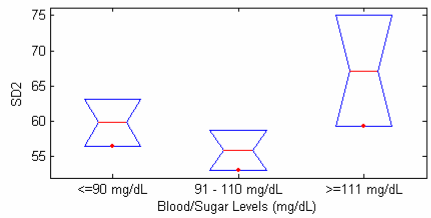

HF (fft)
40
30
20
10
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

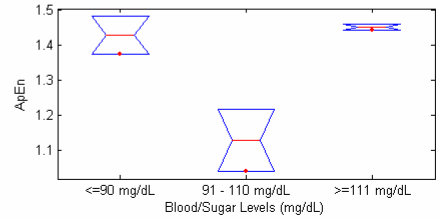

LF/HF (fft)
6
5
4
3
2
1
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)


LF (ar)
90
85
80
75
70
65
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

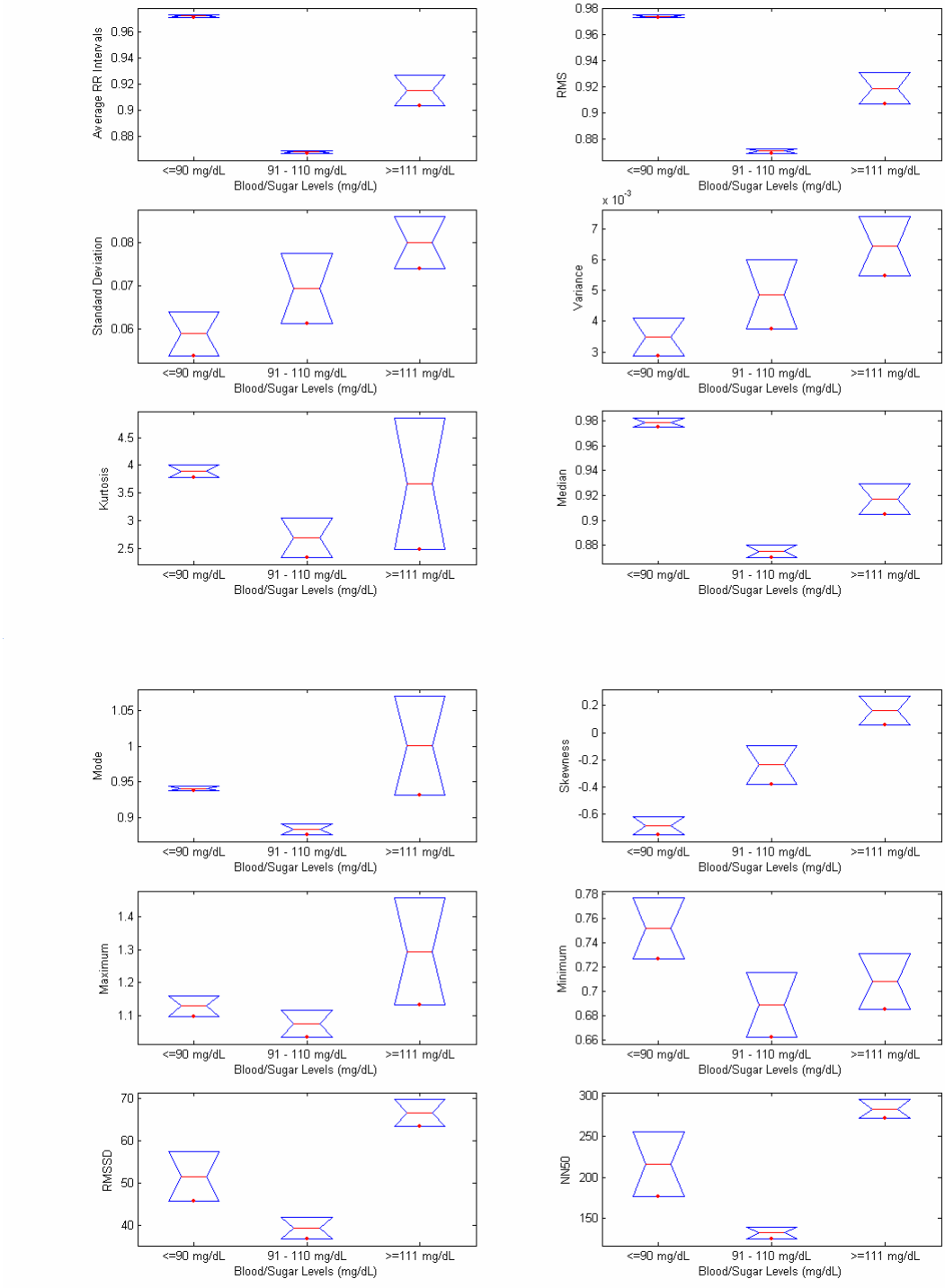

HF (ar)
35
30
25
20
15
10
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

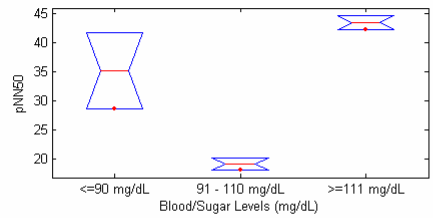

SD1
30
25
20
15
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

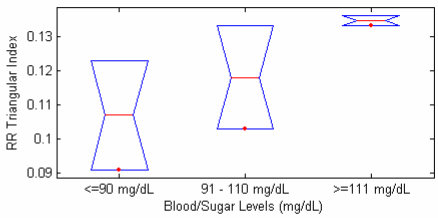

SD2
75
70
65
60
55
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

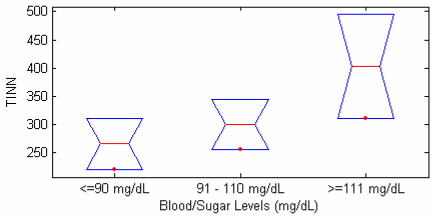

ApEn
1.5
1.4
1.3
1.2
1.1
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

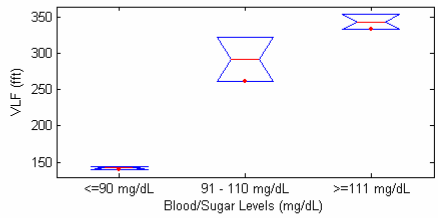
A.3.4 Healthy Subject 4

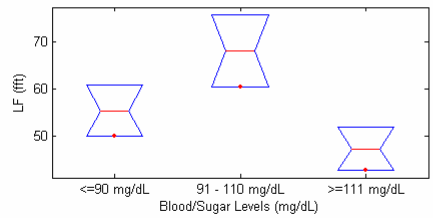


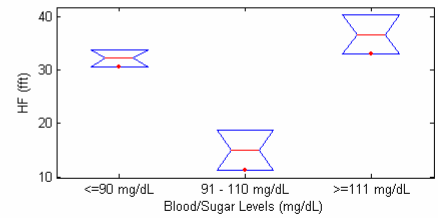

pNN50
45
40
35
30
25
20
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

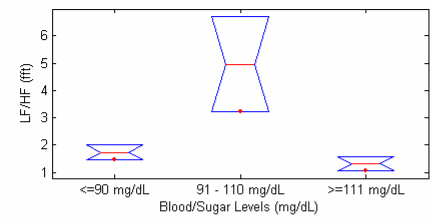

RR Triangular Index
0.13
0.12
0.11
0.1
0.09
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

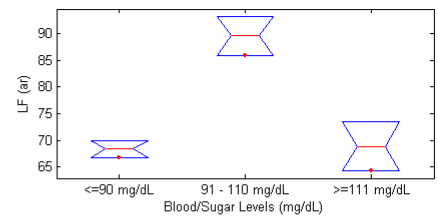

TINN
500
450
400
350
300
250
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

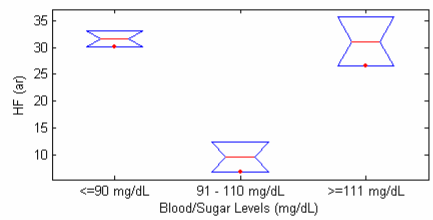

VLF (fft)
350
300
250
200
150
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

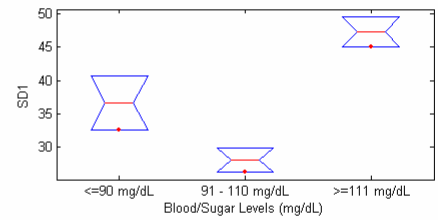

LF (fft)
70
60
50
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

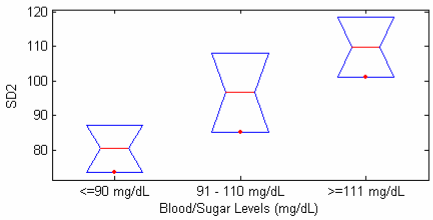

HF (fft)
40
30
20
10
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

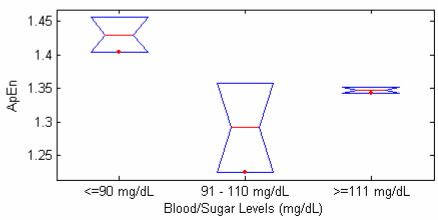

LF/HF (fft)
6
5
4
3
2
1
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)


LF (ar)
90
85
80
75
70
65
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

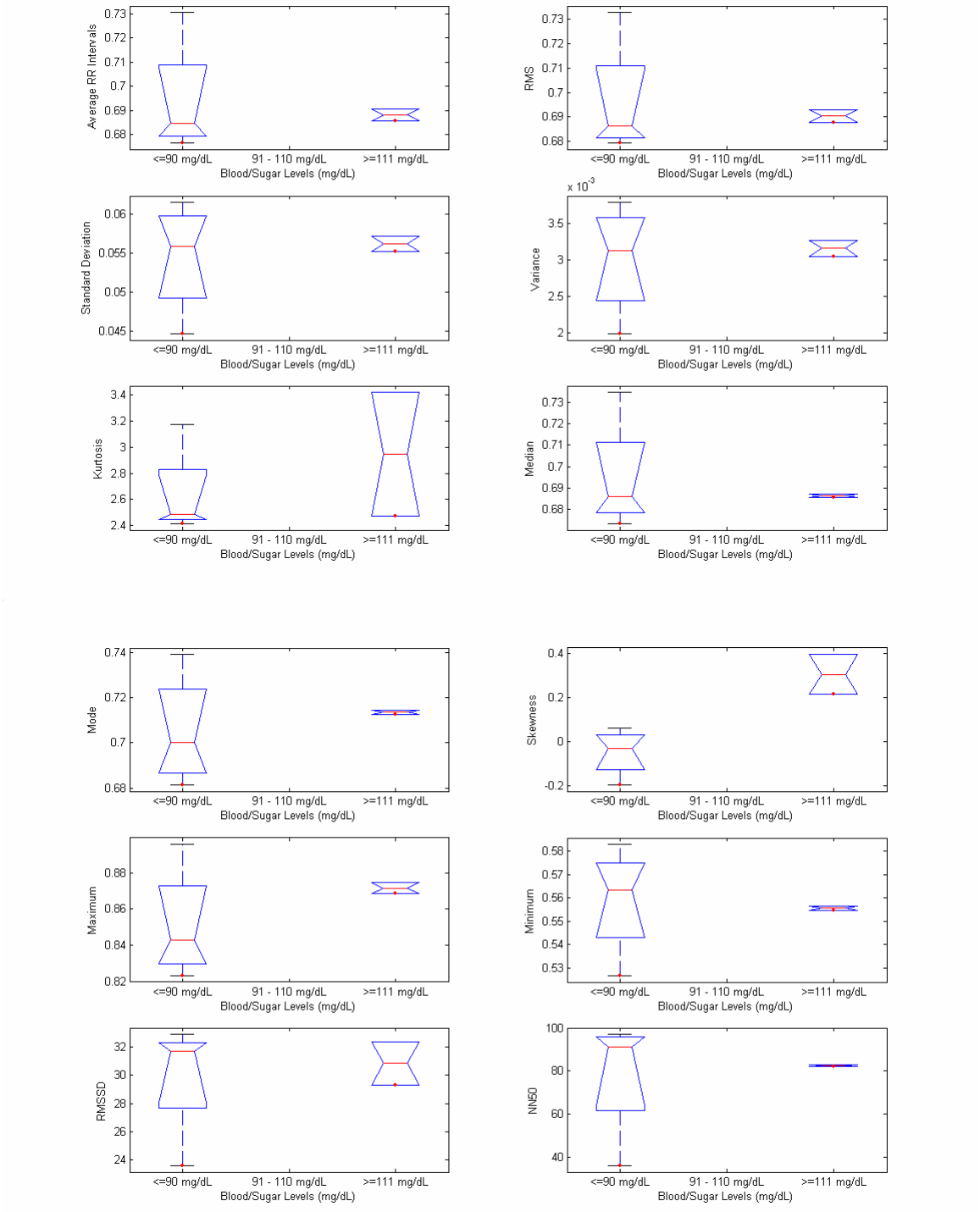

HF (ar)
35
30
25
20
15
10
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

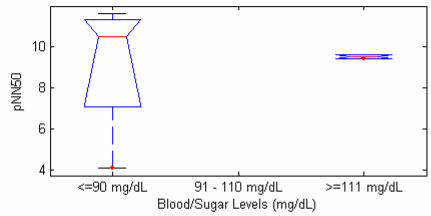

SD1
50
45
40
35
30
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

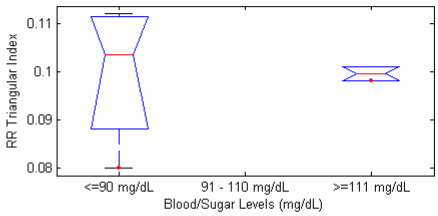

SD2
120
110
100
90
80
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

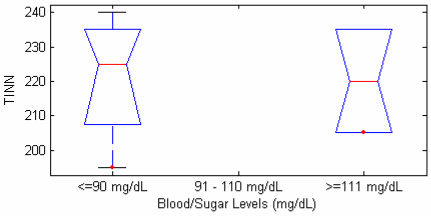

ApEn
1.45
1.4
1.35
1.3
1.25
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

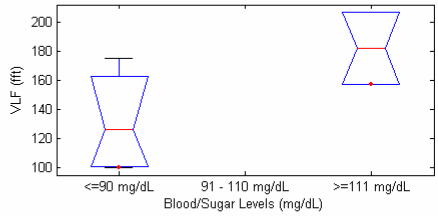
A.3.5 Healthy Subject 5

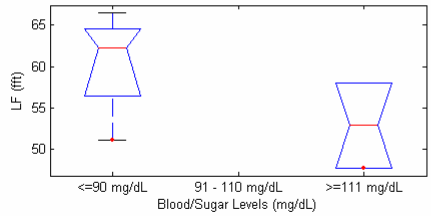


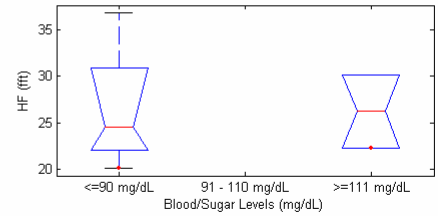

pNN50
10
8
6
4
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

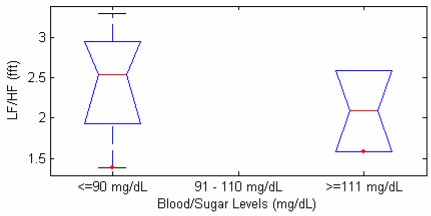

RR Triangular Index
0.11
0.1
0.09
0.08
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

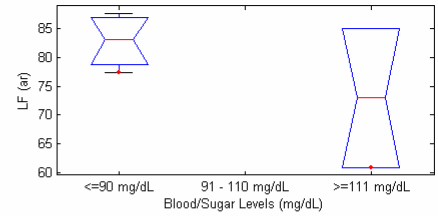

TINN
240
230
220
210
200
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

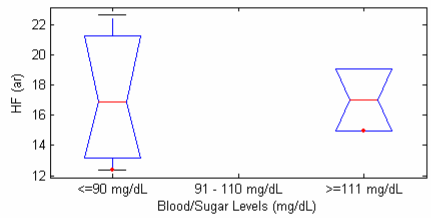

VLF (fft)
200
180
160
140
120
100
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

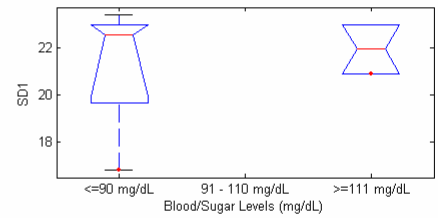

LF (fft)
65
60
55
50
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

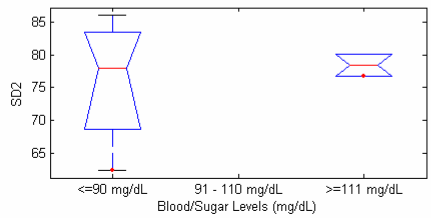

HF (fft)
35
30
25
20
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

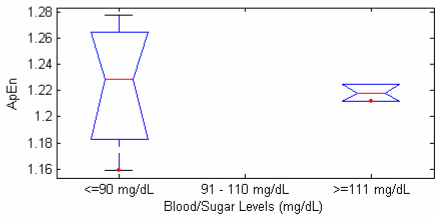

LF/HF (fft)
3
2.5
2
1.5
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)


LF (ar)
85
80
75
70
65
60
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

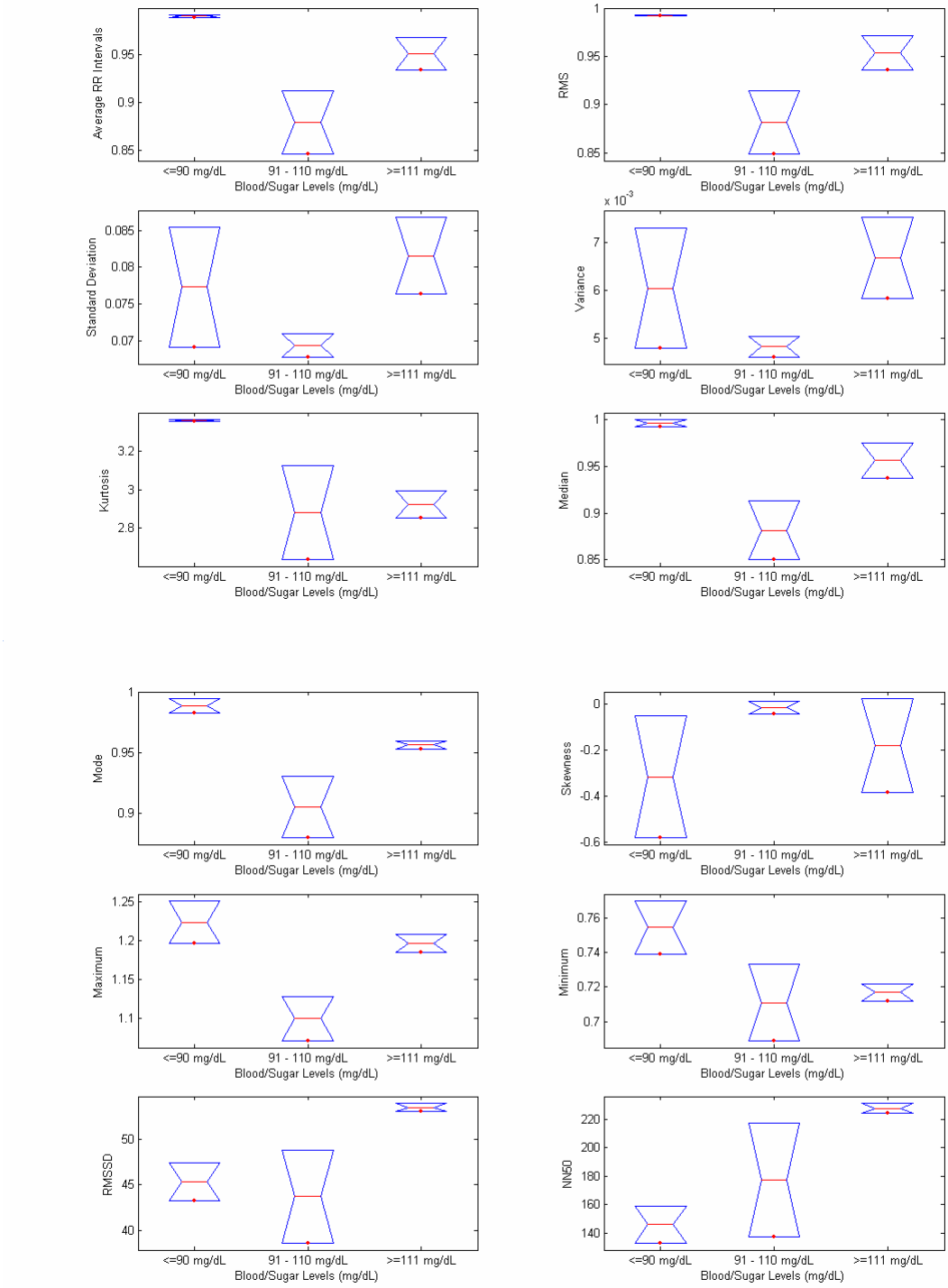

HF (ar)
22
20
18
16
14
12
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

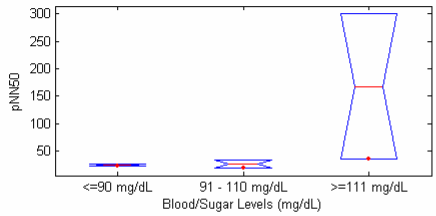

SD1
22
20
18
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

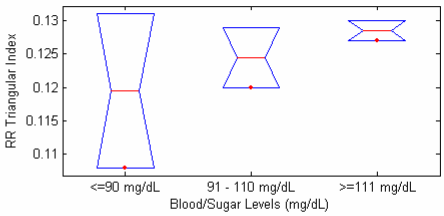

SD2
85
80
75
70
65
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

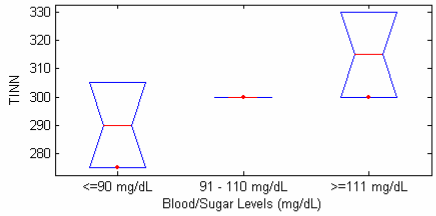

ApEn
1.28
1.26
1.24
1.22
1.2
1.18
1.16
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

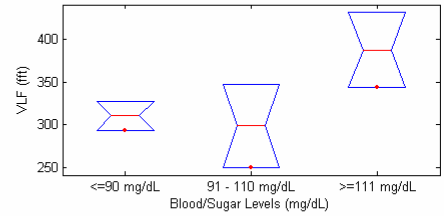
A.3.6 Healthy Subject 6

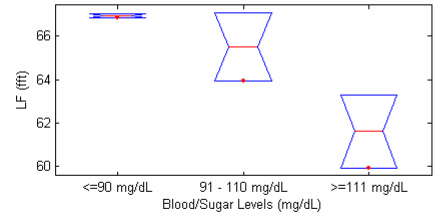


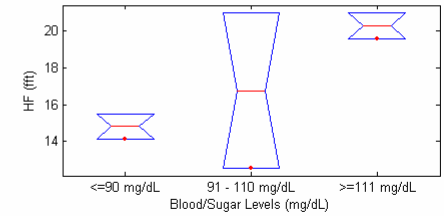

pNN50
300
250
200
150
100
50
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

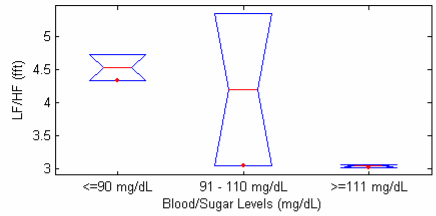

RR Triangular Index
0.13
0.125
0.12
0.115
0.11
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

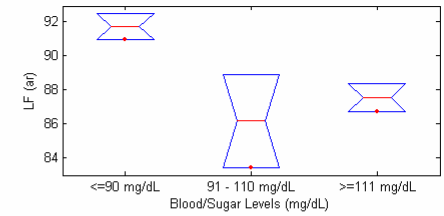

TINN
330
320
310
300
290
280
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

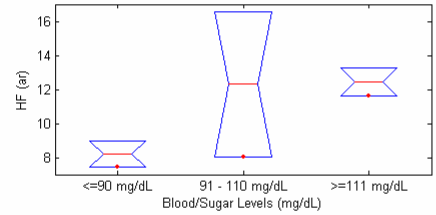

VLF (fft)
400
350
300
250
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

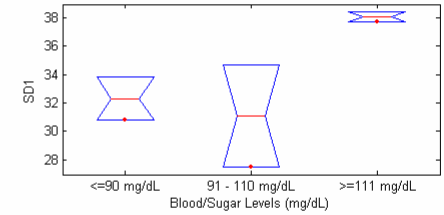

LF (fft)
66
64
62
60
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

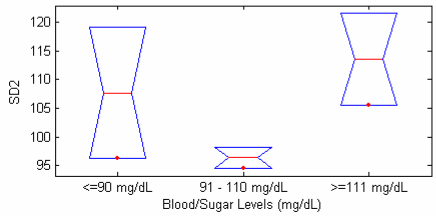

HF (fft)
20
18
16
14
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

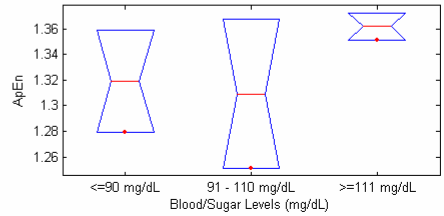

LF/HF (fft)
5
4.5
4
3.5
3
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)


LF (ar)
92
90
88
86
84
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

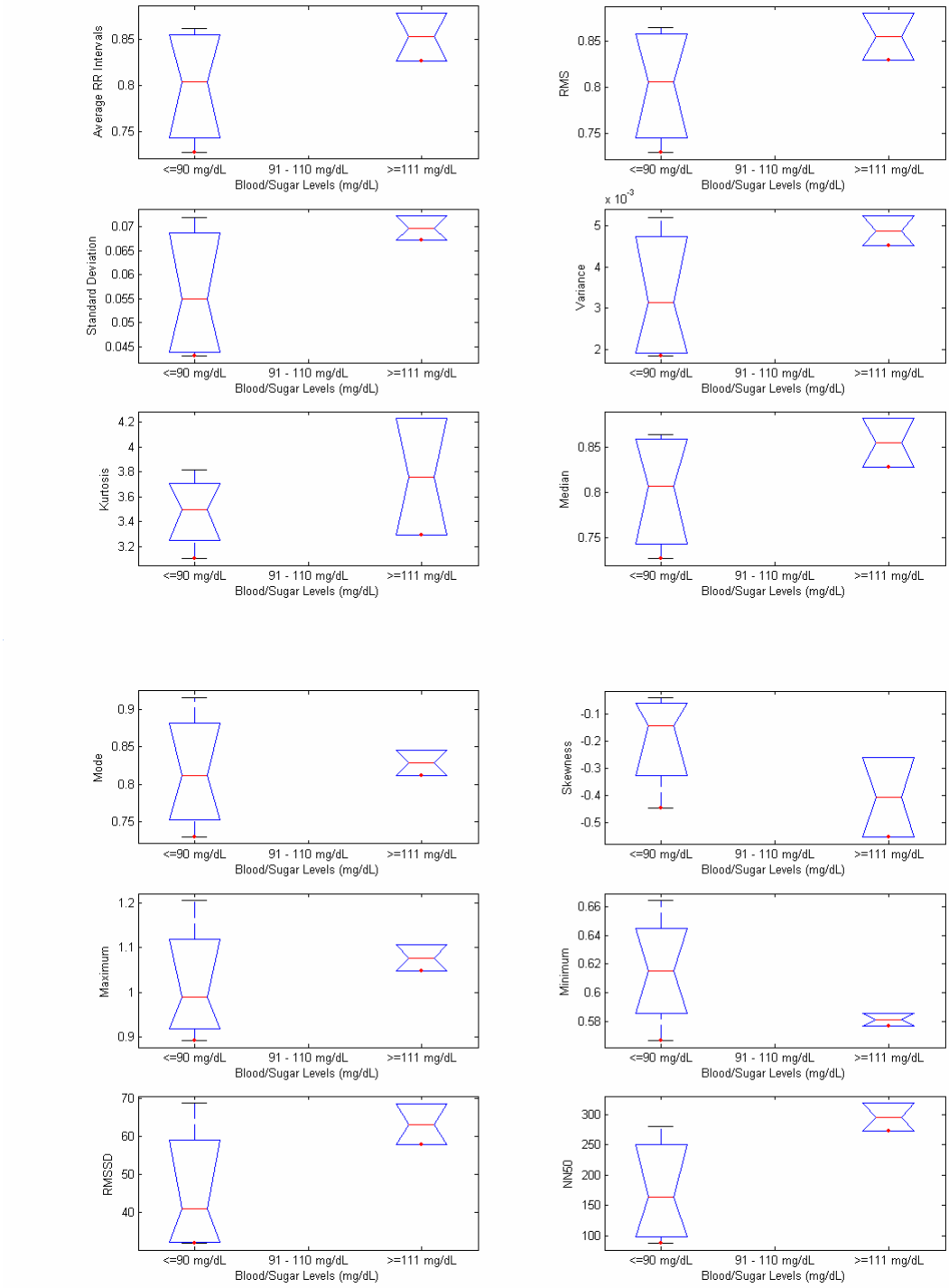

HF (ar)
16
14
12
10
8
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

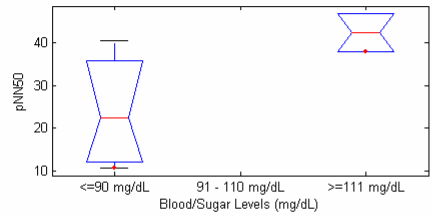

SD1
38
36
34
32
30
28
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

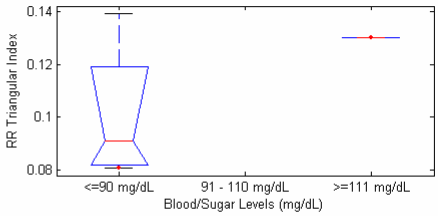

SD2
120
115
110
105
100
95
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

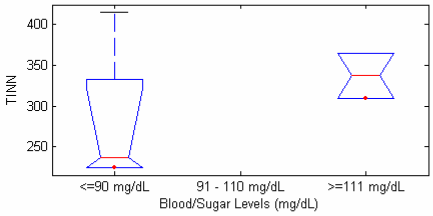

ApEn
1.36
1.34
1.32
1.3
1.28
1.26
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

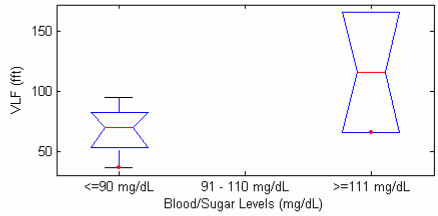
A.3.7 Healthy Subject 7

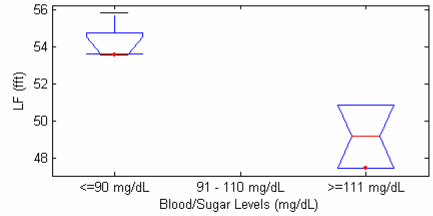


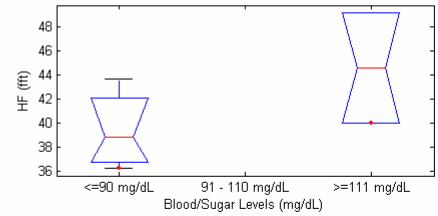

pNN50
40
30
20
10
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

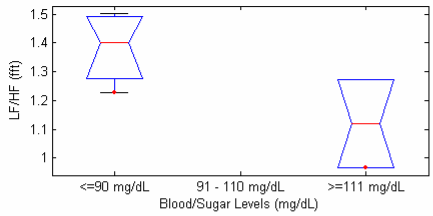

RR Triangular Index
0.14
0.12
0.1
0.08
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

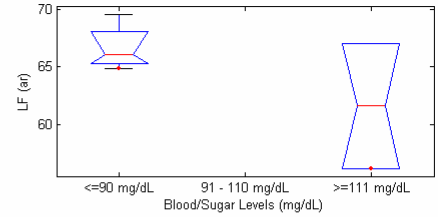

TINN
400
350
300
250
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

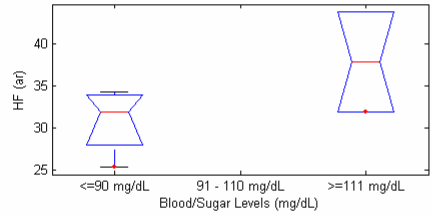

VLF (fft)
150
100
50
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

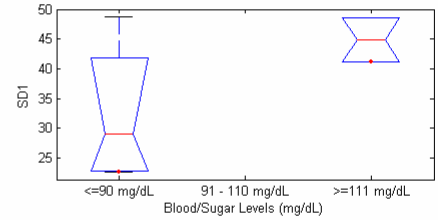

LF (fft)
56
54
52
50
48
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

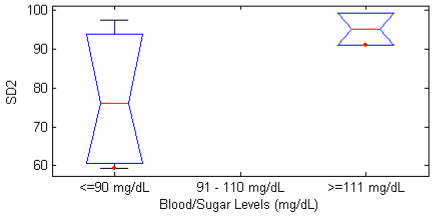

HF (fft)
48
46
44
42
40
38
36
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

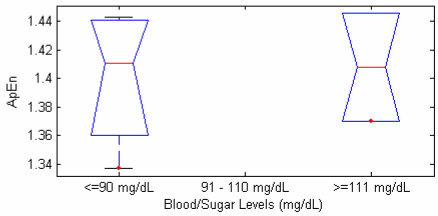

LF/HF (fft)
1.5
1.4
1.3
1.2
1.1
1
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)


LF (ar)
70
65
60
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

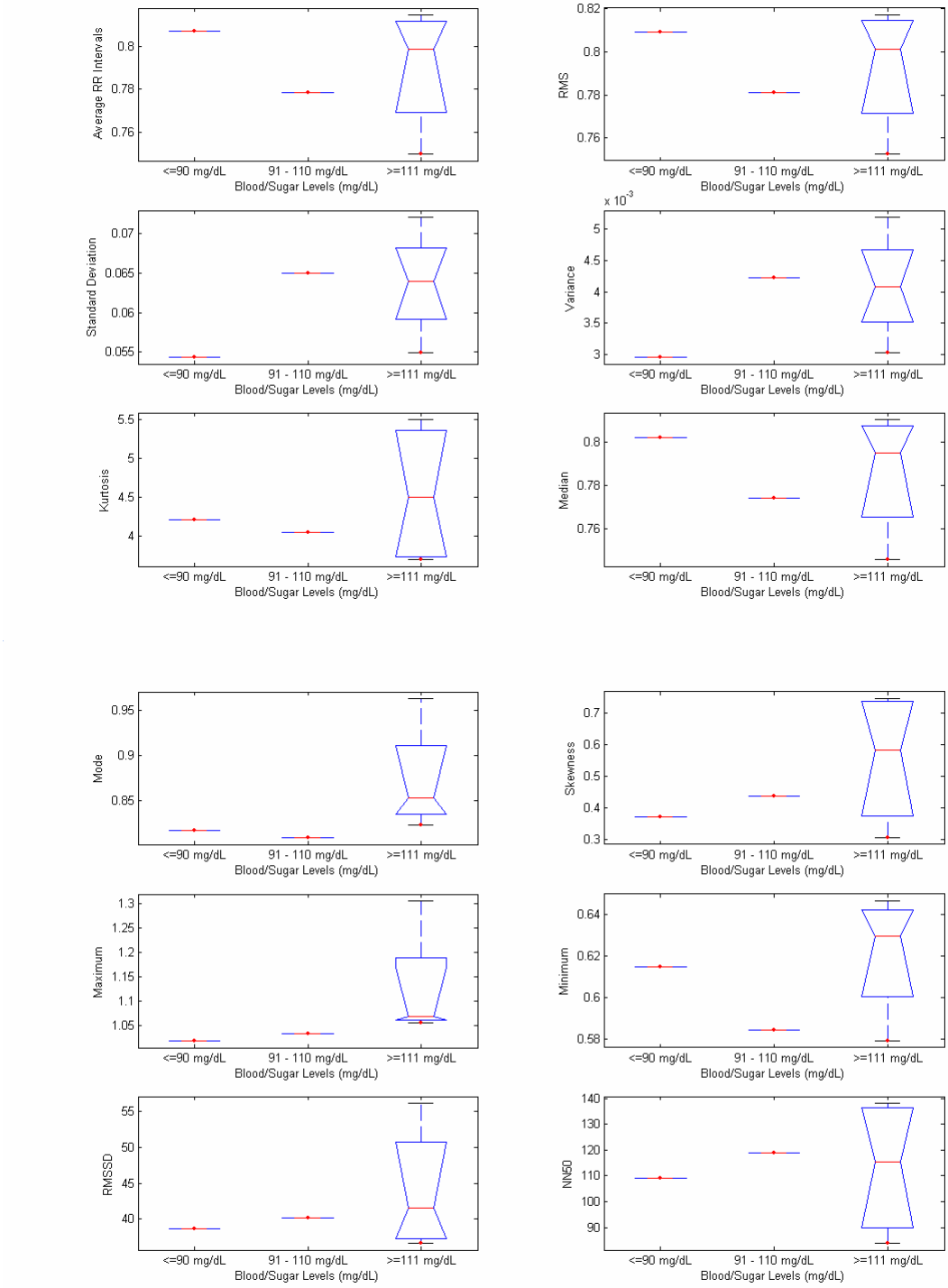

HF (ar)
40
35
30
25
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

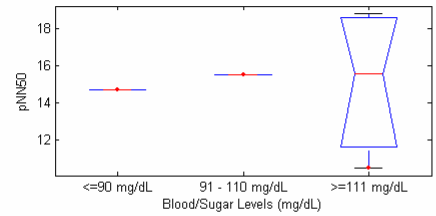

SD1
50
45
40
35
30
25
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

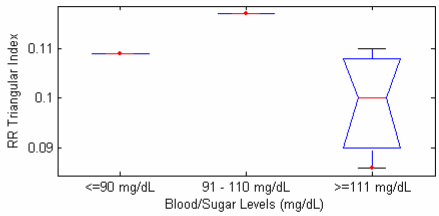

SD2
100
90
80
70
60
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

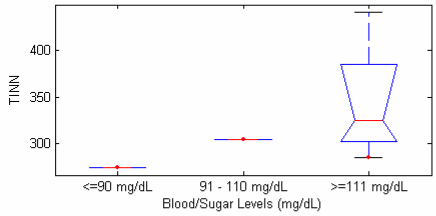

ApEn
1.44
1.42
1.4
1.38
1.36
1.34
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

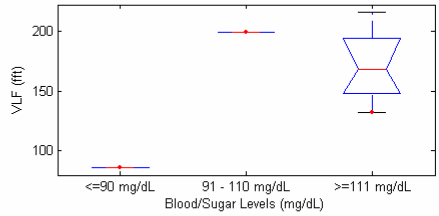
A.3.8 Healthy Subject 8

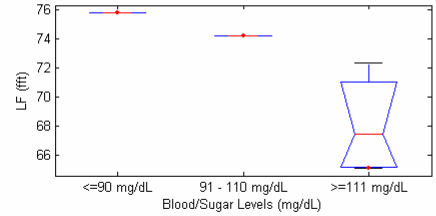


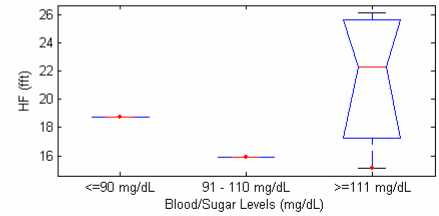

pNN50
18
16
14
12
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

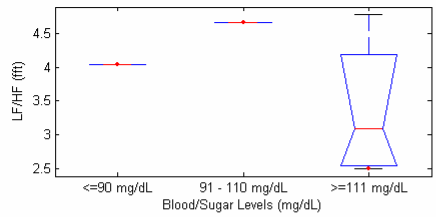

RR Triangular Index
0.11
0.1
0.09
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

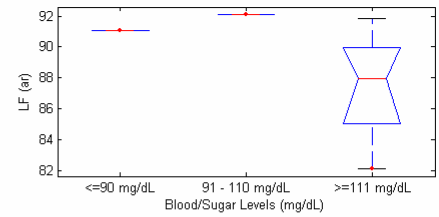

TINN
400
350
300
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

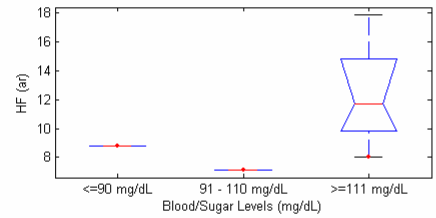

VLF (fft)
200
150
100
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

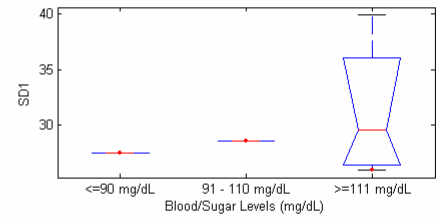

LF (fft)
76
74
72
70
68
66
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

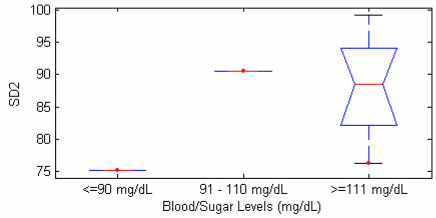

HF (fft)
26
24
22
20
18
16
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

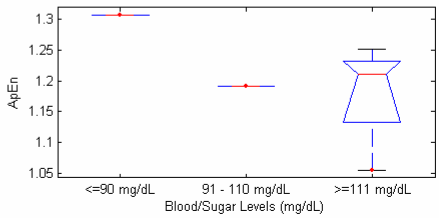

LF/HF (fft)
4.5
4
3.5
3
2.5
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)


LF (ar)
92
90
88
86
84
82
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

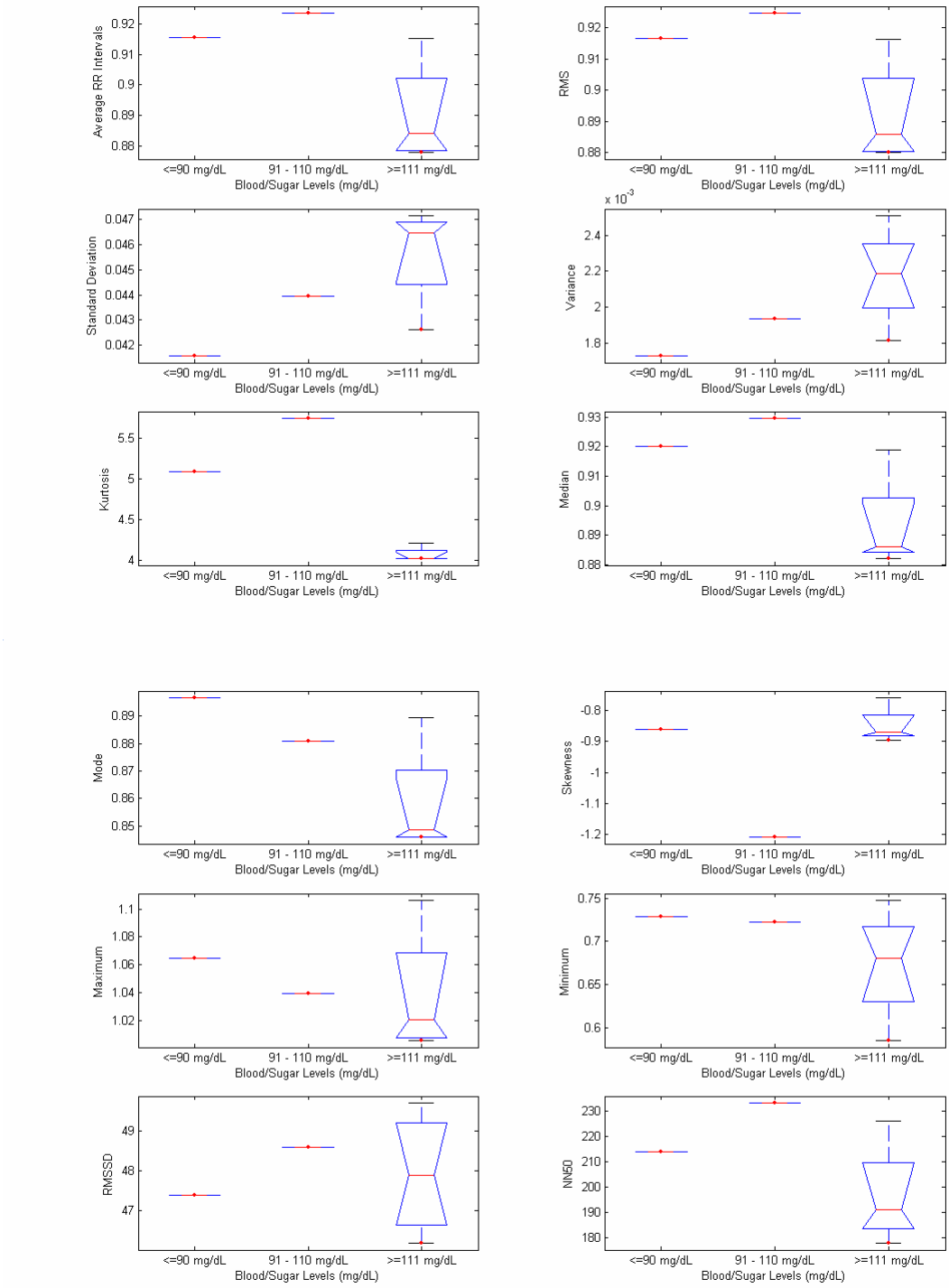

HF (ar)
18
16
14
12
10
8
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

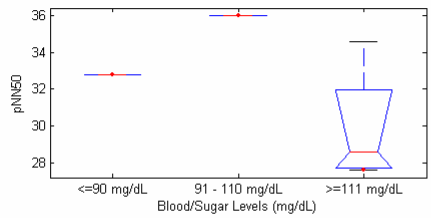

SD1
40
35
30
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

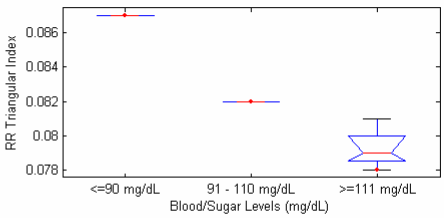

SD2
100
95
90
85
80
75
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

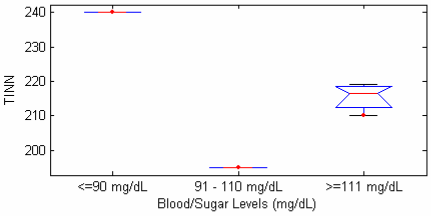

ApEn
1.3
1.25
1.2
1.15
1.1
1.05
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

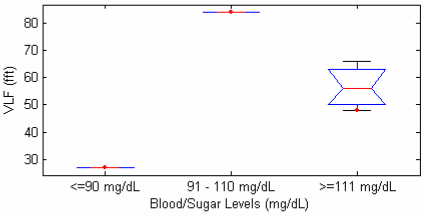
A.3.9 Healthy Subject 9

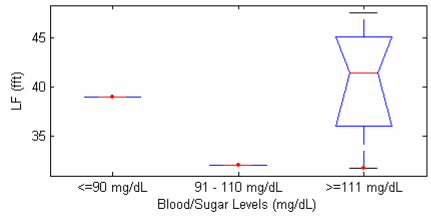


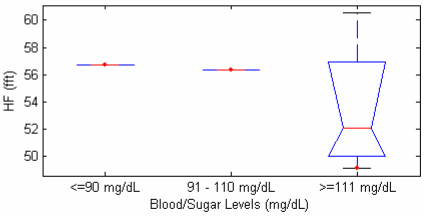

pNN50
36
34
32
30
28
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

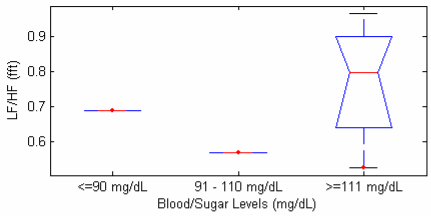

RR Triangular Index
0.086
0.084
0.082
0.08
0.078
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

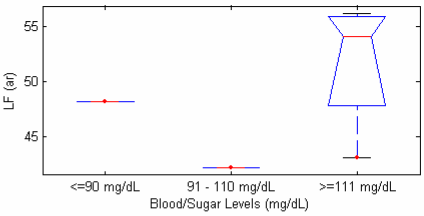

TINN
240
230
220
210
200
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

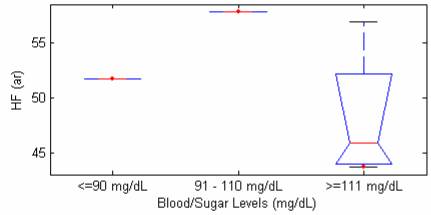

VLF (fft)
80
70
60
50
40
30
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

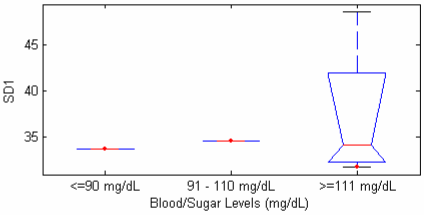

LF (fft)
45
40
35
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

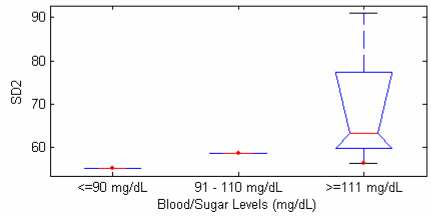

HF (fft)
60
58
56
54
52
50
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

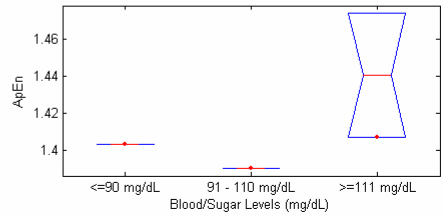

LF/HF (fft)
0.9
0.8
0.7
0.6
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)


LF (ar)
55
50
45
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

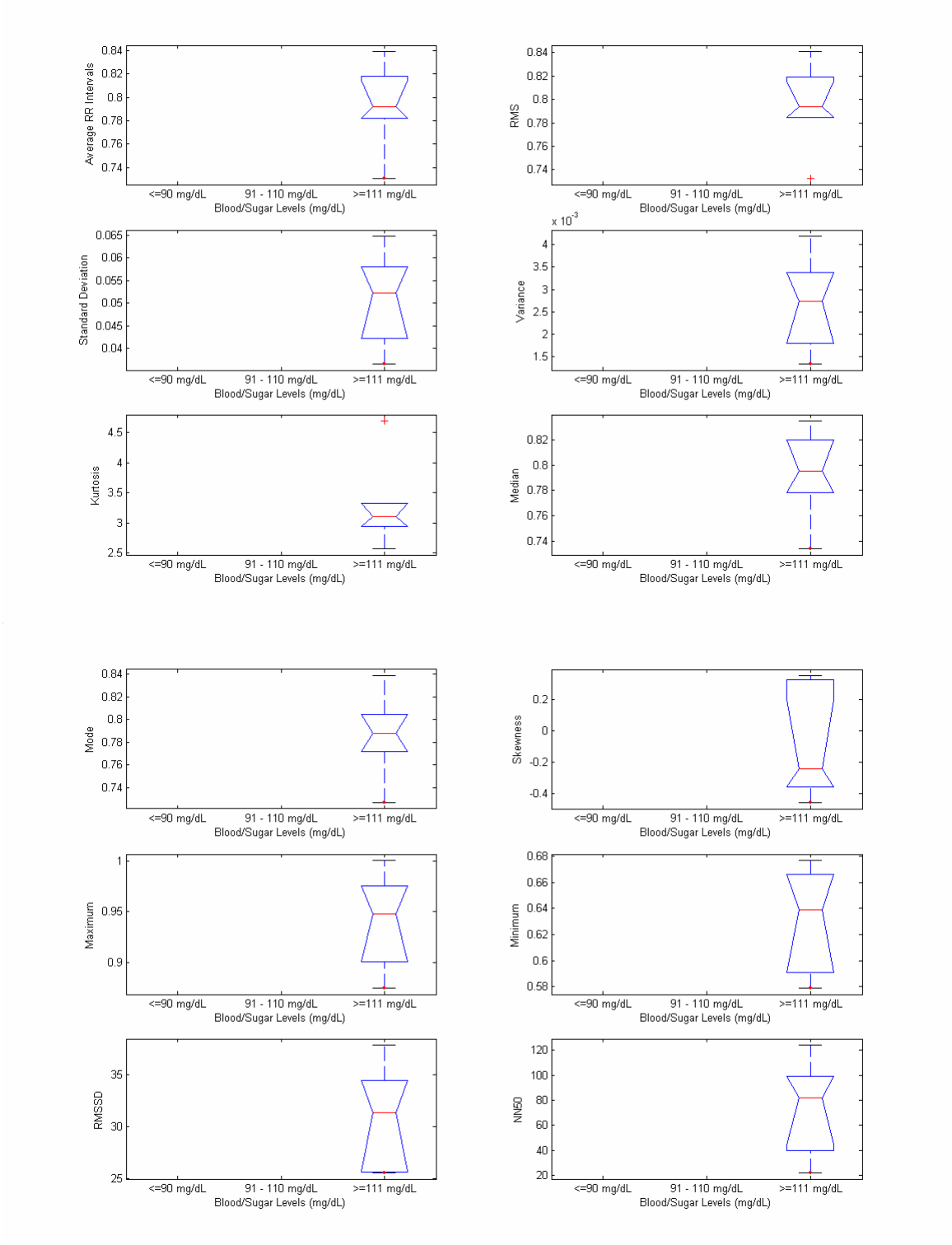

HF (ar)
55
50
45
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

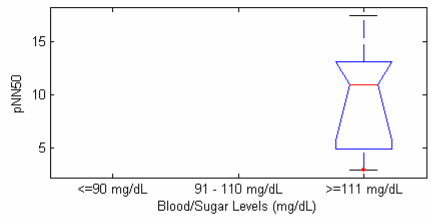

SD1
45
40
35
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

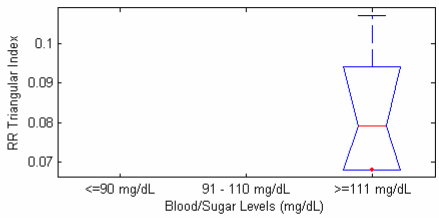

SD2
90
80
70
60
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

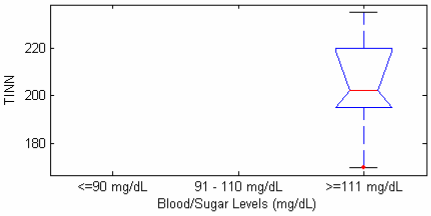

ApEn
1.46
1.44
1.42
1.4
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

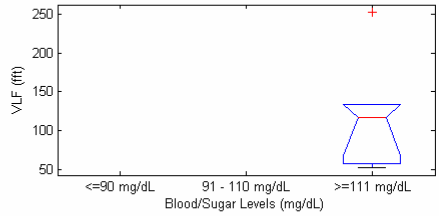
A.3.10 Healthy Subject 10

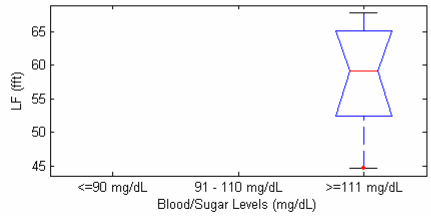


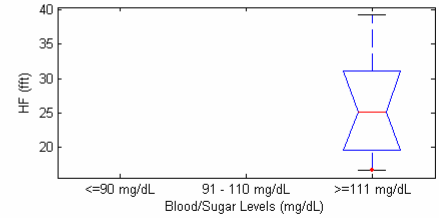

pNN50
15
10
5
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

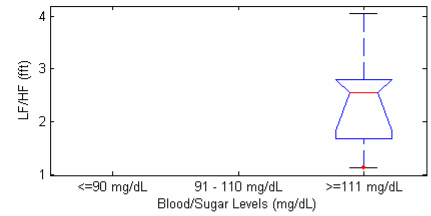

RR Triangular Index
0.1
0.09
0.08
0.07
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

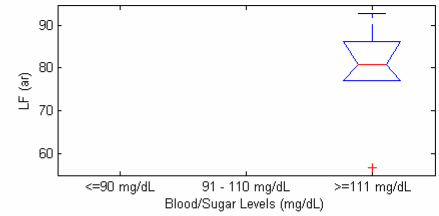

TINN
220
200
180
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

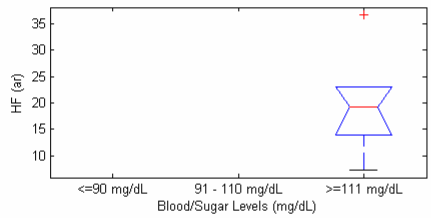

VLF (fft)
250
200
150
100
50
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

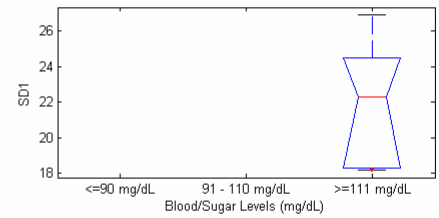

LF (fft)
65
60
55
50
45
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

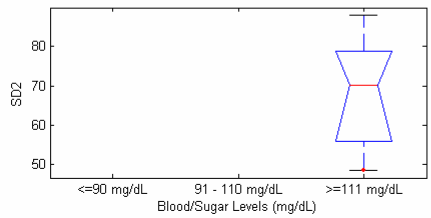

HF (fft)
40
35
30
25
20
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

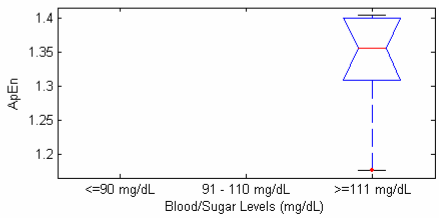

LF/HF (fft)
4
3
2
1
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)


LF (ar)
90
80
70
60
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)


HF (ar)
35
30
25
20
15
10
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

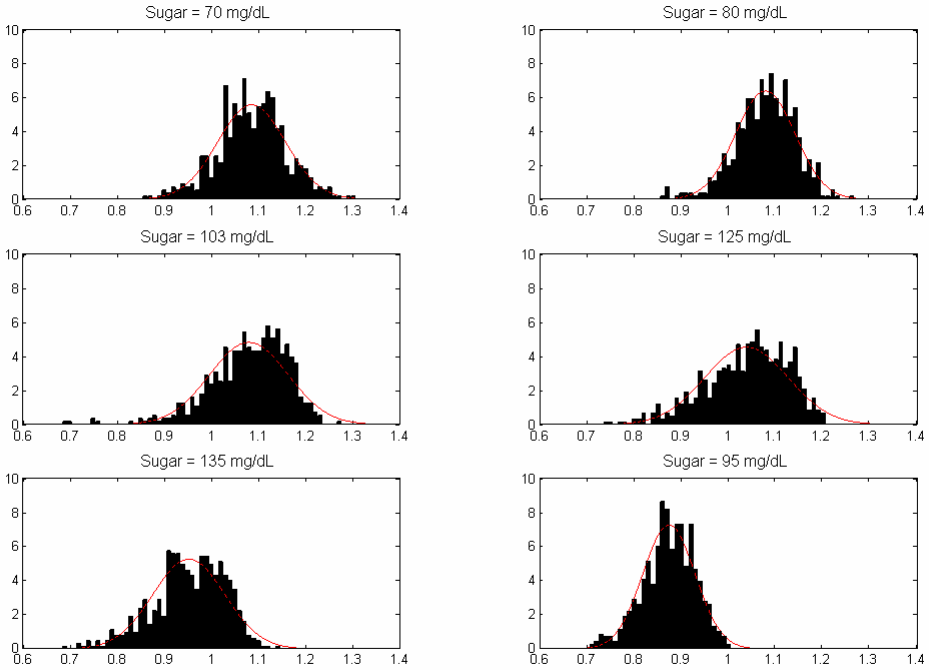

SD1
26
24
22
20
18
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

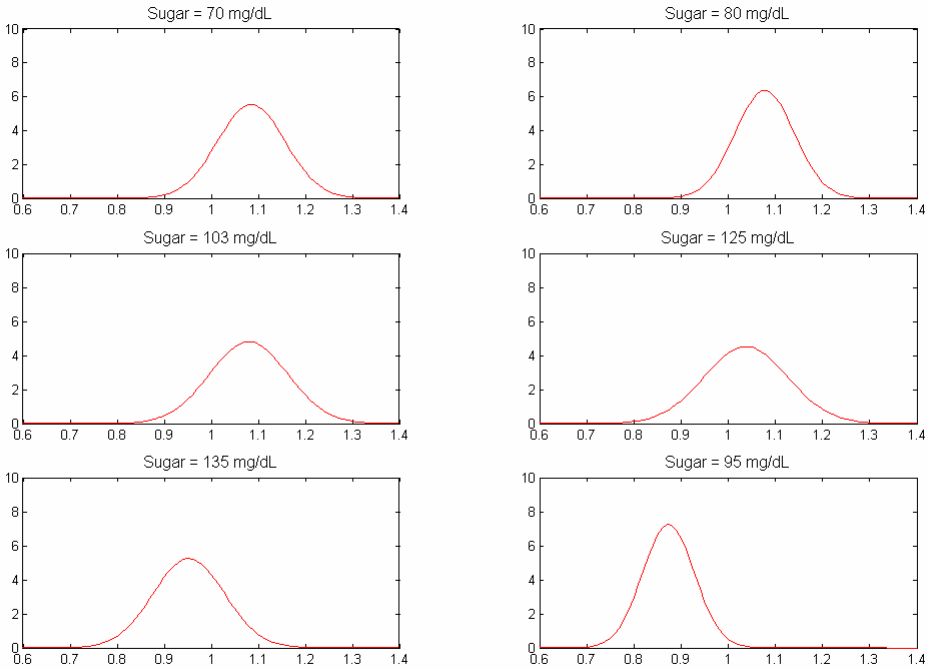

SD2
80
70
60
50
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)


ApEn
1.4
1.35
1.3
1.25
1.2
<=90 mg/dL
91 - 110 mg/dL
>=111 mg/dL
Blood/Sugar Levels (mg/dL)

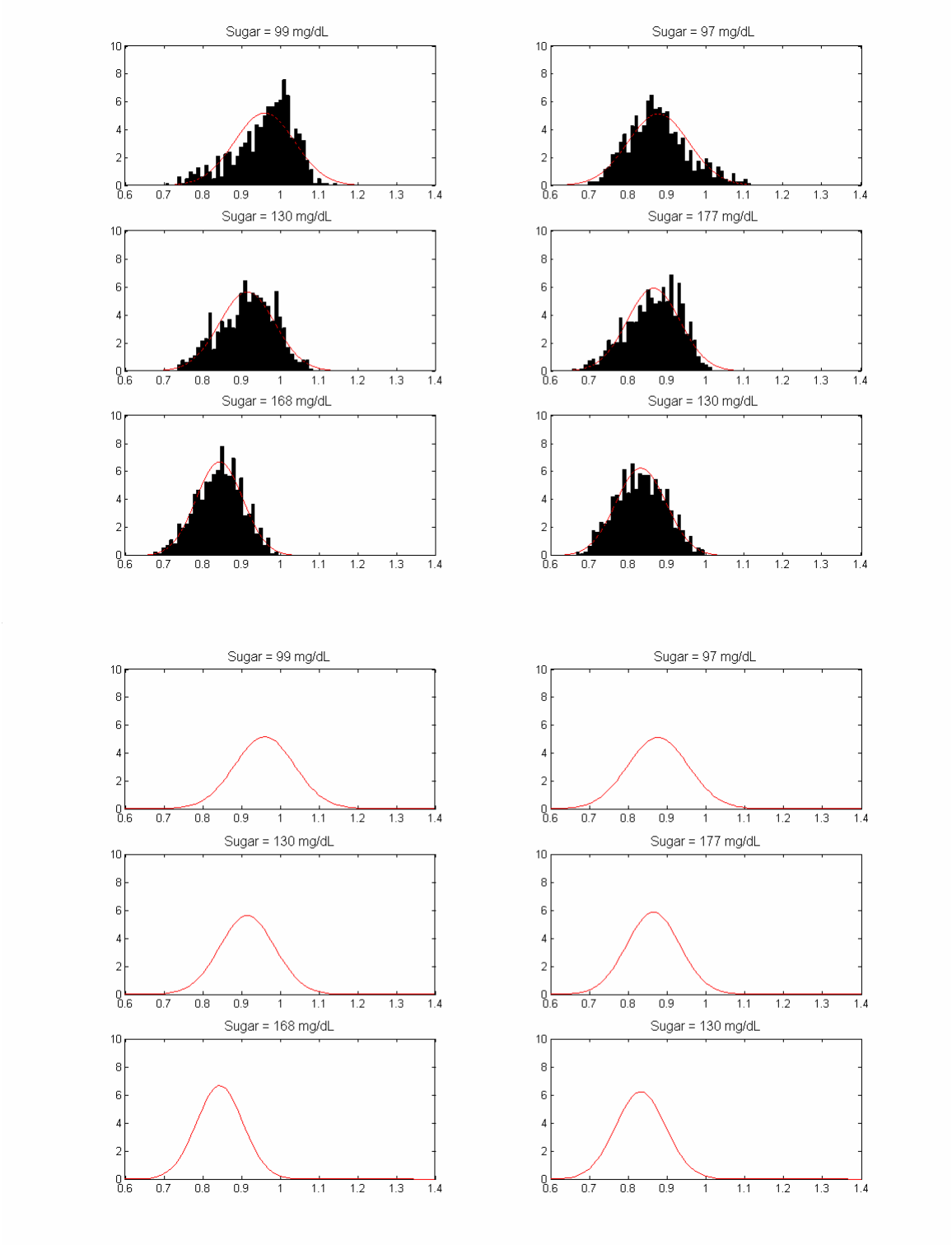
A.4 Non-Diabetic HRV histograms

A.4.1 Healthy Subject 1

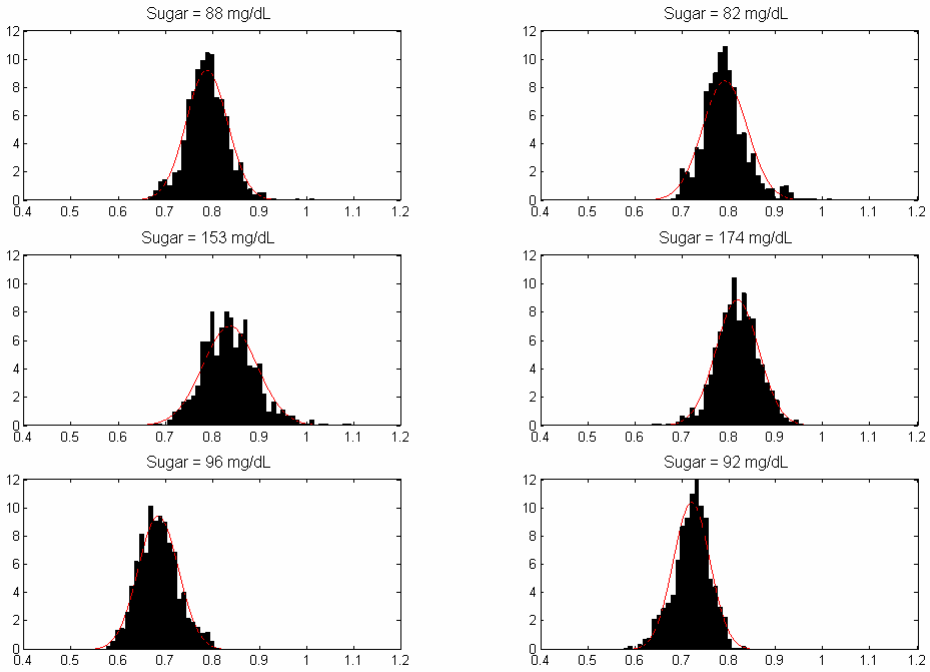


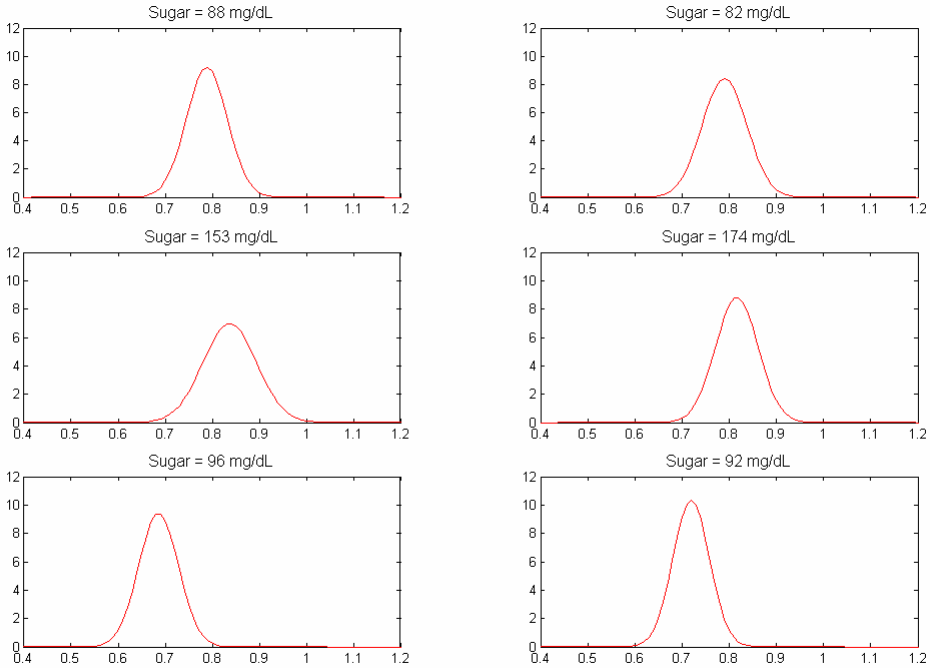


A.4.2 Healthy Subject 2

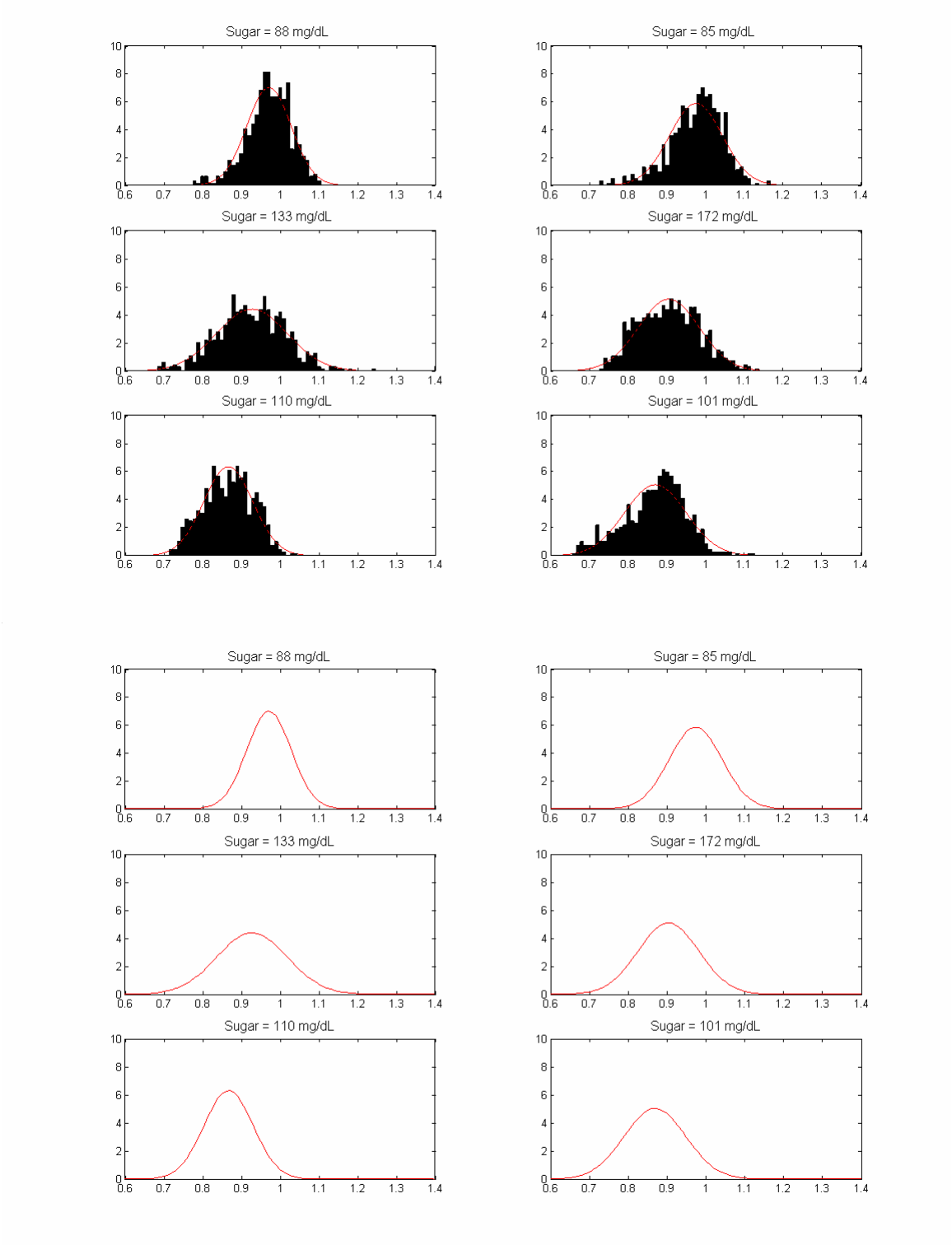


A.4.3 Healthy Subject 3

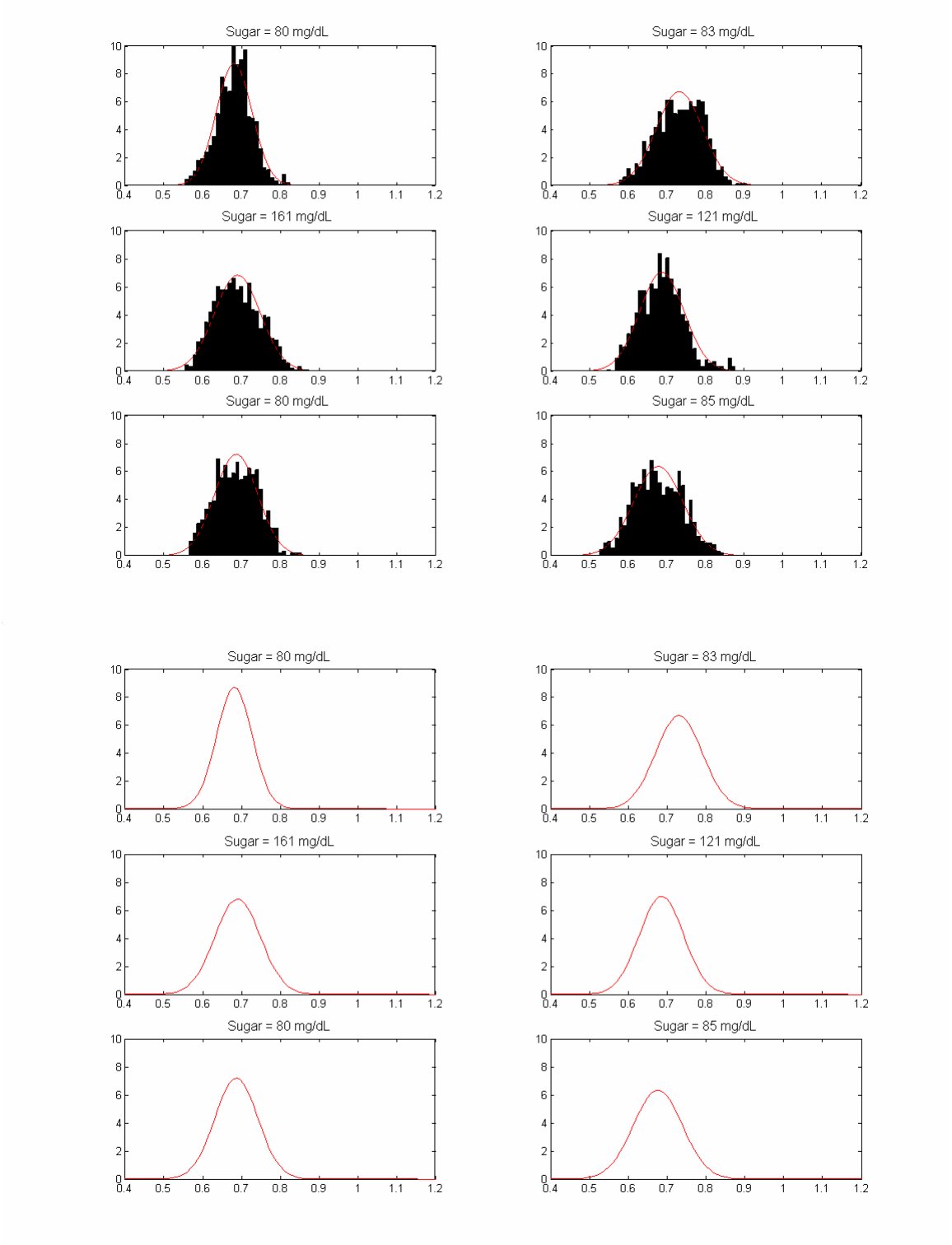




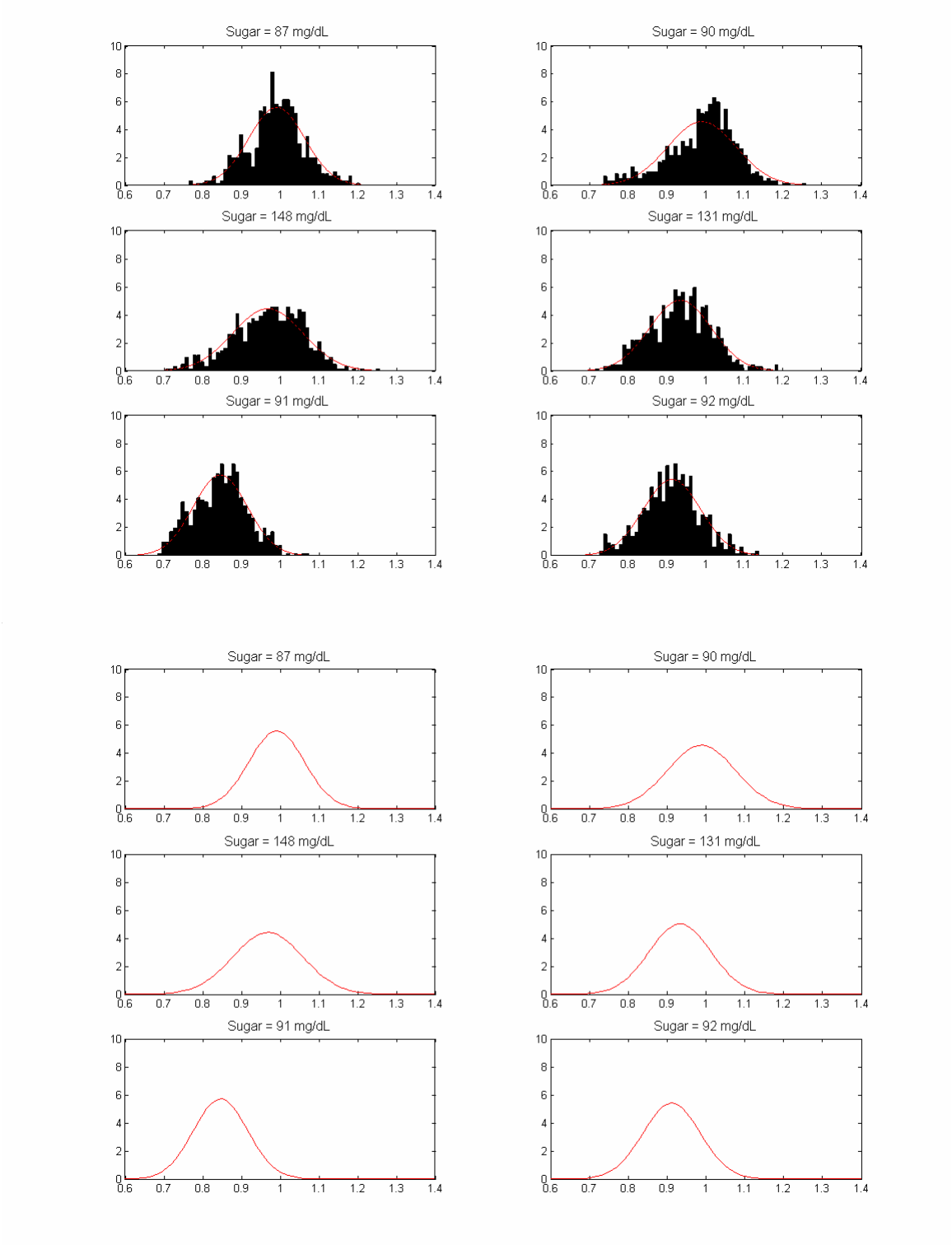
A.4.4 Healthy Subject 4



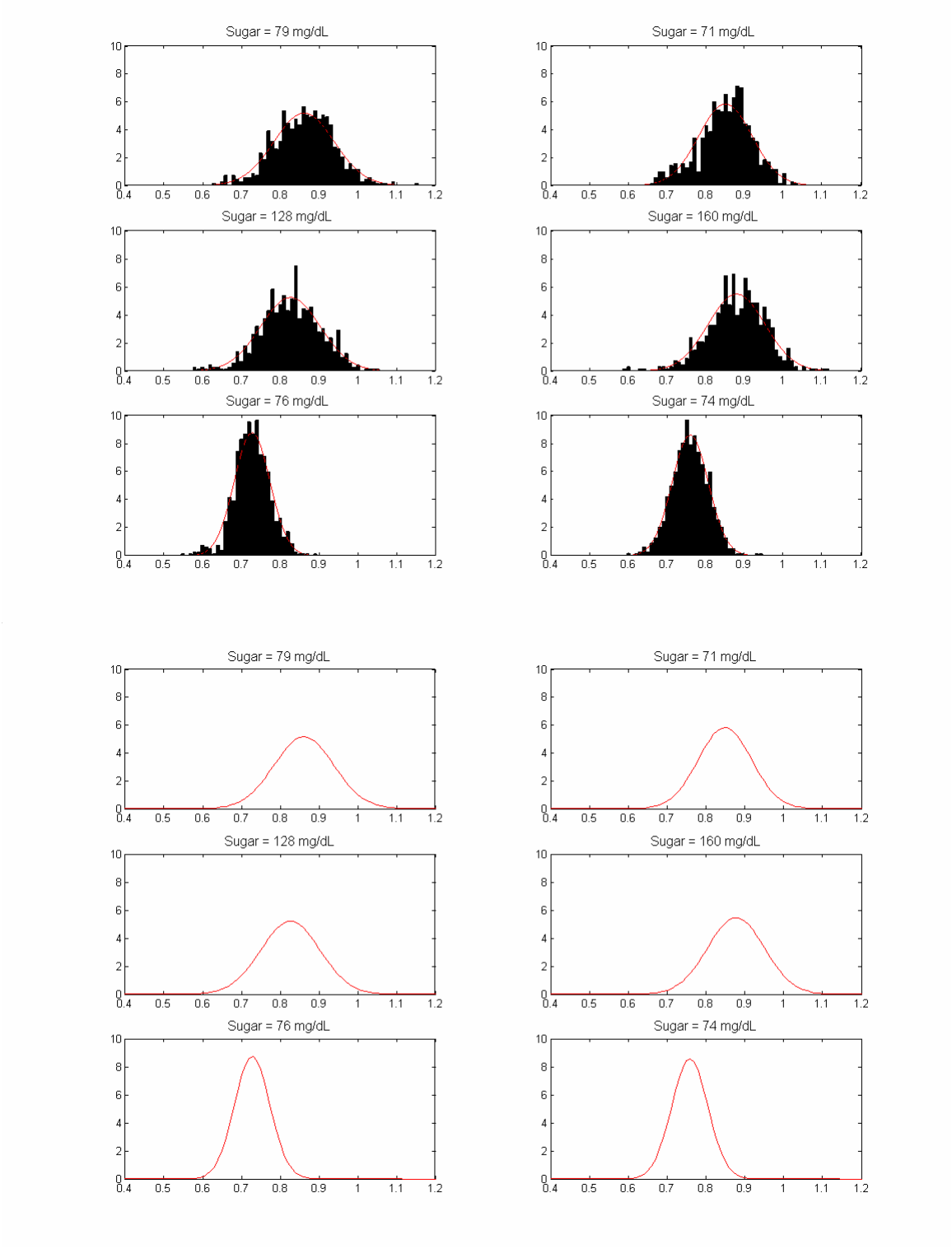
A.4.5 Healthy Subject 5



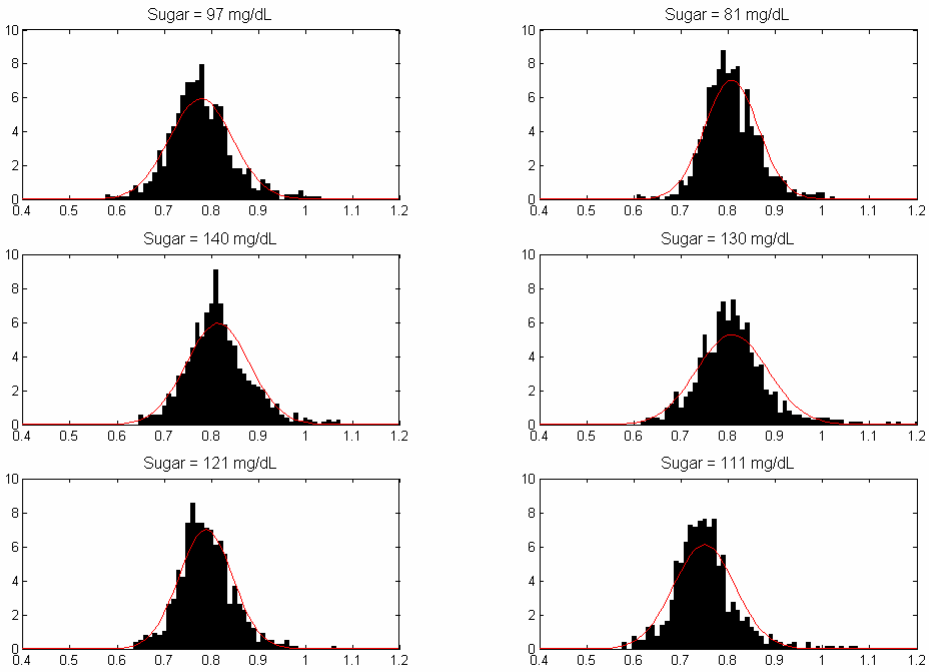
A.4.6 Healthy Subject 6

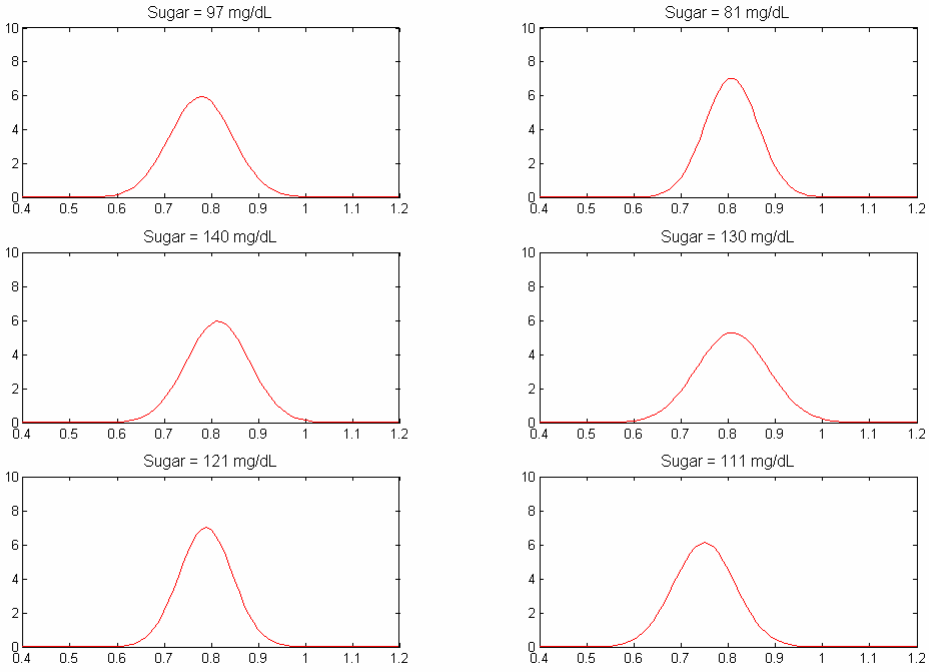


A.4.7 Healthy Subject 7

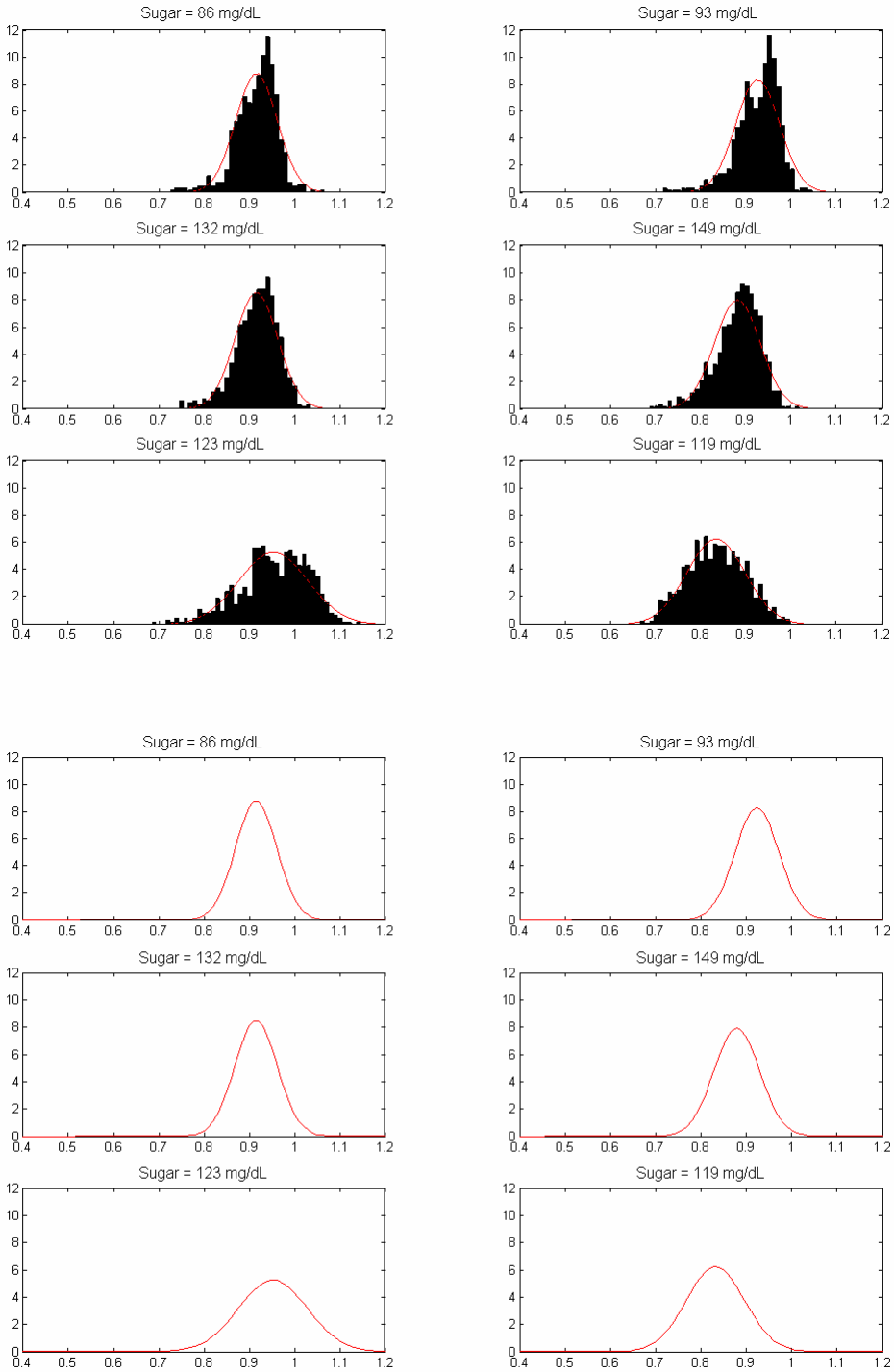


A.4.8 Healthy Subject 8

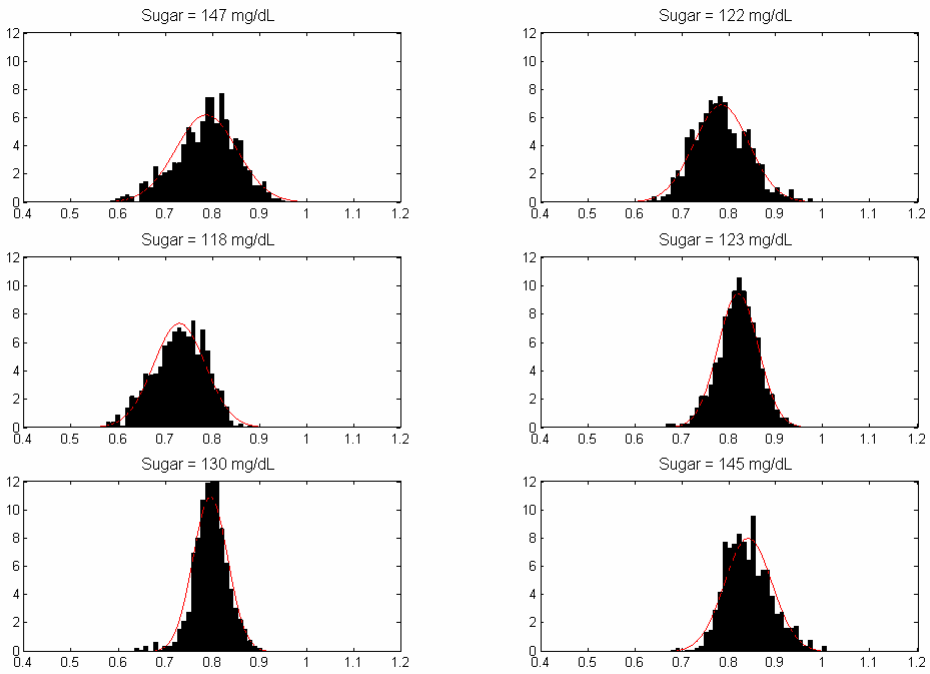


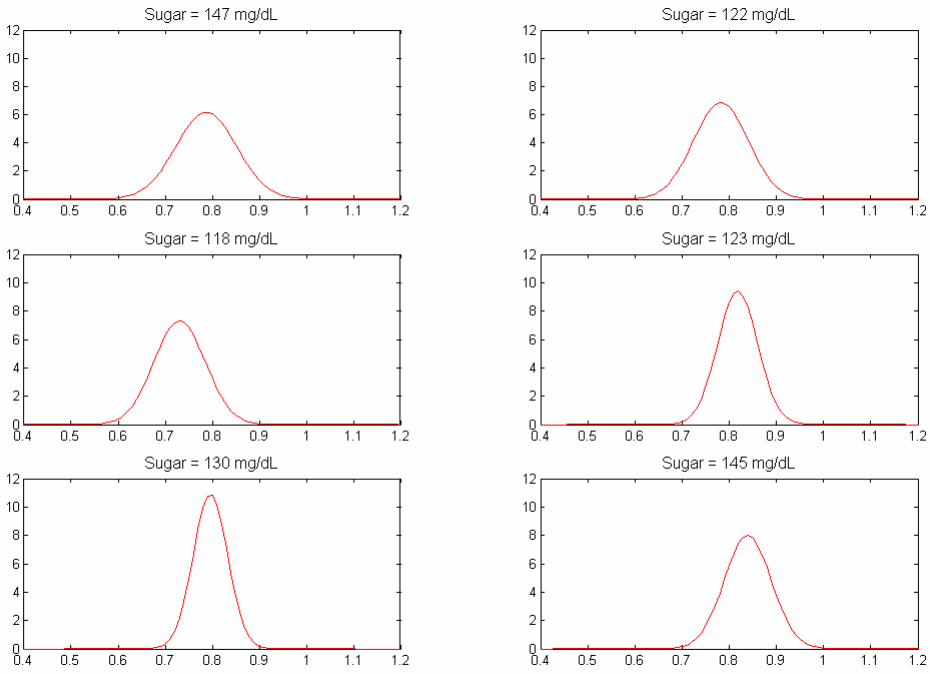


A.4.9 Healthy Subject 9



A.4.10 Healthy Subject 10





A.5 Diabetic HRV parameter measurements (6 subjects)

A.5.1 Subject with Diabetes 1

Hypoglycemic Measurements

Stat	1	2	3	4	5	6	7
Average (s)	0.81	0.80	0.85	0.88	0.90	0.90	0.92
RMS (s)	0.81	0.81	0.85	0.89	0.90	0.90	0.92
SD (s)	0.05	0.06	0.05	0.04	0.04	0.05	0.05
Var	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Kurtosis	4.91	4.03	4.35	8.23	7.82	8.65	6.34
Median (s)	0.81	0.81	0.85	0.88	0.90	0.90	0.92
mode (s)	0.81	0.82	0.84	0.87	0.89	0.89	0.91
skewness	-0.12	-0.44	-0.36	-0.26	-0.26	-0.25	-0.04
maximum (s)	0.98	0.97	1.02	1.08	1.06	1.12	1.15
min (s)	0.66	0.62	0.70	0.69	0.70	0.67	0.71
RMSSD (ms)	71.30	63.50	30.80	51.80	58.20	67.80	76.80
NN50	196.00	160.00	32.00	70.00	85.00	88.00	111.00
pNN50 %	26.50	21.80	4.60	10.40	12.80	13.30	17.10
RR tri indx	0.06	0.07	0.07	0.06	0.05	0.07	0.07
TINN (ms)	220.00	220.00	220.00	270.00	240.00	310.00	295.00
Power(FFT) VLF (s^2/Hz)	23.00	29.00	356.00	43.00	31.00	15.00	93.00
Power(FFT) LF (n.u.)	22.80	32.20	59.10	33.90	22.00	33.10	28.30
Power(FFT) HF	77.20	67.80	40.90	66.10	78.00	66.90	71.70
Power(FFT) LF/HF (n.u.)	0.30	0.48	1.44	0.51	0.28	0.50	0.40
Power(AR) VLF	0.00	228.00	329.00	98.00	52.00	59.00	0.00
Power(AR) LF (n.u.)	20.80	0.00	51.90	0.00	0.00	0.00	31.70
Power(AR) HF (n.u.)	18.20	37.30	25.20	45.70	55.70	58.90	40.90
Power(AR) LF/HF (n.u.)	1.15	0.00	2.06	0.00	0.00	0.00	0.77
SD1(poincare') (ms)	50.70	45.20	22.20	36.80	41.30	48.20	54.50
SD2(poincare') (ms)	41.30	67.10	59.70	41.20	38.70	42.50	54.20
ApEn	0.38	0.41	0.32	0.50	0.46	0.43	0.42

Stat	8	9	10	11	12	13	14	15
Average (s)	0.92	0.88	0.73	0.93	0.92	0.92	0.76	0.92
RMS (s)	0.92	0.89	0.73	0.93	0.93	0.92	0.76	0.92
SD (s)	0.07	0.12	0.04	0.10	0.06	0.04	0.03	0.07
Var	0.01	0.01	0.00	0.01	0.00	0.00	0.00	0.01
Kurtosis	4.07	2.18	4.12	3.58	7.48	9.67	4.03	4.07
Median (s)	0.92	0.92	0.72	0.94	0.92	0.92	0.76	0.92
mode (s)	0.96	0.97	0.70	0.95	0.93	0.91	0.76	0.96
skewness	0.26	-0.66	0.80	0.14	-0.11	0.06	0.35	0.26

maximum (s)	1.21	1.11	0.93	1.24	1.14	1.12	0.89	1.21
min (s)	0.71	0.60	0.63	0.67	0.71	0.73	0.67	0.71
RMSSD (ms)	40.10	29.50	14.40	117.40	85.50	63.40	17.70	40.10
NN50	51.00	23.00	7.00	180.00	102.00	63.00	6.00	51.00
pNN50 %	7.80	3.40	0.90	28.50	15.80	9.70	0.80	7.80
RR tri indx	0.07	0.01	0.05	0.09	0.06	0.05	0.06	0.07
TINN (ms)	265.00	295.00	190.00	430.00	290.00	280.00	145.00	265.00
Power(FFT) VLF (s^2/Hz)	127.00	152.00	37.00	201.00	44.00	14.00	32.00	127.00
Power(FFT) LF (n.u.)	69.90	66.30	91.70	19.50	20.90	18.20	82.50	69.90
Power(FFT) HF	30.10	33.70	8.30	80.50	79.10	81.80	17.50	30.10
Power(FFT) LF/HF (n.u.)	2.33	1.97	11.04	0.24	0.27	0.22	4.70	2.33
Power(AR) VLF	0.00	0.00	0.00	213.00	0.00	83.00	0.00	0.00
Power(AR) LF (n.u.)	71.30	77.00	95.10	0.00	19.90	0.00	92.70	71.30
Power(AR) HF (n.u.)	20.40	18.40	3.40	76.80	48.30	62.00	3.60	20.40
Power(AR) LF/HF (n.u.)	3.50	4.24	27.70	0.00	0.41	0.00	25.54	3.50
SD1(poincare') (ms)	28.60	21.10	10.30	83.40	60.70	45.00	12.60	28.60
SD2(poincare') (ms)	98.10	168.10	62.30	114.40	50.60	42.40	40.80	98.10
ApEn	0.27	0.17	0.21	0.29	0.32	0.38	0.38	0.27

Normal Measurements

Stat	1	2	3	4	5	6	7
Average (s)	0.61	0.65	0.66	0.70	0.79	0.81	0.77
RMS (s)	0.61	0.65	0.66	0.71	0.79	0.81	0.77
SD (s)	0.04	0.04	0.03	0.05	0.10	0.04	0.06
Var	0.00	0.00	0.00	0.00	0.01	0.00	0.00
Kurtosis	3.39	2.48	3.20	4.37	2.16	2.44	2.45
Median (s)	0.62	0.64	0.66	0.72	0.79	0.81	0.77
mode (s)	0.63	0.65	0.67	0.73	0.88	0.84	0.83
skewness	-0.31	0.26	0.20	-1.07	-0.04	0.29	-0.02
maximum (s)	0.73	0.75	0.78	0.86	1.00	0.95	0.93
min (s)	0.50	0.55	0.59	0.54	0.43	0.70	0.60
RMSSD (ms)	9.40	10.90	11.50	13.20	38.90	18.90	17.60
NN50	1.00	3.00	2.00	4.00	35.00	11.00	11.00
pNN50 %	0.10	0.30	0.20	0.50	4.70	1.50	1.40
RR tri indx	0.03	0.04	0.05	0.04	0.08	0.07	0.08
TINN (ms)	90.00	130.00	130.00	135.00	350.00	165.00	185.00
Power(FFT) VLF (s^2/Hz)	30.00	26.00	19.00	19.00	191.00	101.00	269.00

Power(FFT) LF (n.u.)	81.40	76.90	88.30	81.30	83.60	82.60	87.30
Power(FFT) HF	18.60	23.10	11.70	18.70	16.40	17.40	12.70
Power(FFT) LF/HF (n.u.)	4.37	3.33	7.57	4.35	5.08	4.74	6.87
Power(AR) VLF	2.00	0.00	0.00	0.00	0.00	26.00	0.00
Power(AR) LF (n.u.)	92.30	89.60	92.00	85.30	81.90	96.20	97.40
Power(AR) HF (n.u.)	4.60	6.90	5.90	9.80	0.20	2.40	1.40
Power(AR) LF/HF (n.u.)	20.21	12.96	15.61	8.74	335.91	40.73	67.75
SD1(poincare') (ms)	6.80	7.80	8.20	9.40	27.90	13.50	12.70
SD2(poincare') (ms)	60.60	51.30	41.20	74.60	138.20	61.60	90.30
ApEn	0.15	0.24	0.38	0.16	0.16	0.36	0.22

Stat	8	9	10	11	12	13	14	15
Average (s)	0.75	0.77	0.71	0.71	0.72	0.87	0.86	0.75
RMS (s)	0.75	0.77	0.71	0.71	0.72	0.87	0.86	0.75
SD (s)	0.04	0.08	0.04	0.04	0.04	0.04	0.03	0.04
Var	0.00	0.01	0.00	0.00	0.00	0.00	0.00	0.00
Kurtosis	3.37	4.49	3.69	4.31	2.94	8.04	8.57	3.37
Median (s)	0.76	0.77	0.70	0.71	0.72	0.87	0.86	0.76
mode (s)	0.77	0.79	0.69	0.71	0.69	0.87	0.86	0.77
skewness	-0.06	0.15	0.90	0.16	-0.17	-1.03	-0.64	-0.06
maximum (s)	0.90	1.20	0.87	0.89	0.82	1.03	1.04	0.90
min (s)	0.63	0.57	0.60	0.60	0.60	0.70	0.62	0.63
RMSSD (ms)	14.00	41.60	15.60	15.60	10.30	15.40	26.70	14.00
NN50	3.00	46.00	11.00	13.00	0.00	5.00	7.00	3.00
pNN50 %	0.40	6.10	1.30	1.60	0.00	0.70	1.00	0.40
RR tri indx	0.05	0.07	0.05	0.05	0.04	0.04	0.05	0.05
TINN (ms)	145.00	335.00	160.00	190.00	95.00	145.00	290.00	145.00
Power(FFT) VLF (s^2/Hz)	85.00	279.00	70.00	150.00	29.00	134.00	54.00	85.00
Power(FFT) LF (n.u.)	87.50	50.90	87.90	88.30	91.20	68.20	79.60	87.50
Power(FFT) HF	12.50	49.10	12.10	11.70	8.80	31.80	20.40	12.50
Power(FFT) LF/HF (n.u.)	7.02	1.04	7.28	7.53	10.36	2.14	3.91	7.02
Power(AR) VLF	0.00	0.00	0.00	1.00	0.00	0.00	0.00	0.00
Power(AR) LF (n.u.)	92.40	75.40	91.20	94.60	92.50	83.40	65.80	92.40
Power(AR) HF (n.u.)	5.00	10.10	4.70	3.30	4.00	14.80	22.50	5.00
Power(AR) LF/HF (n.u.)	18.52	7.50	19.49	28.79	22.87	5.65	2.93	18.52

SD1(poincare') (ms)	10.10	29.60	11.20	11.20	7.40	11.10	19.00	10.10
SD2(poincare') (ms)	56.80	108.80	61.70	57.00	56.70	55.00	43.10	56.80
ApEn	0.26	0.19	0.21	0.23	0.19	0.35	0.34	0.26

Hyperglycemic Measurements

Stat	1	2	3	4	5	6	7
Average (s)	0.82	0.91	0.91	0.88	0.87	0.88	0.85
RMS (s)	0.82	0.91	0.91	0.88	0.87	0.88	0.85
SD (s)	0.06	0.04	0.03	0.02	0.04	0.04	0.05
Var	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Kurtosis	6.06	3.28	3.49	6.31	5.11	8.51	2.91
Median (s)	0.83	0.91	0.91	0.88	0.87	0.88	0.84
mode (s)	0.89	0.91	0.90	0.88	0.86	0.88	0.83
skewness	-0.57	-0.66	-0.27	-0.69	-0.08	-0.78	0.60
maximum (s)	1.10	0.98	0.99	0.96	0.98	1.04	1.01
min (s)	0.44	0.79	0.80	0.79	0.72	0.70	0.73
RMSSD (ms)	36.20	16.20	16.10	11.90	12.80	12.80	22.30
NN50	11.00	4.00	1.00	0.00	2.00	2.00	25.00
pNN50 %	1.60	0.60	0.20	0.00	0.30	0.30	3.60
RR tri indx	0.07	0.06	0.04	0.03	0.04	0.04	0.07
TINN (ms)	400.00	120.00	110.00	110.00	145.00	165.00	180.00
Power(FFT) VLF (s^2/Hz)	209.00	112.00	60.00	14.00	95.00	20.00	68.00
Power(FFT) LF (n.u.)	72.60	71.20	75.10	68.80	83.70	87.60	87.50
Power(FFT) HF	27.40	28.80	24.90	31.20	16.30	12.40	12.50
Power(FFT) LF/HF (n.u.)	2.65	2.47	3.02	2.21	5.14	7.04	6.99
Power(AR) VLF	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Power(AR) LF (n.u.)	70.30	83.00	77.70	78.70	91.90	93.10	91.70
Power(AR) HF (n.u.)	15.00	14.50	18.90	17.50	6.70	6.10	6.60
Power(AR) LF/HF (n.u.)	4.70	5.72	4.11	4.50	13.74	15.35	13.81
SD1(poincare') (ms)	25.80	11.60	11.50	8.50	9.20	9.30	15.90
SD2(poincare') (ms)	79.00	48.80	39.50	24.50	50.30	55.50	74.20
ApEn	0.22	0.39	0.50	0.57	0.25	0.29	0.32

Stat	8	9	10	11	12	13	14	15
Average (s)	0.81	0.89	0.92	0.99	0.96	0.97	0.98	0.81
RMS (s)	0.81	0.89	0.93	0.99	0.96	0.98	0.98	0.81
SD (s)	0.07	0.07	0.13	0.06	0.07	0.12	0.06	0.07
Var	0.01	0.01	0.02	0.00	0.01	0.01	0.00	0.01

Kurtosis	4.07	3.58	2.38	3.45	3.19	2.97	3.73	4.07
Median (s)	0.80	0.89	0.96	0.99	0.97	1.00	0.99	0.80
mode (s)	0.81	0.85	0.98	1.02	1.01	1.02	0.99	0.81
skewness	0.41	-0.17	-0.62	-0.29	-0.65	-0.67	-0.71	0.41
maximum (s)	1.14	1.12	1.22	1.14	1.16	1.31	1.14	1.14
min (s)	0.63	0.54	0.49	0.77	0.76	0.64	0.77	0.63
RMSSD (ms)	23.30	46.30	47.20	42.70	37.10	48.10	40.60	23.30
NN50	30.00	86.00	139.00	154.00	108.00	156.00	131.00	30.00
pNN50 %	4.10	13.20	21.70	25.90	17.40	25.70	21.70	4.10
RR tri indx	0.07	0.09	0.10	0.08	0.09	0.10	0.09	0.07
TINN (ms)	205.00	390.00	290.00	210.00	265.00	315.00	225.00	205.00
Power(FFT) VLF (s^2/Hz)	184.00	212.00	172.00	120.00	579.00	614.00	119.00	184.00
Power(FFT) LF (n.u.)	90.70	64.10	59.60	55.40	68.50	70.10	47.70	90.70
Power(FFT) HF	9.30	35.90	40.40	44.60	31.50	29.90	52.30	9.30
Power(FFT) LF/HF (n.u.)	9.70	1.79	1.48	1.24	2.18	2.35	0.91	9.70
Power(AR) VLF	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Power(AR) LF (n.u.)	93.40	63.70	66.80	57.10	80.70	74.50	62.10	93.40
Power(AR) HF (n.u.)	6.60	23.90	26.50	39.80	18.40	25.10	35.40	6.60
Power(AR) LF/HF (n.u.)	14.05	2.66	2.52	1.44	4.39	2.97	1.76	14.05
SD1(poincare') (ms)	16.70	32.90	33.70	30.30	26.50	34.40	28.90	16.70
SD2(poincare') (ms)	104.70	97.40	181.70	81.80	98.20	164.20	81.90	104.70
ApEn	0.22	0.35	0.26	0.54	0.45	0.36	0.51	0.22

A.5.2 Subject with Diabetes 2

Hypoglycemic Measurements

Stat	1	2	3	4	5	6	7	8
Average (s)	0.69	0.66	0.68	0.69	0.73	0.71	0.71	0.64
RMS (s)	0.69	0.66	0.68	0.70	0.73	0.71	0.71	0.64
SD (s)	0.04	0.04	0.05	0.04	0.07	0.05	0.04	0.06
Var	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Kurtosis	4.44	5.29	4.64	4.69	10.42	11.63	5.09	3.24
Median (s)	0.69	0.66	0.67	0.69	0.73	0.71	0.71	0.64
mode (s)	0.66	0.65	0.68	0.69	0.72	0.71	0.71	0.67
skewness	1.02	1.08	0.95	0.28	0.88	0.60	-0.50	0.32
maximum (s)	0.87	0.85	0.94	0.90	1.18	1.02	0.86	0.91

min (s)	0.61	0.58	0.58	0.54	0.52	0.51	0.56	0.52
RMSSD (ms)	23.00	18.50	25.50	23.30	45.00	30.40	22.00	28.50
NN50	42.00	19.00	38.00	33.00	83.00	34.00	20.00	44.00
pNN50 %	5.00	2.20	4.60	3.90	10.80	4.10	2.40	5.20
RR tri indx	0.08	0.06	0.07	0.07	0.08	0.07	0.05	0.08
TINN (ms)	175.00	190.00	240.00	235.00	450.00	315.00	215.00	280.00
Power(FFT) VLF (s^2/Hz)	46.00	60.00	63.00	181.00	218.00	85.00	44.00	157.00
Power(FFT) LF (n.u.)	77.60	81.30	71.80	83.50	68.60	59.60	59.60	74.40
Power(FFT) HF	22.40	18.70	28.20	16.50	31.40	40.40	40.40	25.60
Power(FFT) LF/HF (n.u.)	3.47	4.33	2.54	5.06	2.19	1.47	1.47	2.91
Power(AR) VLF	0.00	0.00	0.00	0.00	0.00	23.00	0.00	0.00
Power(AR) LF (n.u.)	84.50	86.40	84.50	85.20	77.10	81.20	76.90	81.30
Power(AR) HF (n.u.)	13.20	11.40	13.50	12.40	19.60	16.70	20.10	15.30
Power(AR) LF/HF (n.u.)	6.41	7.57	6.27	6.88	3.94	4.87	3.82	5.30
SD1(poincare') (ms)	16.40	13.20	18.10	16.60	32.00	21.60	15.70	20.30
SD2(poincare') (ms)	53.00	50.20	67.40	59.10	88.00	69.10	47.70	78.80
ApEn	0.45	0.39	0.33	0.34	0.35	0.36	0.47	0.31

Normal Measurements

Stat	1	2	3	4	5	6	7	8
Average (s)	0.68	0.69	0.69	0.69	0.64	0.73	0.75	0.73
RMS (s)	0.68	0.69	0.69	0.69	0.65	0.73	0.75	0.73
SD (s)	0.04	0.03	0.04	0.04	0.05	0.04	0.03	0.04
Var	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Kurtosis	3.85	3.21	4.65	4.47	3.57	5.40	10.48	3.73
Median (s)	0.68	0.69	0.69	0.69	0.64	0.73	0.75	0.74
mode (s)	0.67	0.69	0.69	0.70	0.66	0.74	0.74	0.74
skewness	-0.10	0.19	0.03	-0.01	0.45	-1.14	1.00	-0.49
maximum (s)	0.81	0.80	0.85	0.85	0.89	0.88	0.93	0.89
min (s)	0.57	0.60	0.58	0.58	0.53	0.55	0.63	0.61
RMSSD (ms)	16.90	15.40	16.90	17.20	26.40	17.70	18.10	21.40
NN50	12.00	7.00	11.00	10.00	58.00	12.00	10.00	21.00
pNN50 %	1.40	0.80	1.30	1.40	3.50	1.30	1.20	2.60
RR tri indx	0.06	0.05	0.07	0.07	0.06	0.05	0.04	0.05
TINN (ms)	180.00	140.00	195.00	210.00	230.00	150.00	200.00	150.00
Power(FFT) VLF (s^2/Hz)	52.00	50.00	58.00	71.00	95.00	33.00	52.00	27.00
Power(FFT) LF (n.u.)	76.20	84.70	79.40	69.70	74.50	63.90	68.20	59.20
Power(FFT) HF	23.80	15.30	20.60	30.30	25.50	36.10	31.80	40.80
Power(FFT) LF/HF (n.u.)	3.20	5.54	3.84	2.30	2.91	1.77	2.15	1.45
Power(AR) VLF	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Power(AR) LF (n.u.)	94.40	88.60	93.30	93.80	82.00	67.00	63.60	55.50

Power(AR) HF (n.u.)	2.70	7.70	4.90	4.30	11.90	29.10	33.40	38.90
Power(AR) LF/HF (n.u.)	34.37	11.57	19.15	21.73	6.89	2.31	1.90	1.43
SD1(poincare') (ms)	12.00	11.00	12.10	12.30	18.80	12.60	12.80	15.20
SD2(poincare') (ms)	50.30	36.80	50.80	53.10	71.50	59.50	34.90	53.70
ApEn	0.36	0.44	0.39	0.38	0.27	0.34	0.47	0.41

Hyperglycemic Measurements
< No measurements during hyperglycemia were available for diabetic subject 2>

A.5.3 Subject with Diabetes 3

Hypoglycemic Measurements
< No measurements during hypoglycemia were available for diabetic subject 2>

Normal Measurements

Stat	1	2	3	4	5	6	7
Average	0.56	0.57	0.57	0.54	0.54	0.54	0.55
RMS	0.56	0.57	0.57	0.54	0.55	0.54	0.55
SD	0.02	0.03	0.04	0.03	0.03	0.02	0.03
Var	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Kurtosis	4.32	5.85	3.98	3.51	4.47	3.04	2.70
Median	0.56	0.57	0.58	0.53	0.54	0.53	0.56
mode	0.55	0.57	0.58	0.53	0.52	0.52	0.57
skewness	0.38	0.60	-0.82	0.28	1.08	0.49	-0.58
maximum	0.66	0.70	0.68	0.62	0.66	0.63	0.62
min	0.50	0.49	0.46	0.47	0.49	0.48	0.46
RMSSD	8.10	7.70	8.80	7.30	8.30	7.60	7.50
NN50	1.00	0.00	0.00	0.00	0.00	0.00	0.00
pNN50	0.10	0.00	0.00	0.00	0.00	0.00	0.00
RR tri indx	0.03	0.03	0.05	0.03	0.04	0.03	0.03
TINN	115.00	105.00	120.00	80.00	100.00	75.00	85.00
Power(FFT) VLF	27.00	39.00	62.00	17.00	46.00	10.00	18.00
Power(FFT) LF	97.00	94.50	95.00	93.60	95.00	92.90	93.70
Power(FFT) HF	3.00	5.50	5.00	6.40	5.00	7.10	6.30
Power(FFT) LF/HF	32.39	17.17	19.14	14.55	18.98	13.11	14.85
Power(AR) LF	96.90	95.30	97.50	95.60	97.20	93.00	91.60
Power(AR) HF	0.00	0.00	0.00	0.60	0.00	0.00	0.00
Power(AR) LF/HF	inf	inf	inf	163.40	inf	inf	inf
SD1(poincare')	5.80	5.60	6.40	5.20	6.00	5.50	5.40
SD2(poincare')	31.90	35.00	50.60	35.00	37.10	34.90	42.90
ApEn	0.27	0.21	0.20	0.24	0.26	0.27	0.19

Stat	8	9	10	11	12	13	14
Average	0.59	0.54	0.52	0.54	0.54	0.55	0.55
RMS	0.59	0.55	0.52	0.54	0.54	0.55	0.55
SD	0.03	0.05	0.05	0.04	0.03	0.02	0.04
Var	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Kurtosis	7.66	2.92	1.71	2.01	7.36	5.16	6.23
Median	0.59	0.54	0.53	0.53	0.54	0.55	0.55
mode	0.60	0.51	0.48	0.52	0.54	0.55	0.55
skewness	1.51	0.62	0.10	0.29	0.43	0.97	0.13
maximum	0.73	0.71	0.64	0.64	0.70	0.66	0.76
min	0.54	0.47	0.44	0.47	0.46	0.51	0.45
RMSSD	8.40	8.80	7.50	7.10	7.80	7.80	8.20
NN50	0.00	2.00	0.00	0.00	0.00	0.00	1.00
pNN50	0.00	0.20	0.00	0.00	0.00	0.00	0.10
RR tri indx	0.03	0.04	0.03	0.03	0.03	0.04	0.04
TINN	120.00	140.00	70.00	65.00	140.00	90.00	160.00
Power(FFT) VLF	36.00	64.00	30.00	15.00	14.00	20.00	19.00
Power(FFT) LF	97.00	96.90	86.80	93.50	94.70	95.40	94.10
Power(FFT) HF	3.00	3.10	13.20	6.50	5.30	3.60	5.90
Power(FFT) LF/HF	32.49	31.51	6.60	14.43	17.87	26.72	15.98
Power(AR) LF	96.30	97.40	92.60	92.90	96.10	96.30	98.50
Power(AR) HF	0.00	0.00	0.70	0.00	0.00	0.00	0.00
Power(AR) LF/HF	inf	inf	130.88	inf	inf	inf	inf
SD1(poincare')	6.00	6.40	5.40	5.10	5.60	5.60	5.90
SD2(poincare')	36.30	63.40	67.40	50.80	38.30	30.10	50.80
ApEn	0.22	0.10	0.10	0.16	0.23	0.28	0.17

Hyperglycemic Measurements

Stat	1	2	3	4	5	6	7
Average	0.65	0.74	0.72	0.71	0.72	0.71	0.72
RMS	0.65	0.75	0.72	0.71	0.72	0.71	0.72
SD	0.07	0.02	0.04	0.03	0.04	0.06	0.05
Var	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Kurtosis	2.76	3.13	5.46	5.91	8.76	4.74	3.52
Median	0.66	0.75	0.73	0.72	0.73	0.72	0.72
mode	0.68	0.75	0.74	0.71	0.73	0.72	0.71
skewness	-0.83	-0.37	-1.63	-1.46	-2.21	-1.27	-0.55
maximum	0.75	0.81	0.79	0.78	0.80	0.81	0.84
min	0.48	0.67	0.56	0.59	0.50	0.51	0.51
RMSSD	11.10	11.10	10.50	9.80	12.40	14.90	21.70
NN50	1.00	0.00	0.00	0.00	3.00	6.00	8.00
pNN50	0.10	0.00	0.00	0.00	0.40	0.70	1.00
RR tri indx	0.06	0.04	0.04	0.03	0.04	0.06	0.07

TINN	135.00	90.00	130.00	85.00	125.00	135.00	245.00	
Power(FFT) VLF	185.00	28.00	156.00	51.00	33.00	129.00	319.00	
Power(FFT) LF	91.90	86.50	91.80	77.40	92.50	86.20	84.70	
Power(FFT) HF	8.10	13.50	8.20	22.60	7.50	13.80	15.30	
Power(FFT) LF/HF	11.31	6.38	11.22	3.42	12.34	6.22	5.53	
Power(AR) LF	97.10	89.50	95.10	87.90	89.70	90.40	87.40	
Power(AR) HF	0.00	7.80	4.00	9.90	5.90	8.60	10.10	
Power(AR) LF/HF		11.50	23.50	8.88	15.10	10.51	8.63	
SD1(poincare')	8.10	7.90	7.60	7.00	8.90	10.70	15.60	
SD2(poincare')	91.90	29.30	54.90	38.50	60.30	77.10	66.10	
ApEn	0.14	0.42	0.23	0.32	0.18	0.21	0.29	

Stat	8	9	10	11	12	13	14	15
Average	0.70	0.73	0.73	0.71	0.69	0.69	0.67	0.76
RMS	0.70	0.73	0.73	0.71	0.69	0.69	0.67	0.76
SD	0.04	0.04	0.03	0.04	0.02	0.02	0.07	0.04
Var	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Kurtosis	3.93	4.03	3.56	8.44	7.67	2.99	4.26	5.45
Median	0.71	0.73	0.73	0.72	0.70	0.69	0.68	0.77
mode	0.69	0.73	0.72	0.71	0.70	0.69	0.67	0.78
skewness	-0.64	-0.82	-0.18	-1.92	-1.46	0.51	-0.88	-1.16
maximum	0.82	0.83	0.83	0.83	0.74	0.74	0.82	0.85
min	0.56	0.59	0.64	0.50	0.58	0.65	0.47	0.60
RMSSD	9.80	12.10	11.60	11.60	12.70	11.50	17.20	13.50
NN50	0.00	2.00	1.00	2.00	0.00	0.00	4.00	1.00
pNN50	0.00	0.06	0.10	0.20	0.00	0.00	0.50	0.10
RR tri indx	0.04	145.00	0.04	0.04	0.04	0.03	0.04	0.05
TINN	150.00	134.00	125.00	125.00	100.00	70.00	235.00	140.00
Power(FFT) VLF	53.00	93.30	57.00	106.00	10.00	17.00	120.00	41.00
Power(FFT) LF	95.80	6.70	94.40	88.80	69.00	64.50	89.80	84.10
Power(FFT) HF	4.20	13.87	5.60	11.20	31.00	35.50	10.20	15.90
Power(FFT) LF/HF	22.79	0.00	16.97	7.92	2.22	1.82	8.78	5.30
Power(AR) LF	97.10	1.70	94.60	89.60	79.60	70.70	85.00	93.70
Power(AR) HF	1.80	1.70	0.70	8.50	17.80	25.20	13.60	5.10
Power(AR) LF/HF	52.49	55.48	129.10	10.49	4.46	2.81	6.24	18.29
SD1(poincare')	7.10	8.70	8.30	8.30	9.10	8.20	12.30	9.70
SD2(poincare')	60.30	55.10	42.40	62.70	27.80	23.10	93.90	52.10
ApEn	0.16	0.27	0.31	0.22	0.47	0.56	0.12	0.32

A.5.4 Subject with Diabetes 4

Hypoglycemic Measurements

< No measurements during hypoglycemia were available for diabetic subject 4>

Normal Measurements

Stat	1	2	3	4	5	6	7
Average	0.75	0.71	0.66	0.70	0.74	0.73	0.73
RMS	0.75	0.71	0.66	0.70	0.74	0.73	0.74
SD	0.04	0.05	0.04	0.05	0.04	0.05	0.04
Var	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Kurtosis	3.33	2.18	2.63	3.31	2.78	3.51	3.83
Median	0.75	0.71	0.66	0.70	0.74	0.73	0.73
mode	0.78	0.68	0.67	0.70	0.70	0.74	0.71
skewness	0.11	-0.29	-0.36	-0.22	0.21	-4.77	0.30
maximum	0.94	0.82	0.77	0.86	0.88	0.89	0.88
min	0.63	0.59	0.55	0.57	0.65	0.57	0.58
RMSSD	21.00	15.10	18.80	22.00	17.70	19.60	22.00
NN50	11.00	4.00	7.00	11.00	8.00	5.00	13.00
pNN50	1.50	0.50	0.90	1.40	1.00	0.60	1.60
RR tri indx	0.08	0.07	0.05	0.06	0.07	0.07	0.07
TINN	190.00	150.00	180.00	220.00	165.00	205.00	205.00
Power(FFT) VLF	135.00	60.00	25.00	63.00	58.00	98.00	113.00
Power(FFT) LF	85.40	87.90	81.20	77.00	91.30	89.00	90.40
Power(FFT) HF	14.60	12.10	18.80	23.00	8.70	11.00	9.60
Power(FFT) LF/HF	5.85	7.28	4.31	3.35	10.49	8.10	9.43
Power(AR) VLF	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Power(AR) LF	93.80	93.60	83.70	83.50	91.30	91.70	90.00
Power(AR) HF	4.20	4.30	10.30	9.80	5.50	4.60	5.40
Power(AR) LF/HF	22.38	21.74	8.12	8.52	16.47	19.89	16.54
SD1(poincare')	15.00	10.80	13.40	15.70	12.60	13.90	15.70
SD2(poincare')	60.90	72.60	61.10	71.10	55.20	52.70	54.00
ApEn	0.36	0.24	0.24	0.23	0.35	0.31	0.39

Stat	8	9	10	11	12	13
Average	0.74	0.67	0.61	0.64	0.68	0.71
RMS	0.74	0.67	0.61	0.65	0.68	0.71
SD	0.04	0.05	0.04	0.06	0.04	0.03
Var	0.00	0.00	0.00	0.00	0.00	0.00
Kurtosis	3.56	2.86	4.56	2.16	4.18	3.27
Median	0.74	0.66	0.60	0.63	0.68	0.72
mode	0.73	0.66	0.62	0.60	0.66	0.70
skewness	0.48	0.31	1.07	0.44	-0.67	-0.34
maximum	0.88	0.84	0.79	0.80	0.78	0.80

min	0.64	0.52	0.53	0.54	0.54	0.61
RMSSD	19.00	23.20	28.20	24.20	14.90	15.00
NN50	13.00	12.00	30.00	14.00	5.00	4.00
pNN50	1.70	1.40	3.40	1.60	0.60	0.50
RR tri indx	0.07	0.06	0.05	0.07	0.05	0.06
TINN	165.00	240.00	195.00	195.00	135.00	130.00
Power(FFT)						
VLF	91.00	61.00	71.00	77.00	82.00	48.00
Power(FFT) LF	88.90	86.90	66.90	84.40	82.70	79.90
Power(FFT) HF	11.10	13.10	33.10	15.60	17.30	20.10
Power(FFT)						
LF/HF	8.01	6.61	2.02	5.42	4.78	3.97
Power(AR)						
VLF	0.00	0.00	0.00	0.00	0.00	0.00
Power(AR) LF	94.50	82.70	71.70	83.50	97.00	91.30
Power(AR) HF	2.60	7.90	11.80	0.00	0.00	5.40
Power(AR)						
LF/HF	35.75	10.49	6.07	0.00	0.00	16.91
SD1(poincare')	13.60	16.50	20.10	17.40	10.60	10.70
SD2(poincare')	56.20	65.80	55.10	76.40	55.30	40.60
ApEn	0.33	0.22	0.21	0.16	0.34	0.47

Hyperglycemia Measurements

Stat	1	2	3	4	5	6	7
Average	0.86	0.86	0.85	0.81	0.78	0.76	0.79
RMS	0.87	0.87	0.86	0.81	0.78	0.76	0.79
SD	0.05	0.04	0.05	0.04	0.03	0.02	0.06
Var	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Kurtosis	3.98	4.74	6.60	5.69	3.56	3.56	3.19
Median	0.88	0.87	0.85	0.81	0.78	0.76	0.79
mode	0.88	0.88	0.84	0.80	0.77	0.77	0.83
skewness	-0.97	-0.69	-0.93	0.19	0.23	0.23	-0.29
maximum	0.99	0.98	1.02	0.97	0.91	0.84	0.93
min	0.70	0.74	0.66	0.69	0.69	0.70	0.60
RMSSD	36.70	20.00	18.50	16.90	12.70	10.30	18.80
NN50	38.00	10.00	9.00	5.00	2.00	0.00	7.00
pNN50	6.00	1.50	1.30	0.70	0.30	0.00	0.90
RR tri indx	0.08	0.06	0.07	0.05	0.04	0.03	0.04
TINN	220.00	155.00	175.00	175.00	120.00	100.00	195.00
Power(FFT)							
VLF	242.00	212.00	296.00	57.00	45.00	37.00	221.00
Power(FFT) LF	80.60	85.60	81.80	83.20	80.90	85.20	82.40
Power(FFT) HF	19.40	14.40	18.20	16.80	19.10	14.80	17.60
Power(FFT)							
LF/HF	4.16	5.95	4.50	4.95	4.25	5.75	4.68
Power(AR)	0.00	0.00	0.00	0.00	0.00	0.00	0.00

VLF								
Power(AR) LF	81.30	86.10	87.50	90.20	83.80	83.90	89.70	
Power(AR) HF	7.70	10.70	10.10	7.50	12.20	9.60	7.90	
Power(AR)								
LF/HF	10.56	8.06	8.64	11.97	6.86	8.78	11.42	
SD1(poincare')	26.20	14.30	13.30	12.10	9.10	7.40	13.50	
SD2(poincare')	68.30	49.70	65.20	49.80	46.80	29.20	80.00	
ApEn	0.34	0.47	0.34	0.40	0.32	0.36	0.17	

Stat	8	9	10	11	12	13	14	15
Average	0.82	0.81	0.83	0.77	0.81	0.81	0.82	0.84
RMS	0.83	0.82	0.83	0.77	0.81	0.81	0.82	0.84
SD	0.03	0.05	0.02	0.06	0.04	0.03	0.02	0.02
Var	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Kurtosis	9.52	5.63	2.65	2.95	5.11	3.57	2.94	3.03
Median	0.82	0.82	0.83	0.78	0.81	0.81	0.82	0.84
mode	0.82	0.84	0.83	0.81	0.81	0.80	0.82	0.84
skewness	1.16	-0.92	0.21	-0.48	-0.50	0.09	0.15	0.30
maximum	1.05	0.95	0.88	0.93	0.93	0.90	0.88	0.90
min	0.72	0.62	0.76	0.62	0.66	0.71	0.76	0.78
RMSSD	14.30	15.00	13.30	20.40	15.50	16.40	15.60	18.70
NN50	5.00	4.00	0.00	9.00	0.00	5.00	3.00	3.00
pNN50	0.70	0.50	0.00	1.20	0.00	0.70	0.40	0.40
RR tri indx	0.04	0.06	0.04	0.07	0.06	0.05	0.05	0.05
TINN	205.00	195.00	100.00	270.00	175.00	150.00	100.00	95.00
Power(FFT)								
VLF	58.00	260.00	30.00	241.00	173.00	64.00	60.00	36.00
Power(FFT) LF	86.10	92.20	81.20	91.30	89.70	73.90	71.10	60.00
Power(FFT) HF	13.90	7.80	18.80	8.70	10.30	26.10	28.90	40.00
Power(FFT)								
LF/HF	6.21	11.87	4.32	10.54	8.75	2.83	2.46	1.50
Power(AR)								
VLF	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Power(AR) LF	92.50	95.30	87.00	90.90	91.40	80.60	75.00	61.50
Power(AR) HF	5.10	2.90	7.00	5.80	6.60	13.90	17.10	26.70
Power(AR)								
LF/HF	18.29	32.62	12.43	15.76	13.85	5.80	4.38	2.30
SD1(poincare')	10.30	10.80	9.50	14.60	11.10	11.70	11.10	13.30
SD2(poincare')	45.60	69.20	27.30	85.20	52.20	34.40	28.30	25.70
ApEn	0.35	0.24	0.45	0.20	0.38	0.47	0.51	0.58

A.5.5 Subject with Diabetes 5

Hypoglycemic Measurements
< No measurements during hypoglycemia were available for diabetic subject 5>

Normal Measurements

Stat	1	2	3	4	5	6	7
Average	0.90	0.92	0.90	0.94	0.98	0.95	0.95
RMS	0.91	0.92	0.91	0.94	0.98	0.96	0.96
SD	0.06	0.06	0.07	0.10	0.10	0.12	0.12
Var	0.00	0.00	0.00	0.01	0.01	0.01	0.01
Kurtosis	4.58	4.51	9.14	4.67	3.24	3.27	3.42
Median	0.90	0.92	0.90	0.93	0.98	0.96	0.95
mode	0.86	0.88	0.94	0.91	0.94	0.93	0.93
skewness	0.56	0.34	-0.62	0.00	-0.04	-0.27	-0.24
maximum	1.16	1.16	1.20	1.27	1.27	1.30	1.30
min	0.72	0.72	0.59	0.59	0.68	0.65	0.65
RMSSD	55.00	57.20	54.20	74.00	87.50	81.30	82.10
NN50	285.00	297.00	268.00	308.00	363.00	323.00	303.00
pNN50	43.40	45.70	40.90	48.90	59.30	51.50	48.20
RR tri indx	0.09	0.09	0.10	0.12	0.16	0.16	0.16
TINN	265.00	260.00	390.00	410.00	410.00	475.00	475.00
Power(FFT) VLF	151.00	65.00	35.00	623.00	348.00	865.00	1312.00
Power(FFT) LF	37.20	22.90	18.70	59.10	40.20	45.40	65.20
Power(FFT) HF	62.80	77.10	81.30	40.90	59.80	54.60	34.80
Power(FFT) LF/HF	0.59	0.30	0.23	1.45	0.67	0.83	1.88
Power(AR) VLF	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Power(AR) LF	43.20	40.00	61.80	59.00	52.50	66.70	70.30
Power(AR) HF	55.80	60.40	38.10	40.50	46.40	32.50	29.00
Power(AR) LF/HF	0.77	0.66	1.62	1.46	1.13	2.05	2.42
SD1(poincare')	39.00	40.60	38.60	52.50	62.10	57.90	58.40
SD2(poincare')	73.90	70.20	85.00	123.70	120.70	154.20	155.50
ApEn	0.65	0.66	0.57	0.51	0.63	0.53	0.51

Stat	8	9	10	11	12	13	14	15
Average	0.95	0.93	0.92	0.89	0.88	0.90	0.89	0.91
RMS	0.95	0.94	0.93	0.89	0.88	0.90	0.89	0.91
SD	0.10	0.09	0.09	0.06	0.06	0.05	0.06	0.09
Var	0.01	0.01	0.01	0.00	0.00	0.00	0.00	0.01
Kurtosis	4.24	4.28	4.75	3.25	3.44	3.20	3.29	3.96
Median	0.94	0.94	0.92	0.88	0.87	0.89	0.88	0.90
mode	0.95	0.89	0.88	0.86	0.84	0.88	0.86	0.91

skewness	0.18	-0.43	-0.38	0.32	0.35	0.27	-0.07	0.08
maximum	1.34	1.22	1.22	1.10	1.07	1.07	1.07	1.22
min	0.66	0.63	0.63	0.72	0.72	0.75	0.73	0.60
RMSSD	81.20	71.70	62.00	43.10	37.00	42.10	39.90	58.30
NN50	312.00	317.00	274.00	155.00	114.00	168.00	138.00	194.00
pNN50	49.40	49.70	42.40	23.00	16.70	25.20	22.60	30.20
RR tri indx	0.12	0.13	0.12	0.09	0.08	0.08	0.08	0.11
TINN	475.00	370.00	310.00	225.00	220.00	210.00	215.00	405.00
Power(FFT) VLF	645.00	564.00	609.00	101.00	102.00	75.00	148.00	519.00
Power(FFT) LF	54.80	52.30	26.90	45.10	54.30	48.50	51.70	44.50
Power(FFT) HF	45.20	47.70	73.10	54.90	45.70	51.50	48.30	55.50
Power(FFT) LF/HF	1.21	1.10	0.37	0.82	1.19	0.94	1.07	0.80
Power(AR) VLF	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Power(AR) LF	62.20	56.00	51.80	55.50	61.90	58.60	64.80	59.40
Power(AR) HF	37.40	41.30	46.00	41.20	35.10	38.10	30.90	37.40
Power(AR) LF/HF	1.66	1.36	1.13	1.35	1.76	1.54	2.10	1.59
SD1(poincare')	57.70	51.00	44.10	30.60	26.30	29.90	28.40	41.40
SD2(poincare')	121.50	123.30	114.90	81.70	74.20	68.30	72.50	125.30
ApEn	0.59	0.57	0.52	0.50	0.53	0.61	0.55	0.39

Hyperglycemia Measurements

Stat	1	2	3	4	5	6	7
Average	0.51	0.49	0.51	0.51	0.46	0.46	0.47
RMS	0.52	0.49	0.51	0.51	0.47	0.47	0.47
SD	0.05	0.03	0.04	0.05	0.05	0.04	0.05
Var	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Kurtosis	3.95	3.30	3.32	3.02	2.47	3.67	4.18
Median	0.51	0.48	0.51	0.52	0.46	0.47	0.48
mode	0.51	0.48	0.52	0.52	0.47	0.47	0.49
skewness	1.13	0.07	0.03	-0.54	0.12	-0.37	-0.82
maximum	0.70	0.60	0.66	0.66	0.60	0.58	0.58
min	0.44	0.40	0.40	0.38	0.30	0.30	0.30
RMSSD	18.50	18.10	23.70	29.60	28.40	29.80	48.40
NN50	18.00	24.00	32.00	42.00	40.00	56.00	64.00
pNN50	1.60	2.10	2.90	3.90	3.40	5.10	11.90
RR tri indx	0.03	0.03	0.03	0.05	0.03	0.03	0.05
TINN	195.00	155.00	195.00	225.00	235.00	210.00	230.00
Power(FFT) VLF	87.00	8.00	23.00	43.00	46.00	29.00	12.00
Power(FFT) LF	80.10	83.30	68.20	80.30	45.10	68.30	63.70
Power(FFT) HF	19.90	16.70	31.80	19.70	54.90	31.70	36.30

Power(FFT) LF/HF	4.02	4.98	2.15	4.07	0.82	2.16	1.76	
Power(AR) VLF	0.00	0.00	0.00	0.00	43.00	0.00	0.00	
Power(AR) LF	78.90	50.10	60.20	64.50	0.00	43.30	33.40	
Power(AR) HF	10.00	22.70	13.20	12.80	32.80	0.00	0.00	
Power(AR) LF/HF	7.89	2.21	4.58	5.06	0.00	inf	inf	
SD1(poincare')	13.20	13.00	17.10	21.30	20.70	21.80	35.30	
SD2(poincare')	67.60	40.40	56.30	71.10	67.10	55.00	57.80	
ApEn	0.10	0.24	0.13	0.13	0.12	0.13	0.13	

Stat	8	9	10	11	12	13	14	15
Average	0.55	0.57	0.60	0.60	0.58	0.64	0.73	0.73
RMS	0.55	0.57	0.60	0.60	0.58	0.64	0.73	0.73
SD	0.04	0.04	0.03	0.05	0.07	0.10	0.04	0.03
Var	0.00	0.00	0.00	0.00	0.00	0.01	0.00	0.00
Kurtosis	5.47	4.56	4.77	3.74	3.27	1.88	3.76	3.91
Median	0.55	0.57	0.59	0.60	0.58	0.62	0.73	0.73
mode	0.55	0.55	0.58	0.61	0.55	0.73	0.74	0.71
skewness	0.67	0.23	0.89	-0.43	0.05	0.05	-0.65	-0.48
maximum	0.78	0.78	0.73	0.78	0.86	0.85	0.85	0.84
min	0.46	0.46	0.54	0.44	0.35	0.35	0.59	0.60
RMSSD	13.40	12.50	9.90	15.70	23.50	20.00	16.70	14.20
NN50	5.00	5.00	1.00	11.00	31.00	21.00	6.00	1.00
pNN50	0.50	0.30	0.10	1.10	3.10	2.20	0.70	0.10
RR tri indx	0.03	0.04	0.04	0.05	0.05	0.07	0.06	0.04
TINN	175.00	180.00	125.00	150.00	245.00	225.00	175.00	145.00
Power(FFT) VLF	48.00	51.00	19.00	49.00	79.00	168.00	170.00	87.00
Power(FFT) LF	95.30	95.40	94.60	93.00	86.80	90.20	89.00	91.10
Power(FFT) HF	4.70	4.60	5.40	7.00	13.20	9.80	11.00	8.90
Power(FFT) LF/HF	20.18	20.76	17.49	13.37	6.60	9.19	8.12	10.25
Power(AR) VLF	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Power(AR) LF	91.80	92.20	94.30	90.50	87.60	93.80	96.70	96.40
Power(AR) HF	0.00	0.00	3.00	5.10	3.00	1.90	0.00	0.00
Power(AR) LF/HF	inf	inf	31.35	17.88	28.74	48.75	0.00	0.00
SD1(poincare')	9.70	9.00	7.10	11.30	17.00	14.40	12.00	10.10
SD2(poincare')	60.10	58.70	36.40	73.80	93.00	133.70	60.20	47.70
ApEn	0.13	0.15	0.29	0.15	0.15	0.12	0.32	0.36

A.5.6 Subject with Diabetes 6

Hypoglycemic Measurements
< No measurements during hypoglycemia were available for diabetic subject 6>

Normal Measurements

Stat	1	2	3	4	5	6	7
Average	1.00	1.00	1.00	0.98	0.97	0.97	0.98
RMS	1.00	1.00	1.00	0.98	0.97	0.97	0.98
SD	0.01	0.01	0.02	0.03	0.02	0.01	0.02
Var	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Kurtosis	7.17	5.93	3.92	2.70	4.18	6.21	5.53
Median	1.00	1.00	1.00	0.98	0.97	0.97	0.98
mode	1.01	1.00	1.00	0.99	0.97	0.97	0.98
skewness	0.09	-0.01	-0.26	-0.23	0.10	-1.04	1.27
maximum	1.08	1.08	1.06	1.06	1.03	1.00	1.06
min	0.96	0.96	0.94	0.89	0.89	0.90	0.94
RMSSD	9.40	9.40	8.00	8.10	7.30	6.70	8.90
NN50	4.00	4.00	2.00	2.00	0.00	0.00	2.00
pNN50	0.70	0.70	0.30	0.30	0.00	0.00	0.30
RR tri indx	0.02	0.02	0.02	0.03	0.02	0.02	0.02
TINN	80.00	80.00	85.00	95.00	65.00	40.00	85.00
Power(FFT) VLF	12.00	10.00	8.00	57.00	34.00	9.00	11.00
Power(FFT) LF	56.60	61.60	59.70	86.00	85.90	72.40	68.30
Power(FFT) HF	43.40	38.40	40.30	14.00	14.10	27.60	31.70
Power(FFT) LF/HF	1.30	1.61	1.48	6.15	6.07	2.63	2.15
Power(AR) VLF	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Power(AR) LF	68.00	67.40	85.00	90.30	90.40	80.30	72.70
Power(AR) HF	18.90	19.00	8.20	5.00	4.30	8.70	15.50
Power(AR) LF/HF	3.61	3.54	10.37	18.04	20.91	9.18	4.68
SD1(poincare')	6.70	3.70	5.70	5.90	5.20	4.80	6.40
SD2(poincare')	15.30	16.40	20.50	36.60	27.80	16.90	24.00
ApEn	0.33	0.36	0.36	0.26	0.37	0.40	0.37

Stat	8	9	10	11	12	13
Average	0.98	0.99	1.00	1.01	1.02	1.02
RMS	0.98	0.99	1.00	1.01	1.02	1.02
SD	0.02	0.02	0.02	0.01	0.01	0.01
Var	0.00	0.00	0.00	0.00	0.00	0.00
Kurtosis	3.59	2.67	2.91	4.73	3.14	3.05
Median	0.98	0.99	1.00	1.01	1.02	1.02
mode	0.98	0.99	1.01	1.02	1.02	1.02
skewness	0.53	-0.36	-0.52	-0.85	-0.24	-0.33

maximum	1.06	1.02	1.04	1.05	1.05	1.05
min	0.94	0.94	0.95	0.96	0.98	0.98
RMSSD	9.40	7.70	7.70	7.70	7.70	7.70
NN50	2.00	0.00	0.00	0.00	0.00	0.00
pNN50	0.30	0.00	0.00	0.00	0.00	0.00
RR tri indx	0.03	0.02	0.02	0.02	0.02	0.02
TINN	90.00	50.00	40.00	40.00	50.00	50.00
Power(FFT) VLF	16.00	20.00	8.00	11.00	9.00	9.00
Power(FFT) LF	70.20	62.20	61.20	50.10	51.20	63.10
Power(FFT) HF	29.80	37.80	38.80	49.90	48.80	36.90
Power(FFT) LF/HF	2.36	1.65	1.58	1.01	1.05	1.71
Power(AR) VLF	0.00	0.00	0.00	0.00	0.00	0.00
Power(AR) LF	78.50	77.70	66.90	67.40	69.40	72.40
Power(AR) HF	13.40	14.40	22.30	21.10	20.10	17.90
Power(AR) LF/HF	5.86	5.38	3.00	3.20	3.45	4.05
SD1(poincare')	6.70	5.50	5.50	5.50	5.50	5.50
SD2(poincare')	26.50	23.20	22.40	19.80	15.70	15.90
ApEn	0.40	0.39	0.38	0.40	0.40	0.41

Hyperglycemia Measurements

Stat	1	2	3	4	5	6	7
Average	0.79	0.76	0.76	0.76	0.77	0.81	0.79
RMS	0.80	0.76	0.76	0.76	0.77	0.81	0.80
SD	0.05	0.03	0.03	0.03	0.04	0.04	0.05
Var	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Kurtosis	1.75	4.00	2.98	2.83	2.55	2.70	1.99
Median	0.79	0.76	0.76	0.76	0.77	0.81	0.79
mode	0.84	0.77	0.77	0.76	0.79	0.84	0.84
skewness	0.08	0.78	-0.27	-0.18	0.13	-0.27	0.19
maximum	0.88	0.90	0.83	0.83	0.86	0.90	0.90
min	0.70	0.68	0.68	0.67	0.67	0.70	0.70
RMSSD	7.60	12.50	9.70	7.90	8.40	8.60	8.70
NN50	0.00	3.00	2.00	0.00	0.00	0.00	0.00
pNN50	0.00	0.40	0.30	0.00	0.00	0.00	0.00
RR tri indx	0.03	0.03	0.04	0.04	0.04	0.04	0.04
TINN	60.00	145.00	95.00	70.00	75.00	80.00	80.00
Power(FFT) VLF	26.00	31.00	23.00	60.00	60.00	64.00	74.00
Power(FFT) LF	90.70	91.80	85.40	90.90	92.60	92.70	88.90
Power(FFT) HF	9.30	8.20	14.60	9.10	7.40	7.30	11.10
Power(FFT) LF/HF	9.76	11.23	5.86	10.03	12.52	12.67	8.01
Power(AR)	0.00	0.00	0.00	0.00	0.00	0.00	0.00

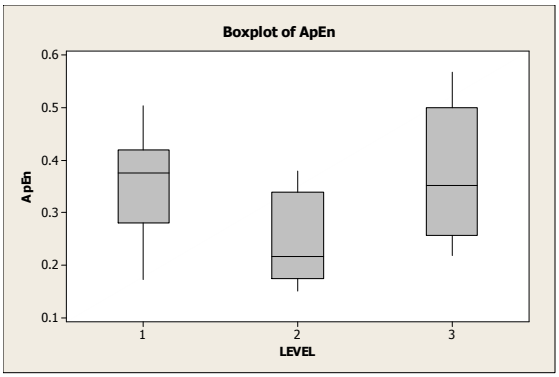
VLF							
Power(AR) LF	89.80	79.20	88.30	93.20	93.30	94.10	93.20
Power(AR) HF	3.40	8.90	5.80	2.50	2.10	3.60	3.90
Power(AR)							
LF/HF	26.28	8.89	15.11	37.52	44.63	25.79	24.11
SD1(poincare')	5.50	8.90	6.90	5.70	6.00	6.30	6.30
SD2(poincare')	67.60	43.40	39.90	43.50	51.80	57.50	69.80
ApEn	0.10	0.21	0.26	0.20	0.19	0.14	0.14

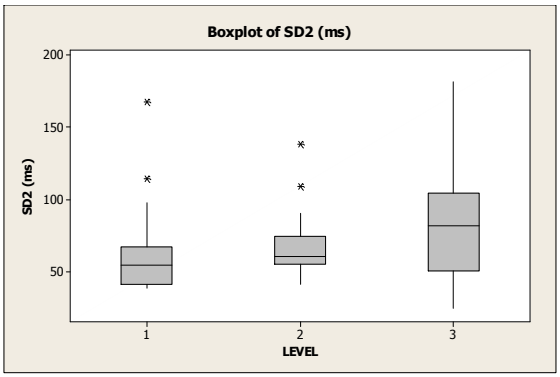
Stat	8	9	10	11	12	13
Average	0.74	0.74	0.79	0.88	0.93	0.93
RMS	0.74	0.74	0.79	0.88	0.93	0.93
SD	0.03	0.03	0.06	0.06	0.02	0.02
Var	0.00	0.00	0.00	0.00	0.00	0.00
Kurtosis	2.14	1.99	2.39	2.49	2.36	2.10
Median	0.74	0.74	0.78	0.90	0.93	0.93
mode	0.76	0.70	0.78	0.94	0.94	0.94
skewness	-0.07	-0.05	0.60	-0.80	-0.11	-0.05
maximum	0.84	0.84	0.94	0.98	0.98	0.98
min	0.66	0.67	0.69	0.73	0.88	0.88
RMSSD	13.80	11.60	8.90	8.80	8.20	8.30
NN50	7.00	5.00	1.00	1.00	0.00	1.00
pNN50	0.90	0.60	0.10	0.20	0.00	0.20
RR tri indx	0.03	0.03	0.04	0.03	0.03	0.02
TINN	175.00	115.00	80.00	75.00	55.00	55.00
Power(FFT)						
VLF	49.00	22.00	61.00	41.00	18.00	19.00
Power(FFT) LF	74.80	72.20	86.30	88.10	87.90	83.10
Power(FFT) HF	25.20	27.80	13.70	11.90	12.10	16.90
Power(FFT)						
LF/HF	2.97	2.59	6.32	7.40	7.24	4.91
Power(AR)						
VLF	0.00	0.00	0.00	0.00	0.00	0.00
Power(AR) LF	78.00	79.70	90.40	90.30	85.80	82.90
Power(AR) HF	10.90	9.80	4.90	5.70	6.20	7.50
Power(AR)						
LF/HF	7.15	8.13	18.63	15.84	13.84	11.12
SD1(poincare')	9.90	8.30	6.40	6.30	5.90	6.00
SD2(poincare')	48.30	48.30	83.80	88.40	26.60	30.80
ApEn	0.21	0.21	0.11	0.08	0.39	0.28

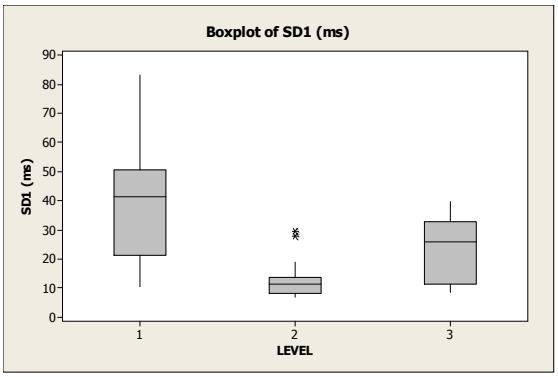
A.6 Diabetic HRV Box plots (6 subjects)

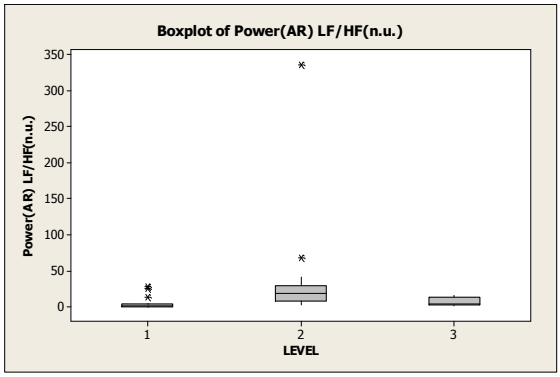
Level 1 = Hypo; Level 2 = Normal; Level 3 = Hyper

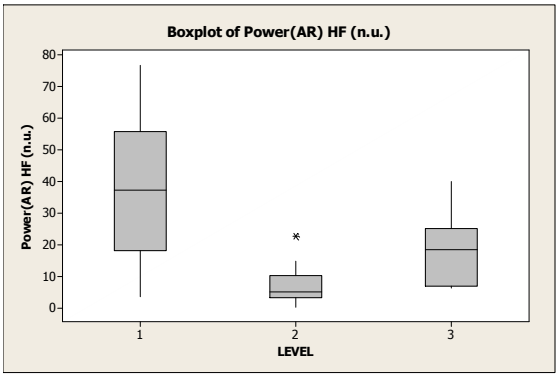
A.6.1 Subject with Diabetes 1

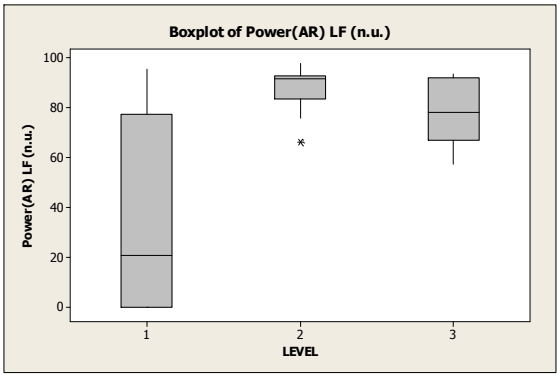


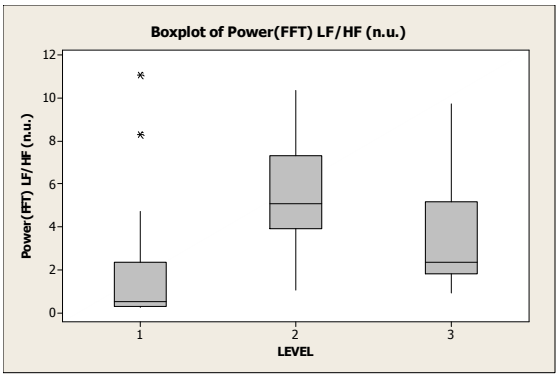


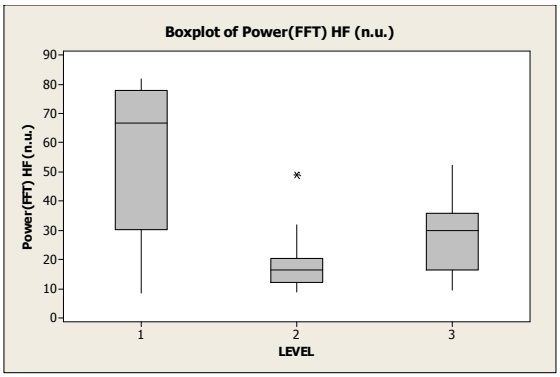


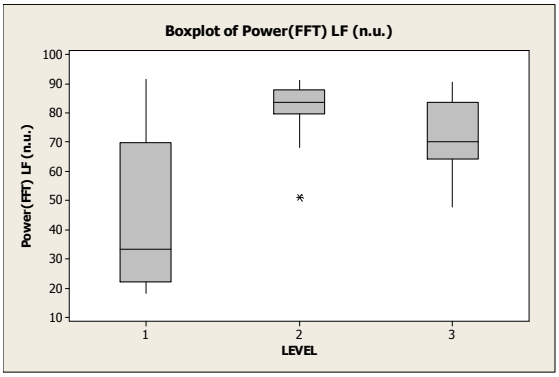


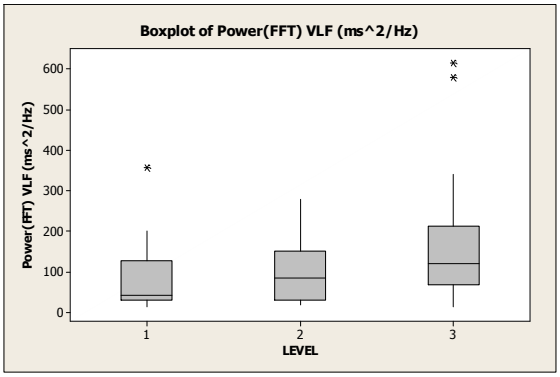


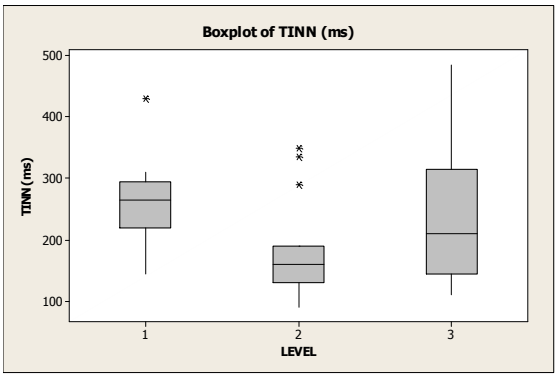


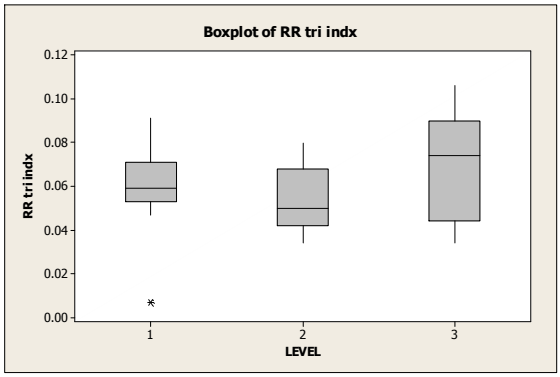

Boxplot of Power(FFT) LF/HF (n.u.)
Power(FFT) LF/HF (n.u.)
LEVEL

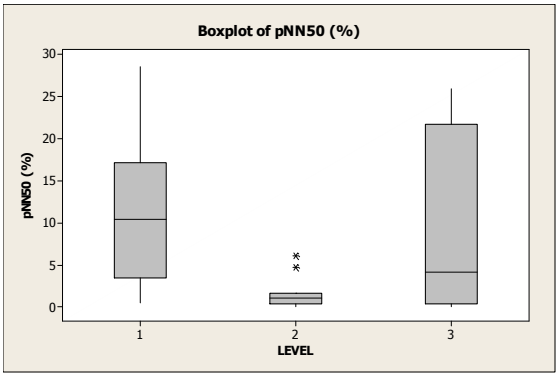

Boxplot of Power(FFT) HF (n.u.)
Power(FFT) HF (n.u.)
LEVEL

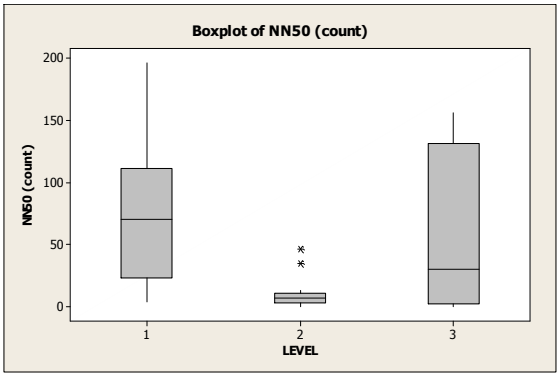

Boxplot of Power(FFT) LF (n.u.)
Power(FFT) LF (n.u.)
LEVEL

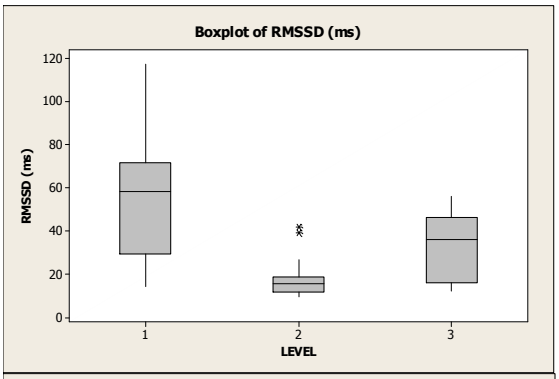

Boxplot of Power(FFT) VLF (ms^2/Hz)
Power(FFT) VLF (ms^2/Hz)
LEVEL

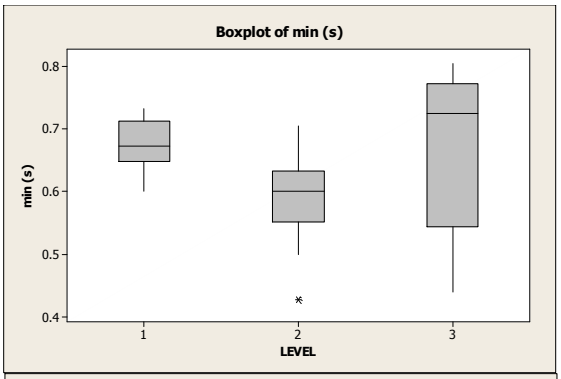

Boxplot of TINN (ms)
TINN (ms)
LEVEL

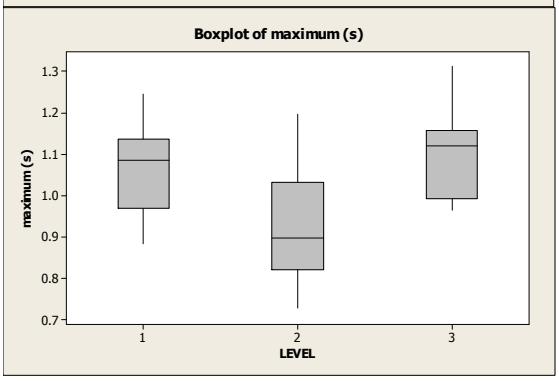

Boxplot of RR tri indx
RR tri indx
LEVEL

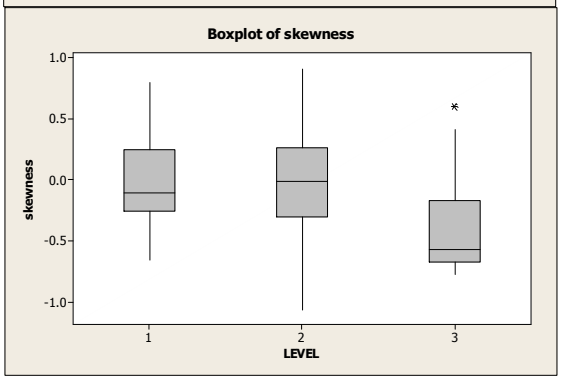

Boxplot of pNN50 (%)
pNN50 (%)
LEVEL

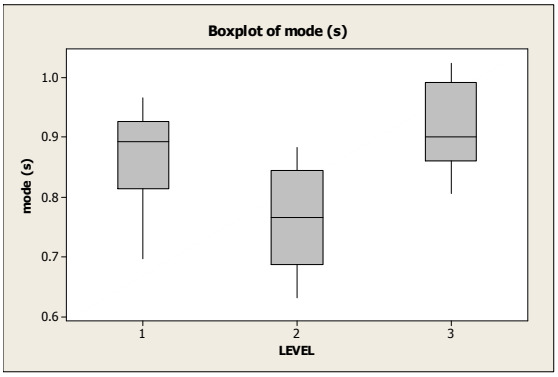

Boxplot of NN50 (count)
NN50 (count)
LEVEL

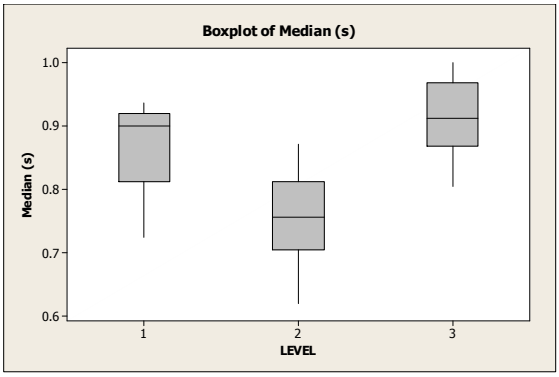

Boxplot of RMSSD (ms)
RMSSD (ms)
LEVEL

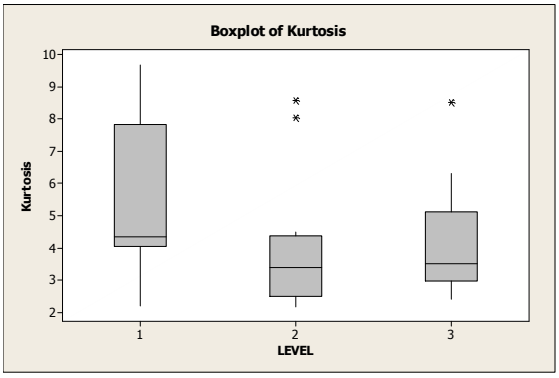

Boxplot of min (s)
min (s)
LEVEL

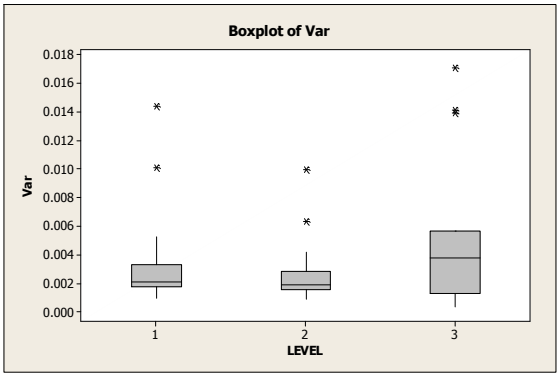

Boxplot of maximum (s)
maximum (s)
LEVEL

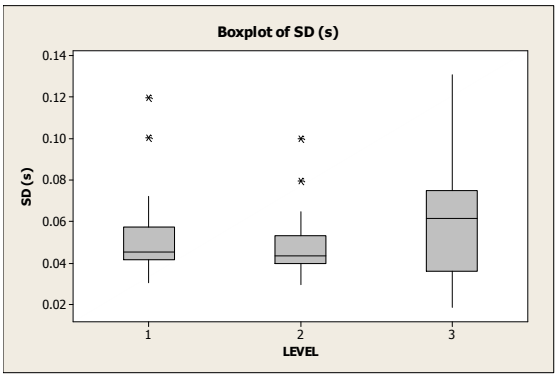

Boxplot of skewness
skewness
LEVEL

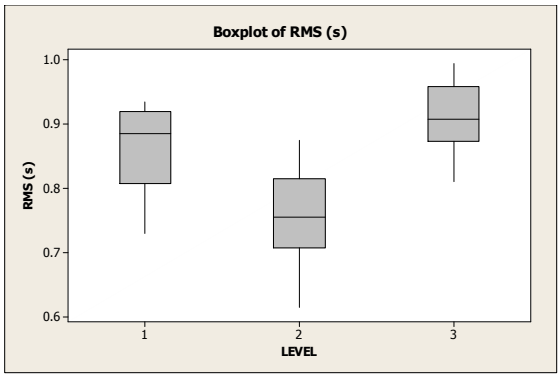

Boxplot of mode (s)
mode (s)
LEVEL

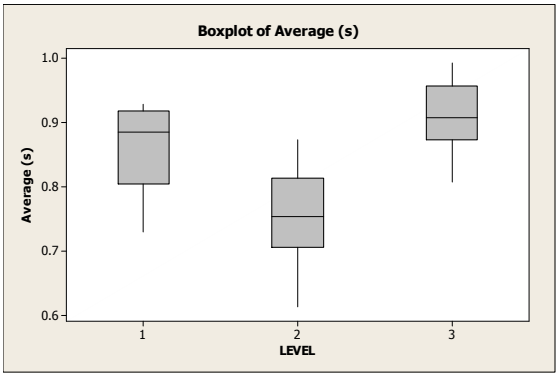

Boxplot of Median (s)
Median (s)
LEVEL


Boxplot of Kurtosis
Kurtosis
LEVEL

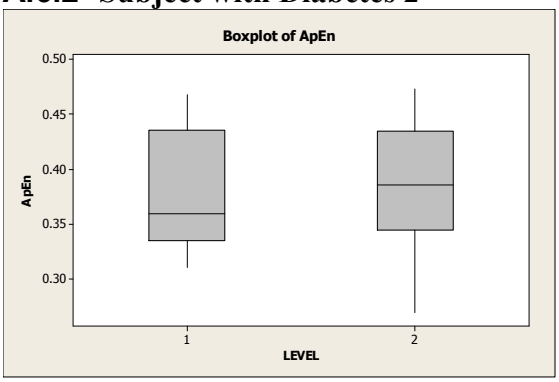

Boxplot of Var
Var
LEVEL

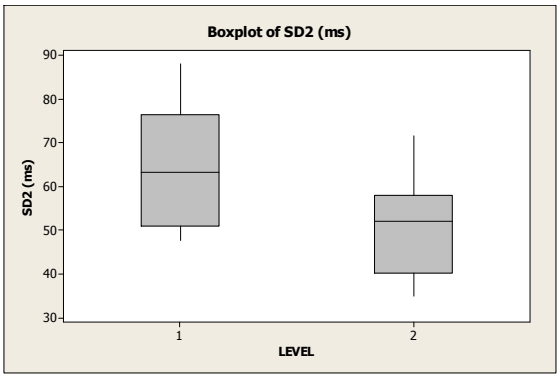


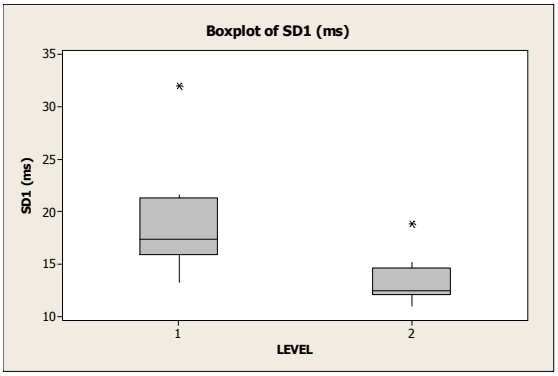


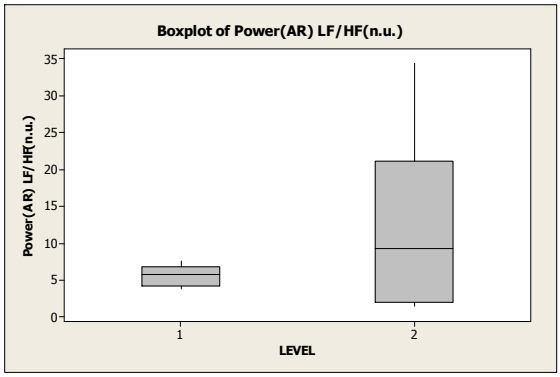


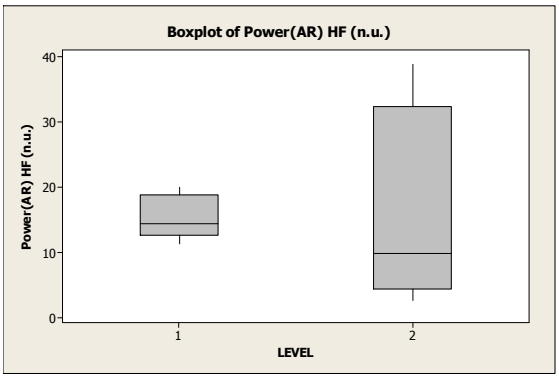
A.6.2 Subject with Diabetes 2

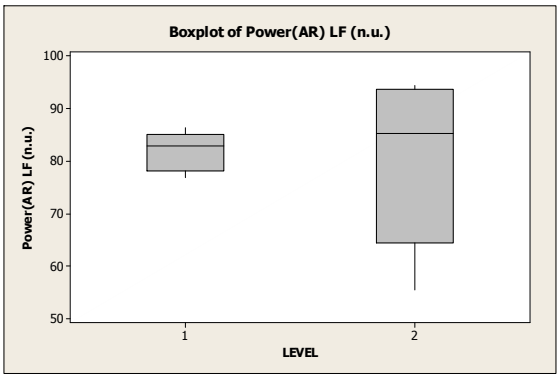


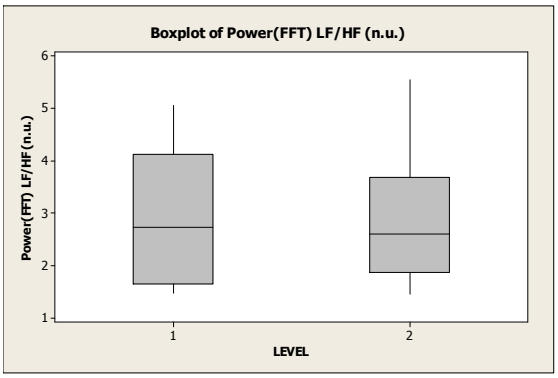


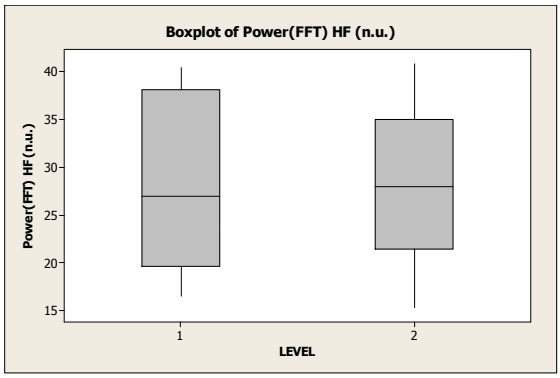


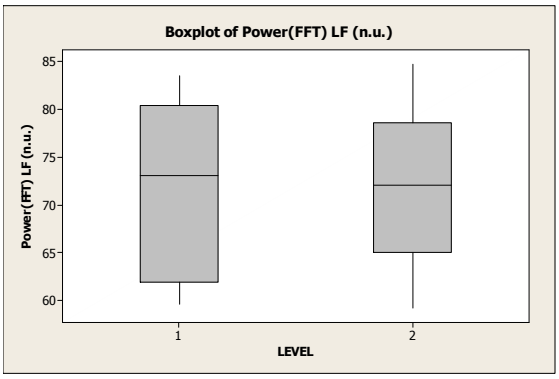


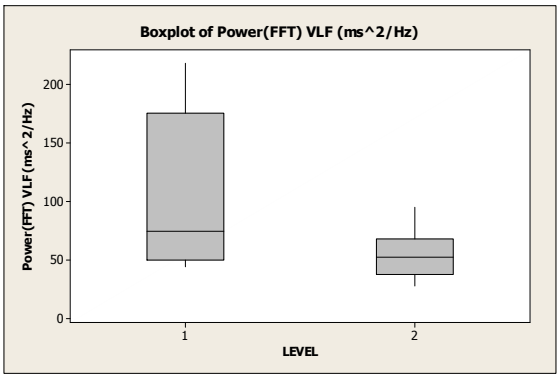

Boxplot of Power(AR) HF (n.u.)
Power(AR) HF (n.u.)
0
10
20
30
40
1
2
LEVEL

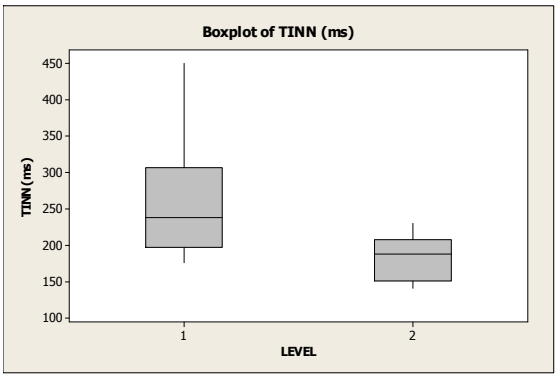

Boxplot of Power(AR) LF (n.u.)
Power(AR) LF (n.u.)
50
60
70
80
90
100
1
2
LEVEL

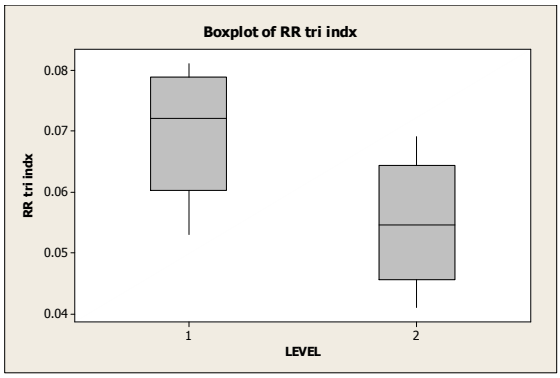

Boxplot of Power(FFT) LF/HF (n.u.)
Power(FFT) LF/HF (n.u.)
1
2
3
4
5
6
1
2
LEVEL

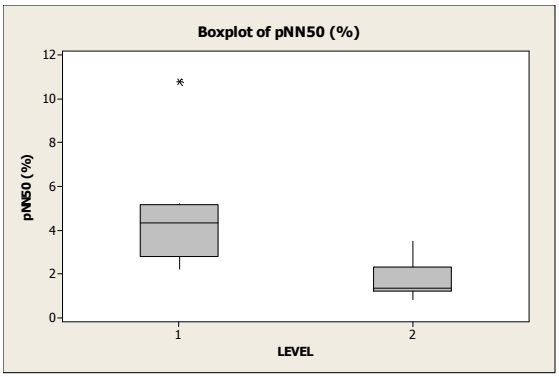

Boxplot of Power(FFT) HF (n.u.)
Power(FFT) HF (n.u.)
15
20
25
30
35
40
1
2
LEVEL

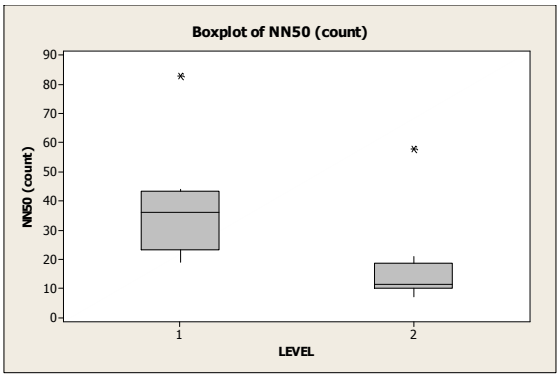

Boxplot of Power(FFT) LF (n.u.)
Power(FFT) LF (n.u.)
60
65
70
75
80
85
1
2
LEVEL

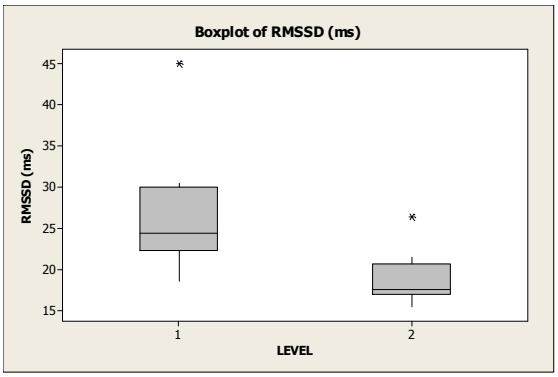

Boxplot of Power(FFT) VLF (ms^2/Hz)
Power(FFT) VLF (ms^2/Hz)
0
50
100
150
200
1
2
LEVEL

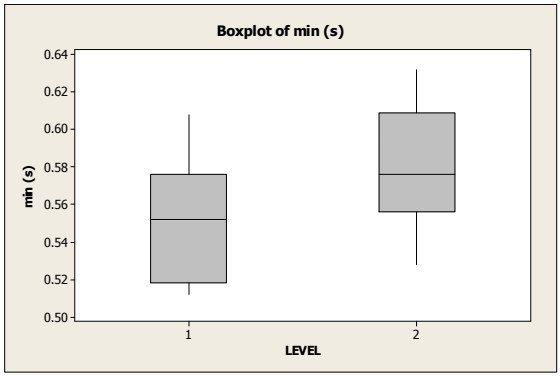

Boxplot of TINN (ms)
TINN (ms)
100
150
200
250
300
350
400
450
1
2
LEVEL

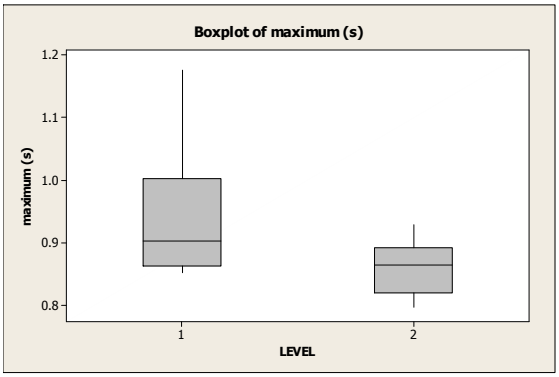

Boxplot of RR tri indx
RR tri indx
0.04
0.05
0.06
0.07
0.08
1
2
LEVEL

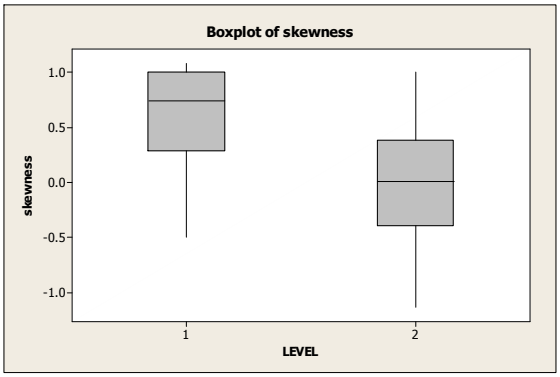

Boxplot of pNN50 (%)
pNN50 (%)
LEVEL

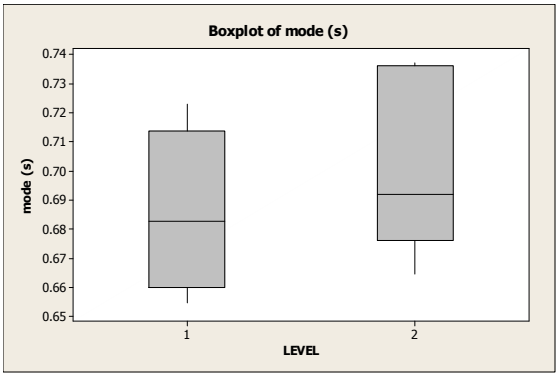

Boxplot of NN50 (count)
NN50 (count)
LEVEL

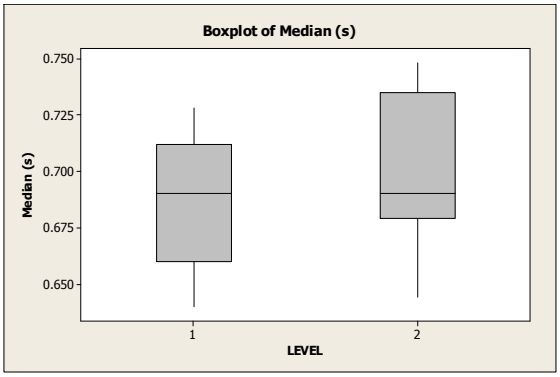

Boxplot of RMSSD (ms)
RMSSD (ms)
LEVEL

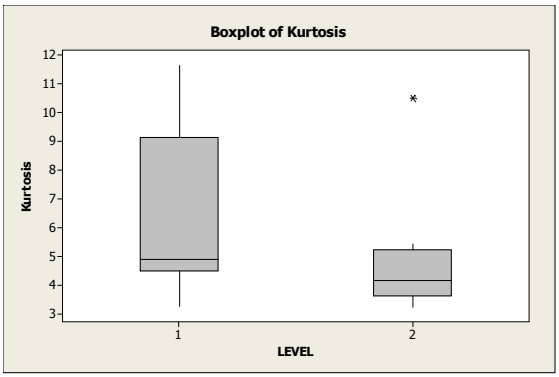

Boxplot of min (s)
min (s)
LEVEL

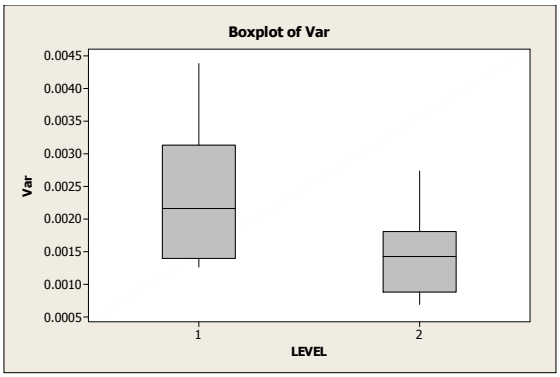

Boxplot of maximum (s)
maximum (s)
LEVEL

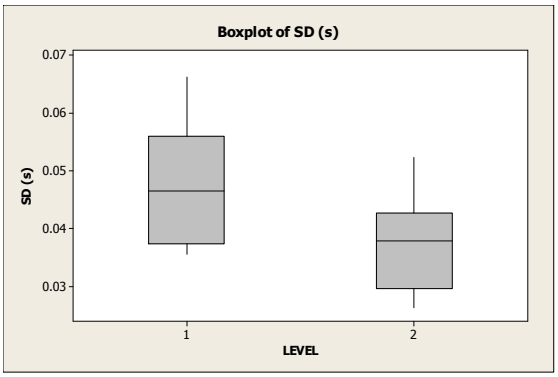

Boxplot of skewness
skewness
LEVEL

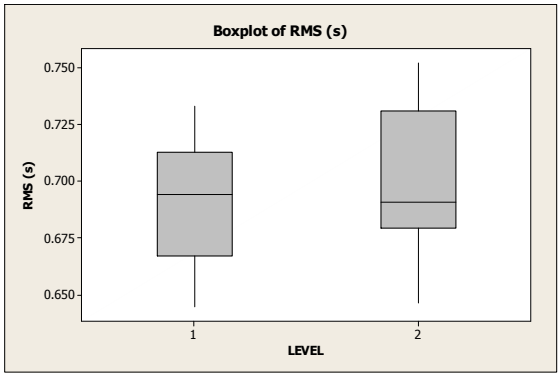

Boxplot of mode (s)
mode (s)
LEVEL

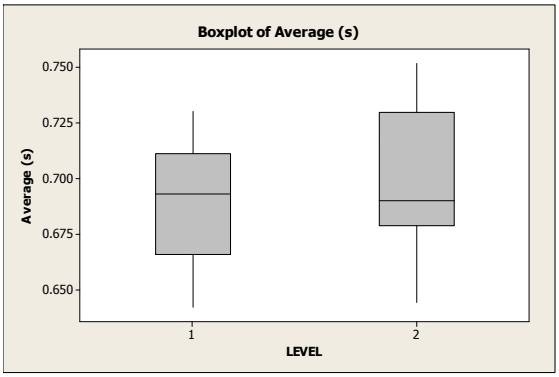

Boxplot of Median (s)
Median (s)
LEVEL



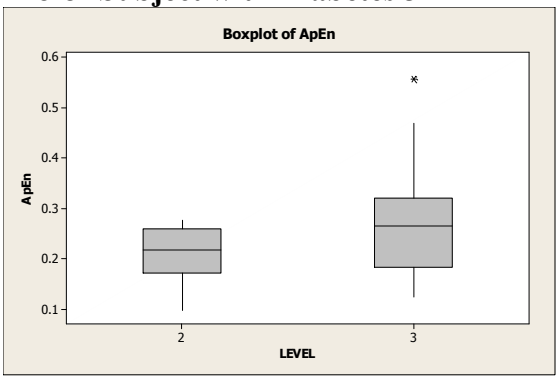


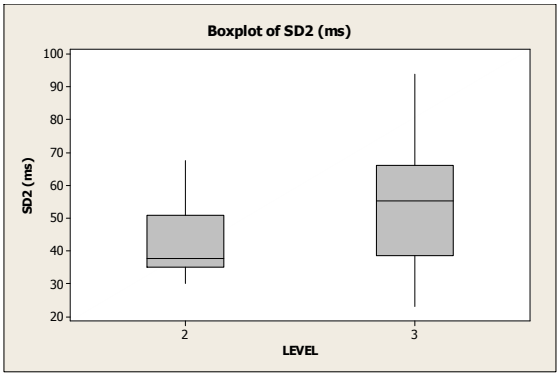


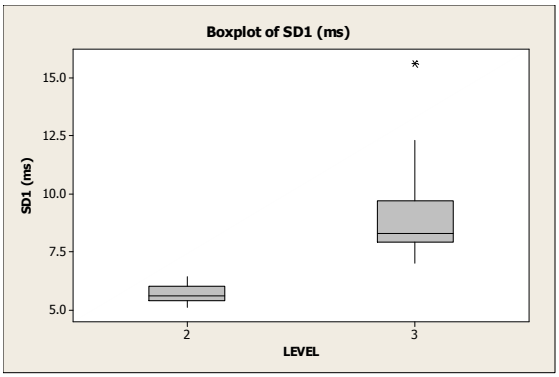


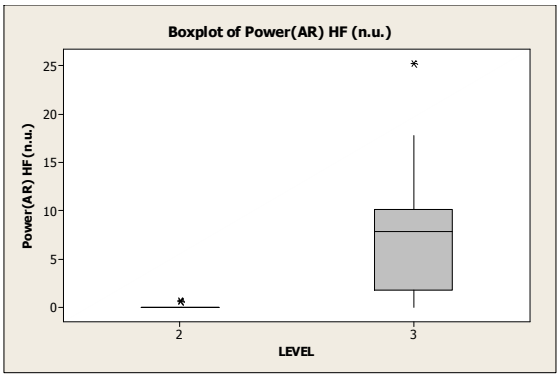


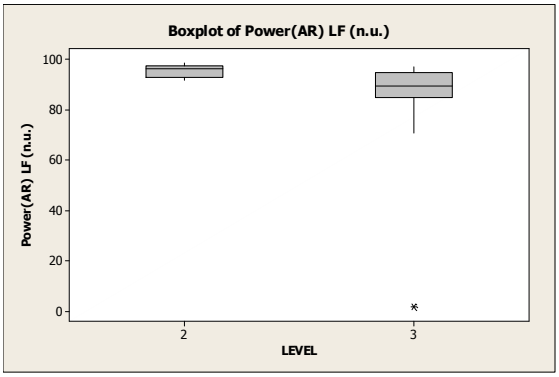
A.6.3 Subject with Diabetes 3

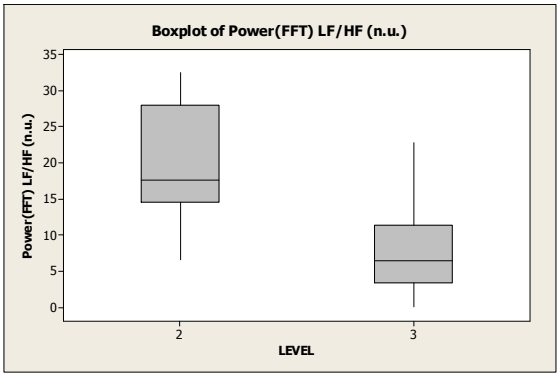


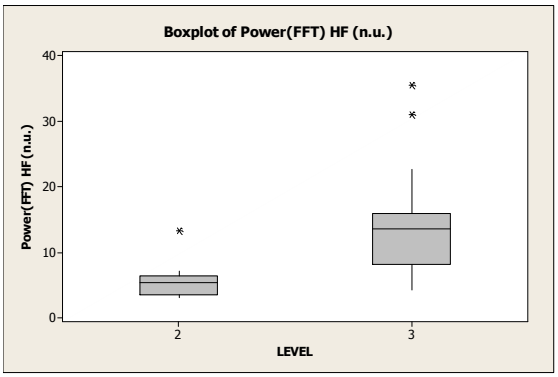


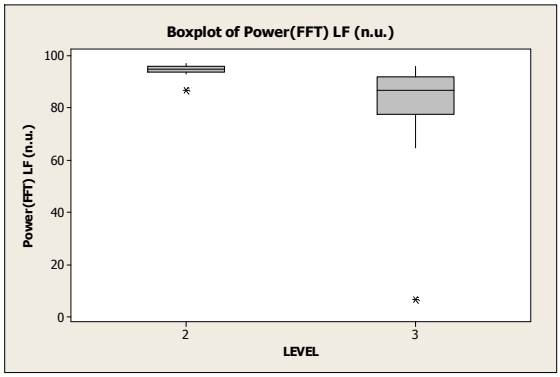

Boxplot of SD1 (ms)
SD1 (ms)
15.0
12.5
10.0
7.5
5.0
2
3
LEVEL

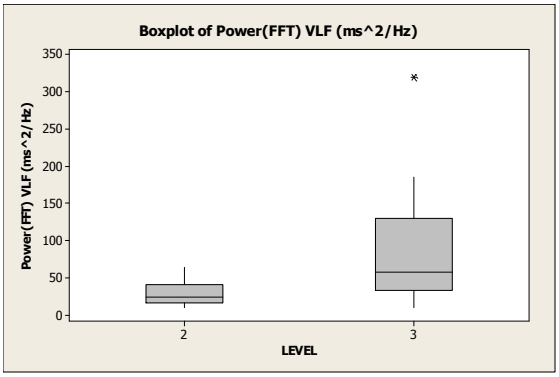

Boxplot of Power(AR) HF (n.u.)
Power(AR) HF (n.u.)
25
20
15
10
5
0
2
3
LEVEL

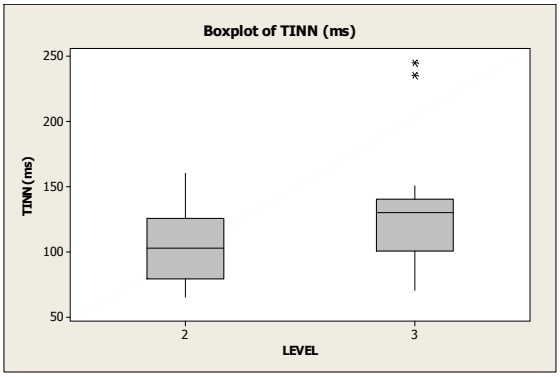

Boxplot of Power(AR) LF (n.u.)
Power(AR) LF (n.u.)
100
80
60
40
20
0
2
3
LEVEL

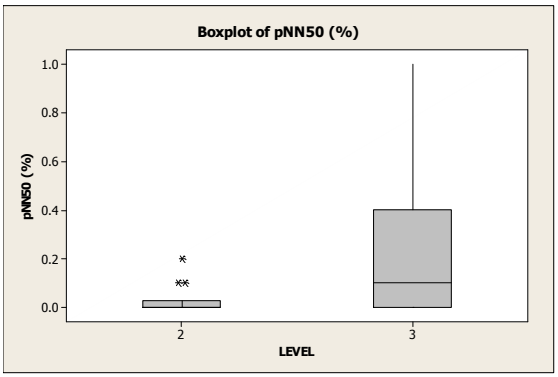

Boxplot of Power(FFT) LF/HF (n.u.)
Power(FFT) LF/HF (n.u.)
35
30
25
20
15
10
5
0
2
3
LEVEL

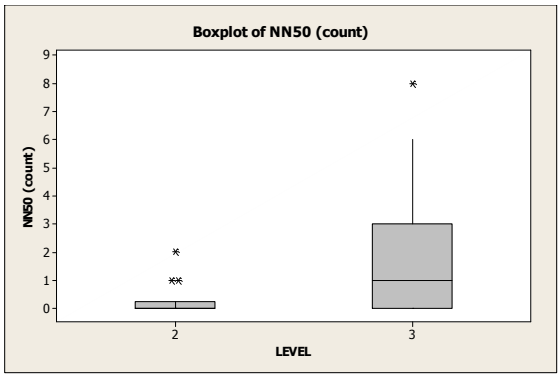

Boxplot of Power(FFT) HF (n.u.)
Power(FFT) HF (n.u.)
40
30
20
10
0
2
3
LEVEL

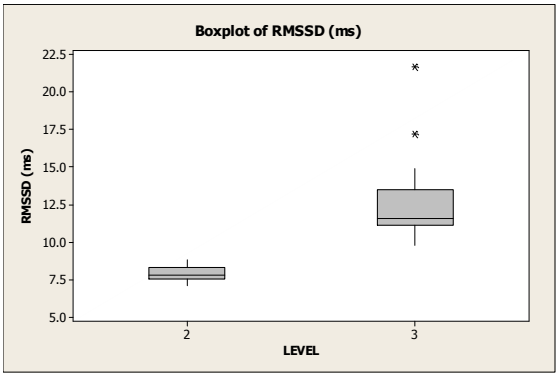

Boxplot of Power(FFT) LF (n.u.)
Power(FFT) LF (n.u.)
100
80
60
40
20
0
2
3
LEVEL

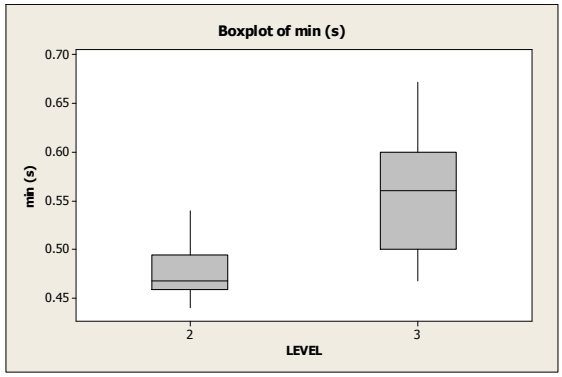

Boxplot of Power(FFT) VLF (ms^2/Hz)
Power(FFT) VLF (ms^2/Hz)
350
300
250
200
150
100
50
0
2
3
LEVEL

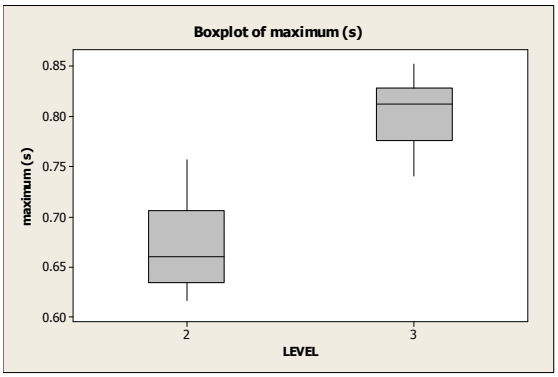

Boxplot of TINN (ms)
TINN (ms)
250
200
150
100
50
2
3
LEVEL

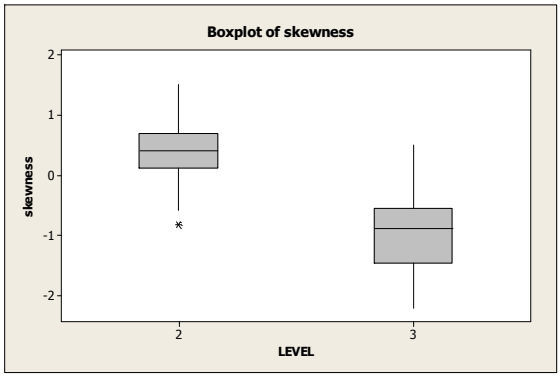

Boxplot of pNN50 (%)
pNN50 (%)
1.0
0.8
0.6
0.4
0.2
0.0
2
3
LEVEL

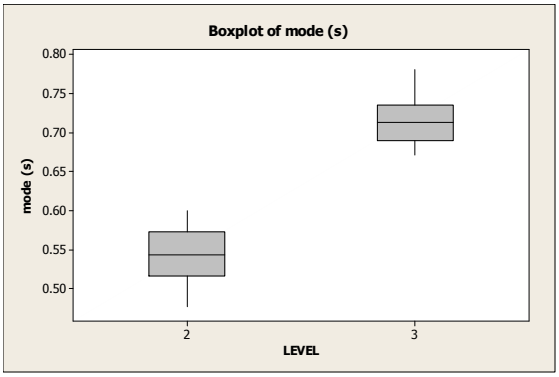

Boxplot of NN50 (count)
NN50 (count)
9
8
7
6
5
4
3
2
1
0
2
3
LEVEL

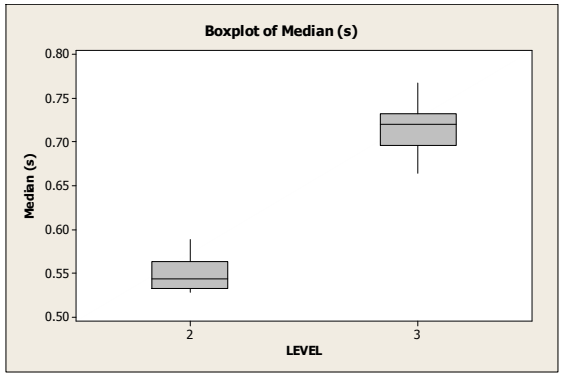

Boxplot of RMSSD (ms)
RMSSD (ms)
22.5
20.0
17.5
15.0
12.5
10.0
7.5
5.0
2
3
LEVEL

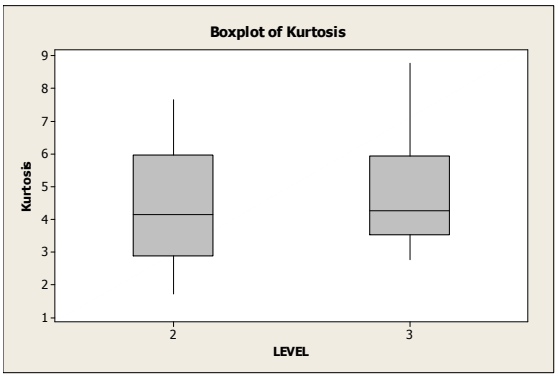

Boxplot of min (s)
min (s)
0.70
0.65
0.60
0.55
0.50
0.45
2
3
LEVEL

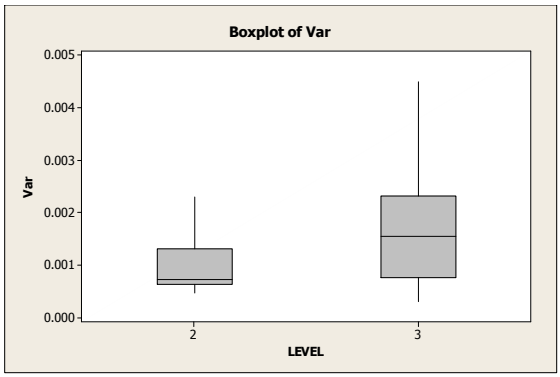

Boxplot of maximum (s)
maximum (s)
0.85
0.80
0.75
0.70
0.65
0.60
2
3
LEVEL

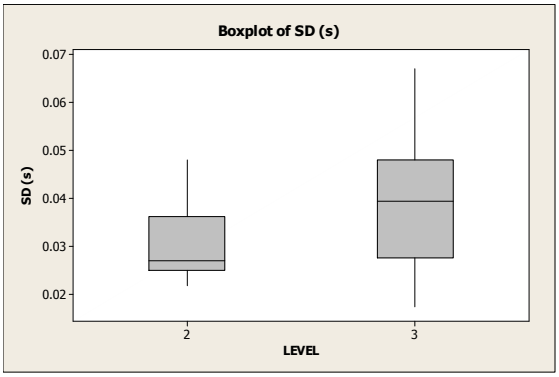

Boxplot of skewness
skewness
2
1
0
-1
-2
2
3
LEVEL

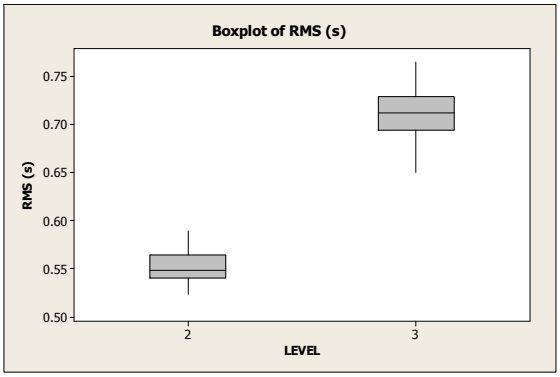

Boxplot of mode (s)
mode (s)
0.80
0.75
0.70
0.65
0.60
0.55
0.50
2
3
LEVEL

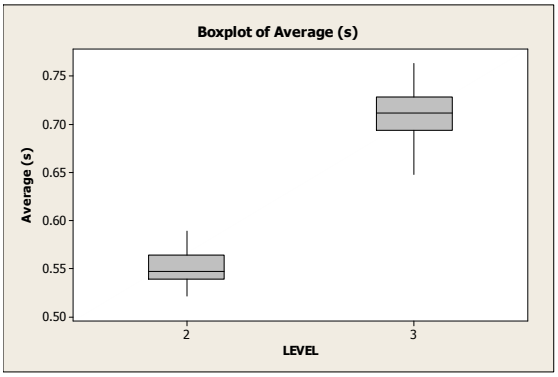

Boxplot of Median (s)
Median (s)
0.80
0.75
0.70
0.65
0.60
0.55
0.50
2
3
LEVEL



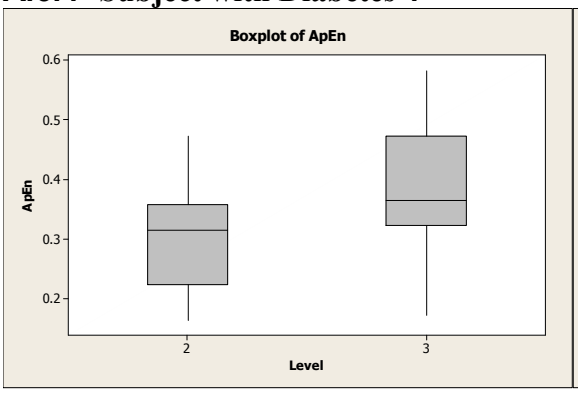


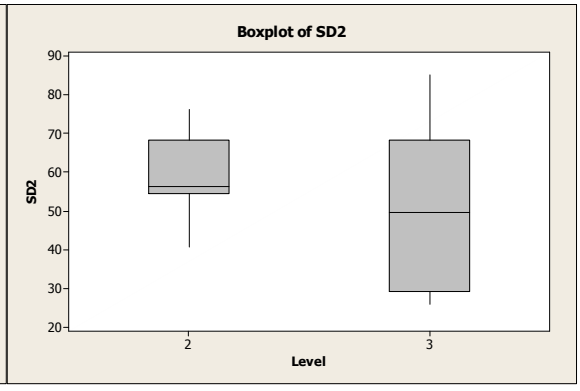


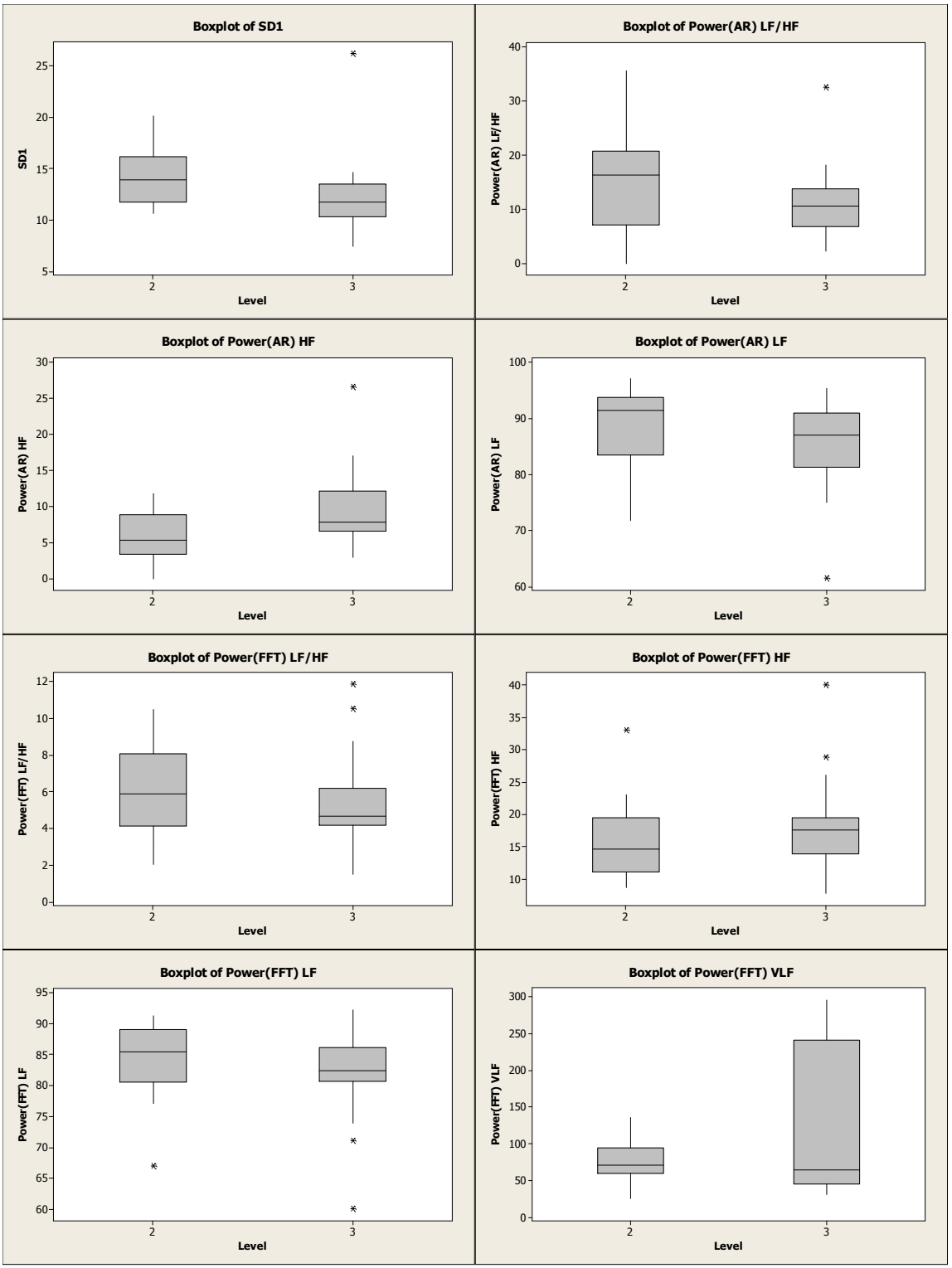


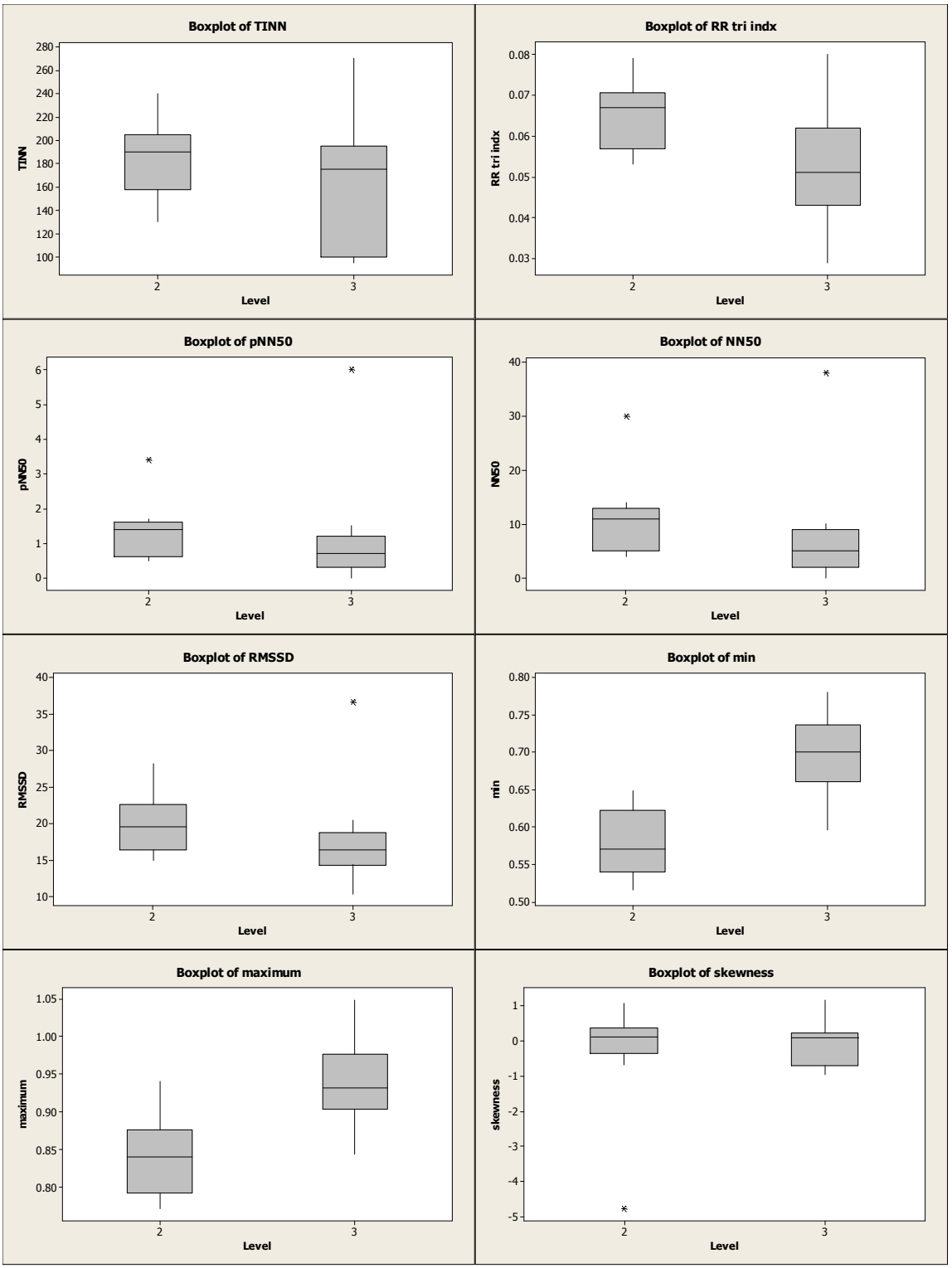


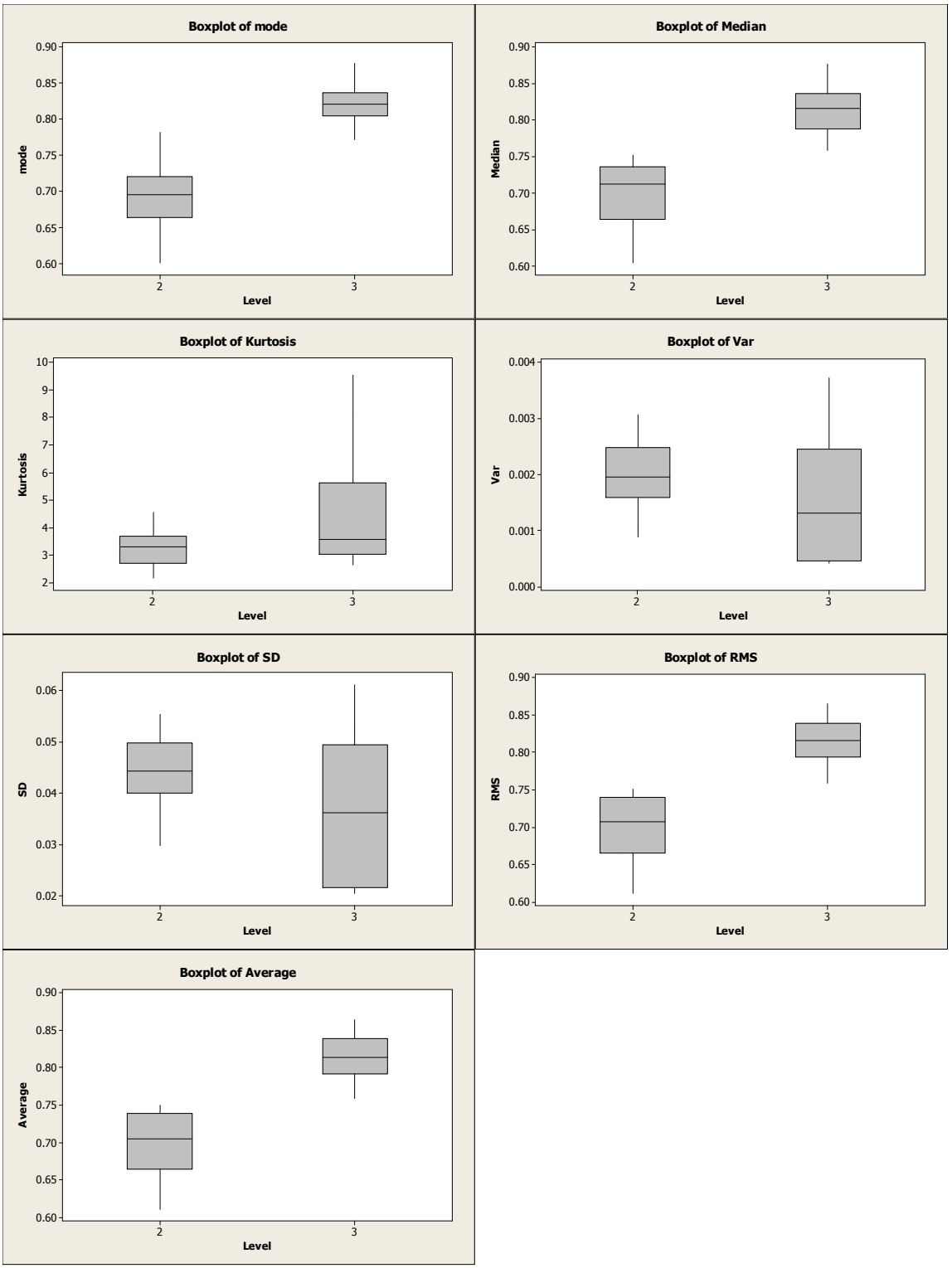
A.6.4 Subject with Diabetes 4



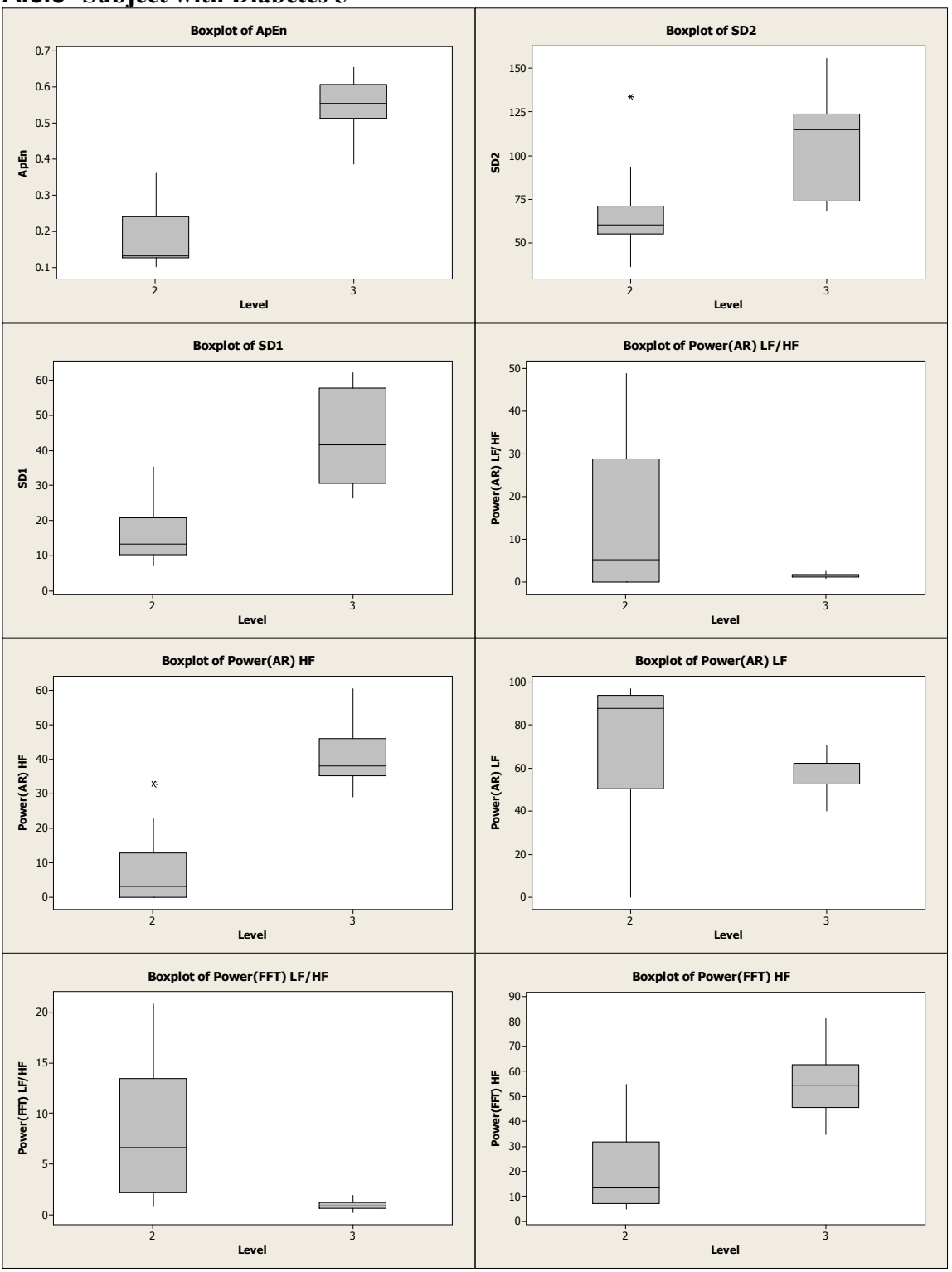


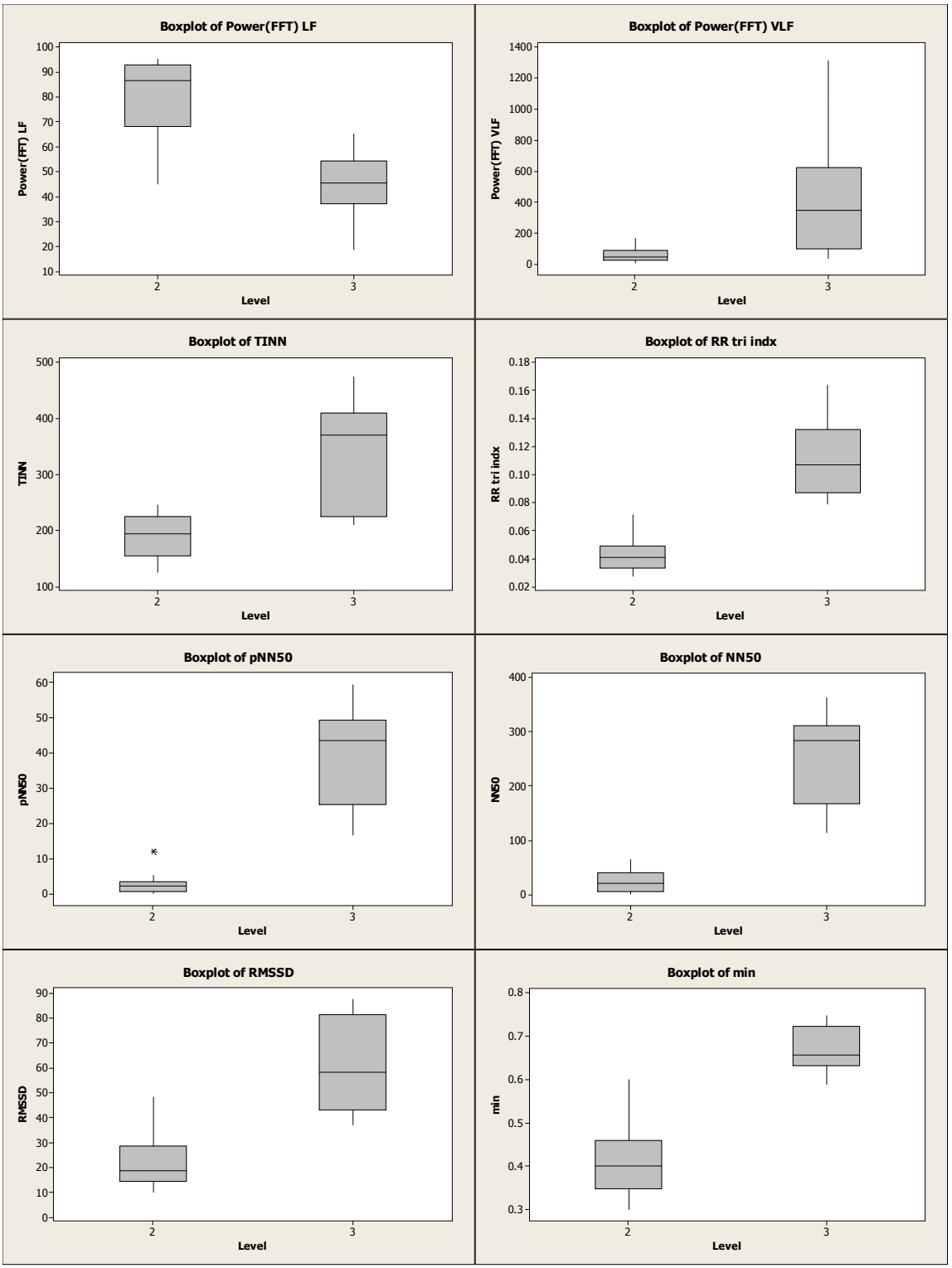

Boxplot of SD1
SD1
Level
Boxplot of Power(AR) LF/HF
Power(AR) LF/HF
Level
Boxplot of Power(AR) HF
Power(AR) HF
Level
Boxplot of Power(AR) LF
Power(AR) LF
Level
Boxplot of Power(FFT) LF/HF
Power(FFT) LF/HF
Level
Boxplot of Power(FFT) HF
Power(FFT) HF
Level
Boxplot of Power(FFT) LF
Power(FFT) LF
Level
Boxplot of Power(FFT) VLF
Power(FFT) VLF
Level

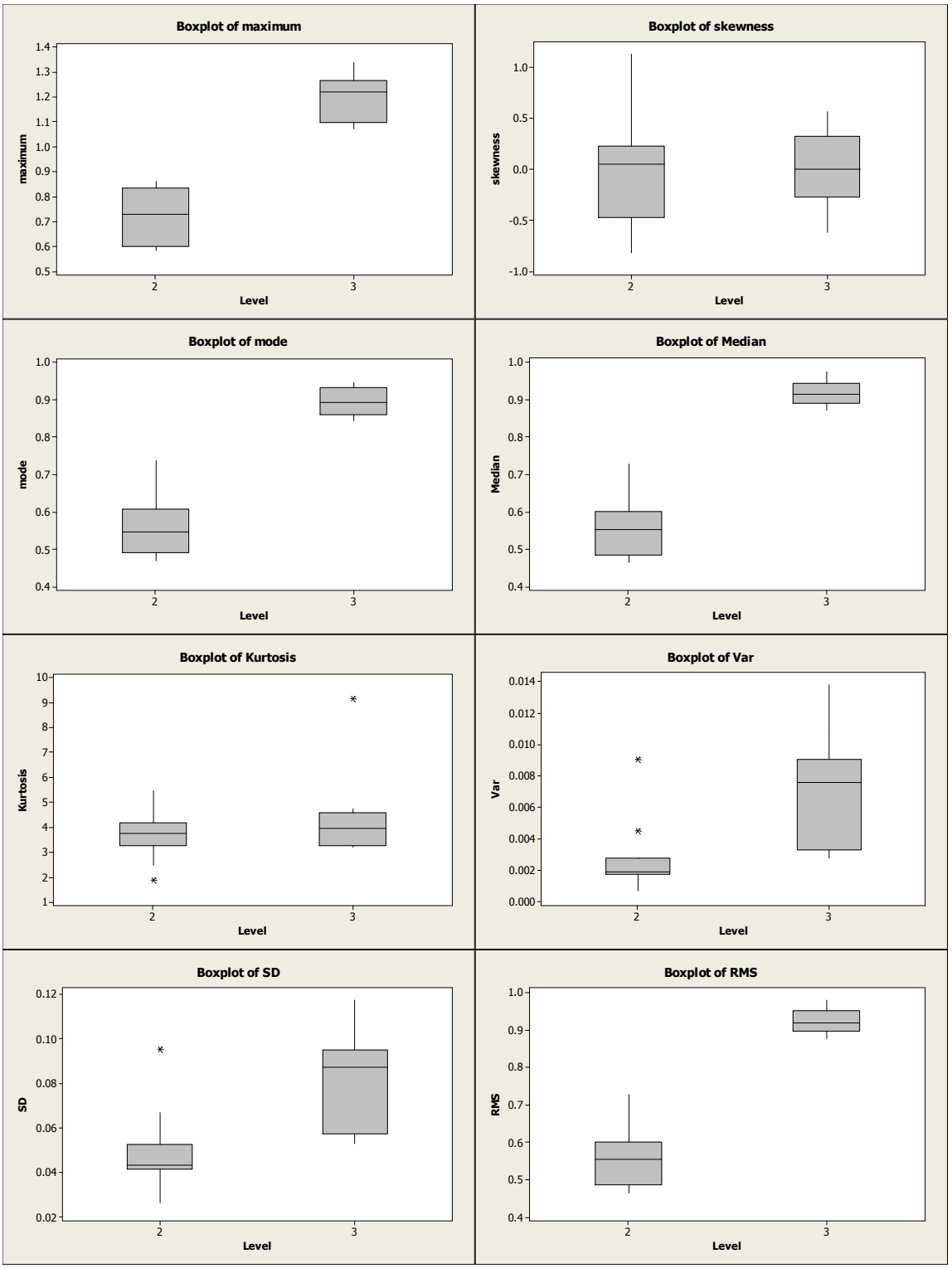

Boxplot of TINN
TINN
Level
Boxplot of RR tri indx
RR tri indx
Level
Boxplot of pNN50
pNN50
Level
Boxplot of NN50
NN50
Level
Boxplot of RMSSD
RMSSD
Level
Boxplot of min
min
Level
Boxplot of maximum
maximum
Level
Boxplot of skewness
skewness
Level

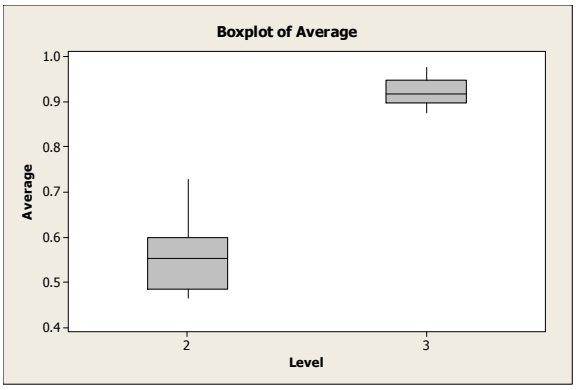

Boxplot of mode
mode
Level
Boxplot of Median
Median
Level
Boxplot of Kurtosis
Kurtosis
Level
Boxplot of Var
Var
Level
Boxplot of SD
SD
Level
Boxplot of RMS
RMS
Level
Boxplot of Average
Average
Level

A.6.5 Subject with Diabetes 5

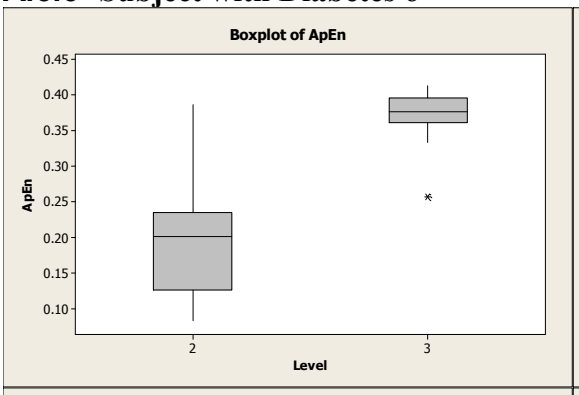


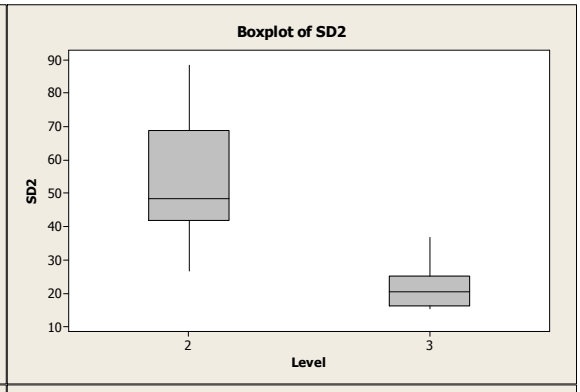

Boxplot of Power(FFT) LF
Power(FFT) LF
Level
Boxplot of Power(FFT) VLF
Power(FFT) VLF
Level
Boxplot of TINN
TINN
Level
Boxplot of RR tri indx
RR tri indx
Level
Boxplot of pNN50
pNN50
Level
Boxplot of NN50
NN50
Level
Boxplot of RMSSD
RMSSD
Level
Boxplot of min
min
Level

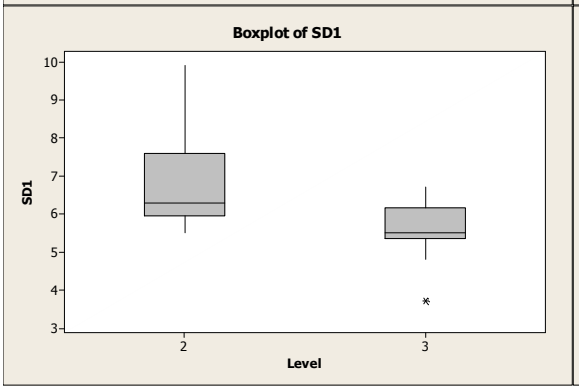

Boxplot of maximum
maximum
Level
Boxplot of skewness
skewness
Level
Boxplot of mode
mode
Level
Boxplot of Median
Median
Level
Boxplot of Kurtosis
Kurtosis
Level
Boxplot of Var
Var
Level
Boxplot of SD
SD
Level
Boxplot of RMS
RMS
Level

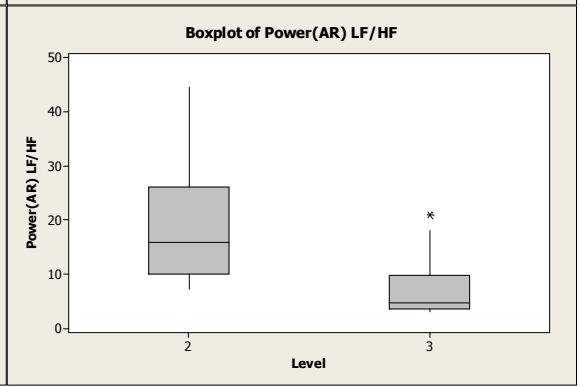


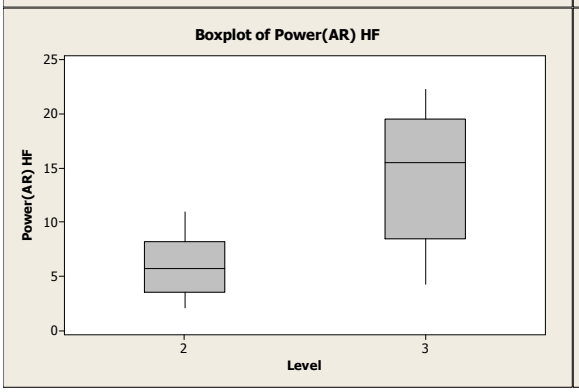
A.6.6 Subject with Diabetes 6

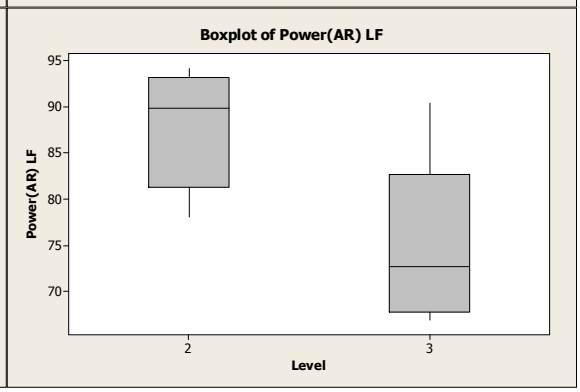


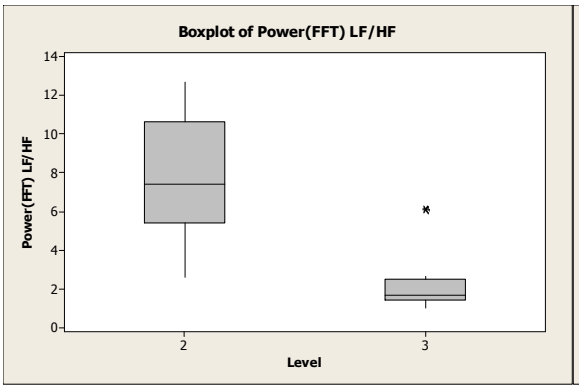


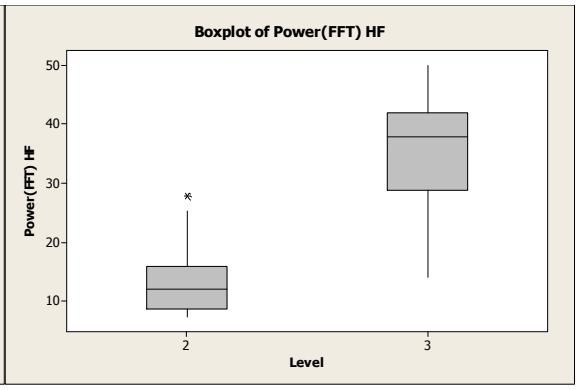


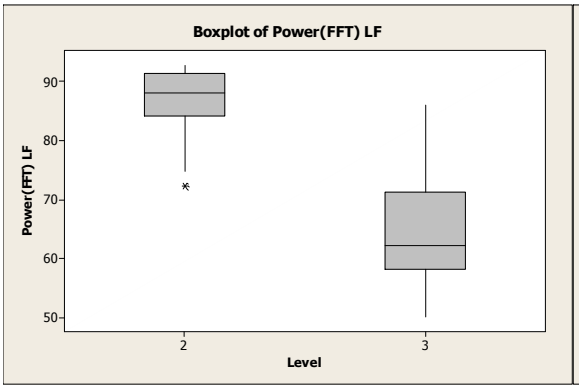


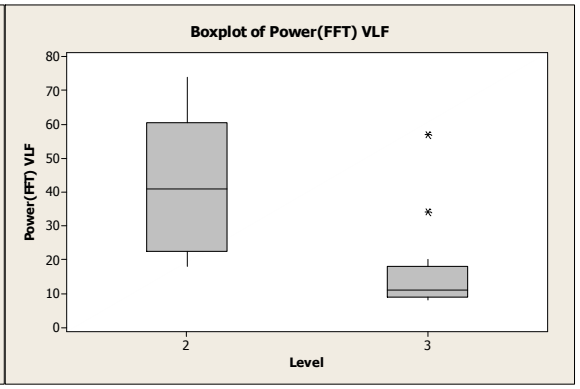


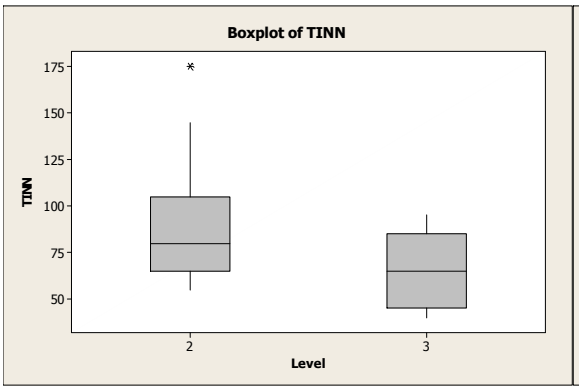


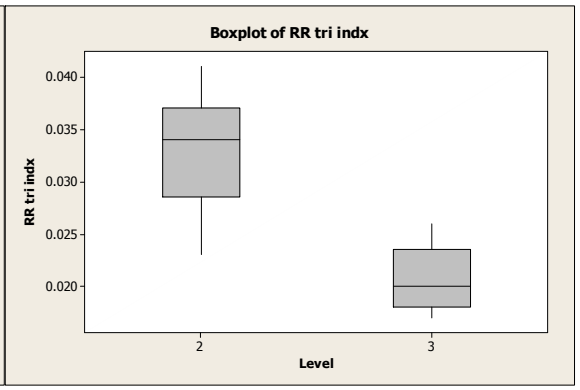

Boxplot of Power(FFT) LF/HF
Power(FFT) LF/HF
Level
2
3

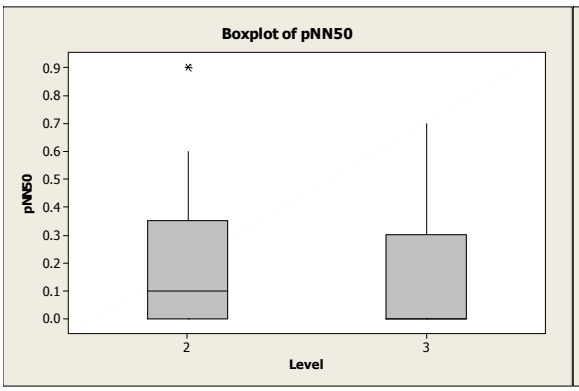

Boxplot of Power(FFT) HF
Power(FFT) HF
Level
2
3

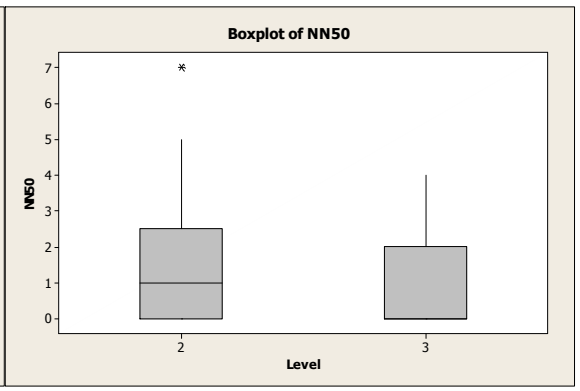

Boxplot of Power(FFT) LF
Power(FFT) LF
Level
2
3

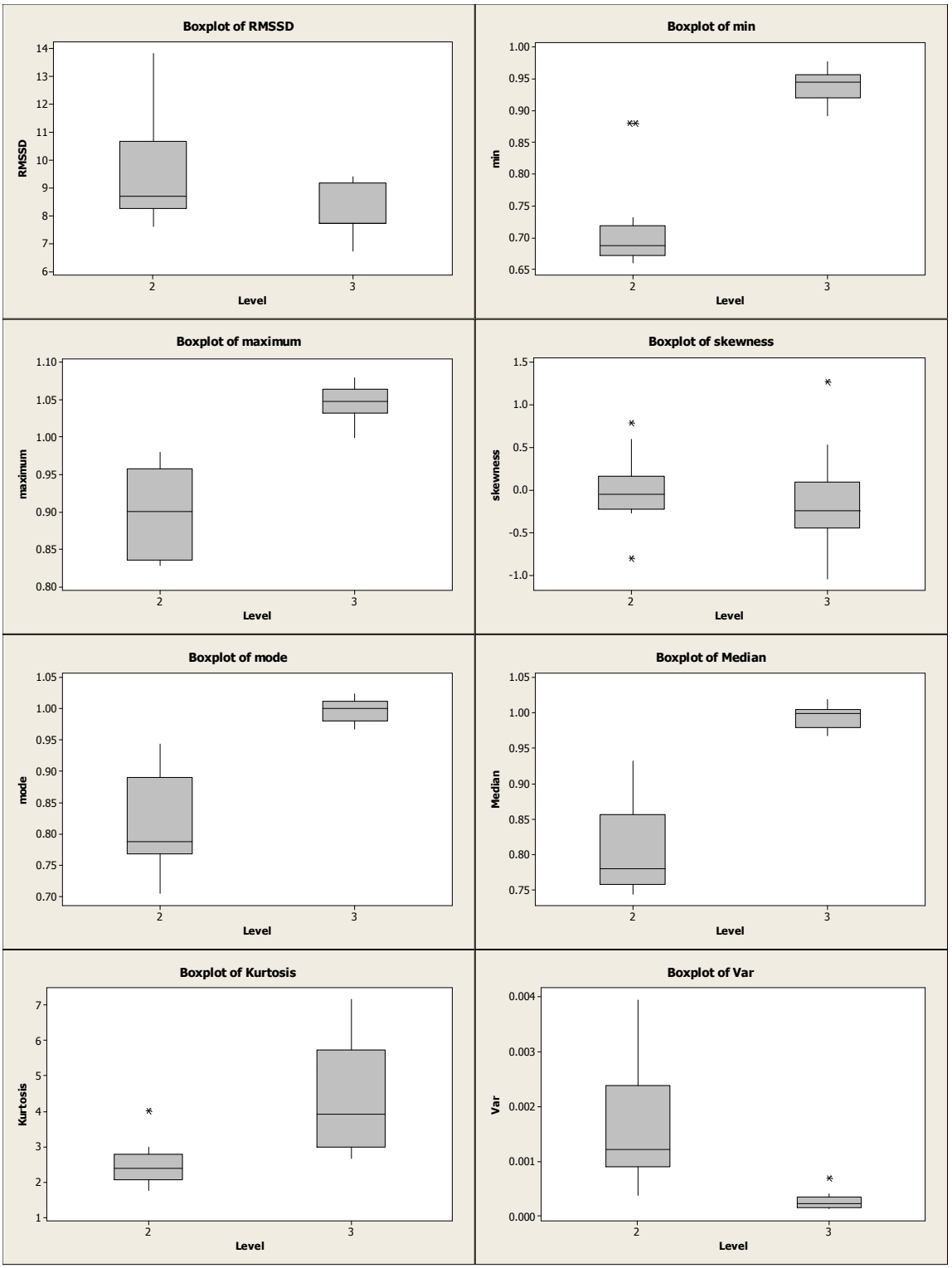

Boxplot of Power(FFT) VLF
Power(FFT) VLF
Level
2
3

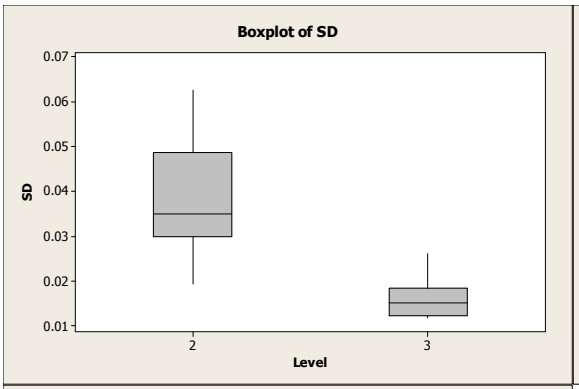

Boxplot of TINN
TINN
Level
2
3

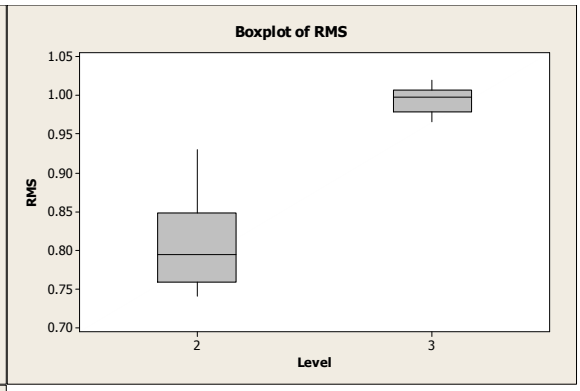

Boxplot of RR tri indx
RR tri indx
Level
2
3

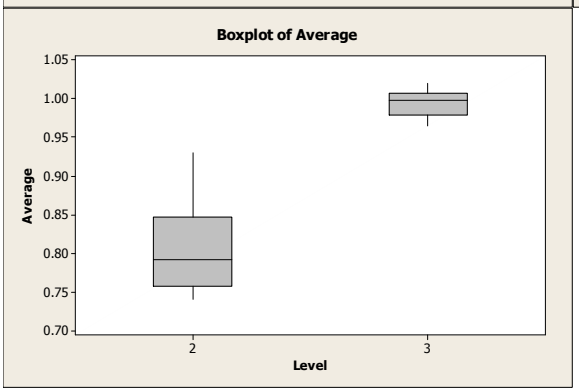

Boxplot of pNN50
pNN50
Level
2
3


Boxplot of NN50
NN50
Level
2
3


Boxplot of RMSSD
RMSSD
Level
Boxplot of min
min
Level
Boxplot of maximum
maximum
Level
Boxplot of skewness
skewness
Level
Boxplot of mode
mode
Level
Boxplot of Median
Median
Level
Boxplot of Kurtosis
Kurtosis
Level
Boxplot of Var
Var
Level

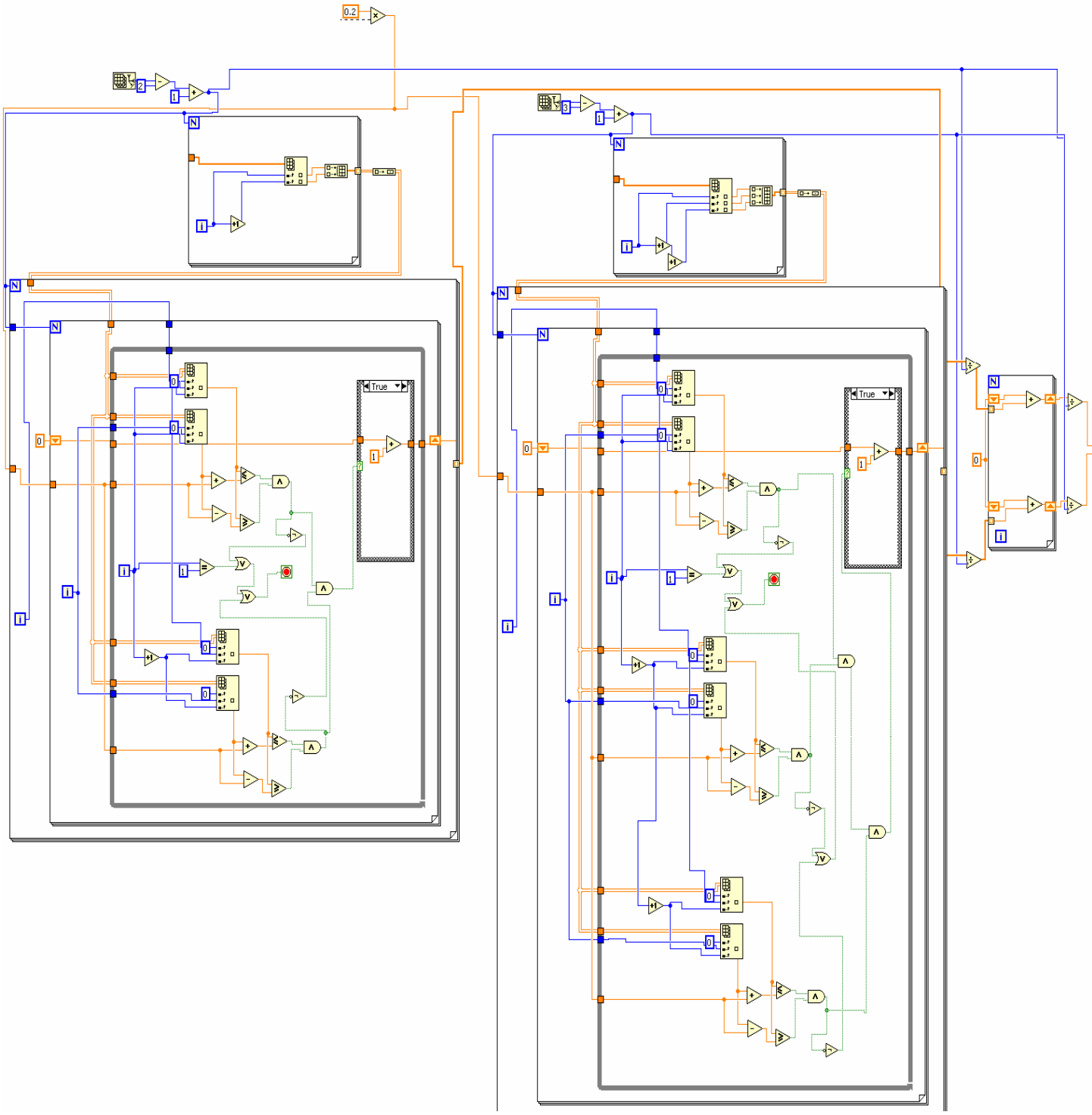

Boxplot of SD
SD
0.07
0.06
0.05
0.04
0.03
0.02
0.01
2
3
Level


Boxplot of RMS
RMS
1.05
1.00
0.95
0.90
0.85
0.80
0.75
0.70
2
3
Level


Boxplot of Average
Average
1.05
1.00
0.95
0.90
0.85
0.80
0.75
0.70
2
3
Level

Appendix B : LabVIEW programs

B.1 Approximate Entropy subroutine



Appendix C : Matlab programs

C.1 Histogram program

```
[A] = textread('HRV file 1.txt','%f');
[B] = textread('HRV file 2.txt','%f');
[C] = textread('HRV file 3.txt','%f');
[D] = textread('HRV file 4.txt','%f');
[E] = textread('HRV file 5.txt','%f');
[F] = textread('HRV file 6.txt','%f');

bin = 0.01
x = .4:bin:1.4;

subplot(3,2,1);
h=hist(A,x);
hn = h/(length(A)*bin);
bar(x,hn,'k')
hold
u = mean (A);
sig = std (A);
f = normpdf(x,u,sig);
plot(x,f,'r')
axis([.4  1.2  0  12])
title('Sugar = 86 mg/dL','FontSize',12)

subplot(3,2,2);
h = hist(B,x)
hn = h/(length(B)*bin);
bar(x,hn,'k')
hold
u = mean (B);
sig = std (B);
f = normpdf(x,u,sig);
plot(x,f,'r')
axis([.4  1.2  0  12])
title('Sugar = 93 mg/dL','FontSize',12)

subplot(3,2,3);
h = hist(C,x)
hn = h/(length(C)*bin);
bar(x,hn,'k')
hold
u = mean (C);
sig = std (C);
f = normpdf(x,u,sig);
plot(x,f,'r')
axis([.4  1.2  0  12])
```

```
title('Sugar = 132 mg/dL','FontSize',12)

subplot(3,2,4);
h = hist(D,x)
hn = h/(length(D)*bin);
bar(x,hn,'k')
hold
u = mean (D);
sig = std (D);
f = normpdf(x,u,sig);
plot(x,f,'r')
axis([.4  1.2  0  12])
title('Sugar = 149 mg/dL','FontSize',12)

subplot(3,2,5);
h = hist(E,x)
hn = h/(length(E)*bin);
bar(x,hn,'k')
hold
u = mean (E);
sig = std (E);
f = normpdf(x,u,sig);
plot(x,f,'r')
axis([.4  1.2  0  12])
title('Sugar = 123 mg/dL','FontSize',12)

subplot(3,2,6);
h = hist(F,x)
hn = h/(length(F)*bin);
bar(x,hn,'k')
hold
u = mean (F);
sig = std (F);
f = normpdf(x,u,sig);
plot(x,f,'r')
axis([.4  1.2  0  12])
title('Sugar = 119 mg/dL','FontSize',12)

set(gcf, 'PaperPosition', [.05 .05 8 10]);
```

C.2 Box plot program

```
[A] = xlsread('HRVstat1','Average');
[B] = xlsread('HRVstat1','RMS');
[C] = xlsread('HRVstat1','SD');
[D] = xlsread('HRVstat1','Variance');
```

```
[E] = xlsread('HRVstat1','Kurtosis');
[F] = xlsread('HRVstat1','Median');
[G] = xlsread('HRVstat1','Mode');
[H] = xlsread('HRVstat1','Skewness');
[I] = xlsread('HRVstat1','Max');
[J] = xlsread('HRVstat1','Min');
[K] = xlsread('HRVstat1','RMSSD');
[L] = xlsread('HRVstat1','NN50');
[M] = xlsread('HRVstat1','pNN50');
[N] = xlsread('HRVstat1','RR tri index');
[O] = xlsread('HRVstat1','TINN');
[P] = xlsread('HRVstat1','VLF(fft)');
[Q] = xlsread('HRVstat1','LF fft n.u.');
[R] = xlsread('HRVstat1','HF fft n.u.');
[S] = xlsread('HRVstat1','LF_HF fft n.u.');
[T] = xlsread('HRVstat1','LF ar n.u.');
[U] = xlsread('HRVstat1','HF ar n.u.');
[V] = xlsread('HRVstat1','LF_HF ar n.u.');
[W] = xlsread('HRVstat1','SD1');
[X] = xlsread('HRVstat1','SD2');
[Y] = xlsread('HRVstat1','ApEn');

Average = [A(:,2) A(:,4) A(:,6) A(:,8) A(:,10)];
RMS = [B(:,2) B(:,4) B(:,6) B(:,8) B(:,10)];
SD = [C(:,2) C(:,4) C(:,6) C(:,8) C(:,10)];
Var = [D(:,2) D(:,4) D(:,6) D(:,8) D(:,10)];
Kurt = [E(:,2) E(:,4) E(:,6) E(:,8) E(:,10)];
Med = [F(:,2) F(:,4) F(:,6) F(:,8) F(:,10)];
Mode = [G(:,2) G(:,4) G(:,6) G(:,8) G(:,10)];
Skew = [H(:,2) H(:,4) H(:,6) H(:,8) H(:,10)];
Max = [I(:,2) I(:,4) I(:,6) I(:,8) I(:,10)];
Min = [J(:,2) J(:,4) J(:,6) J(:,8) J(:,10)];
RMSSD = [K(:,2) K(:,4) K(:,6) K(:,8) K(:,10)];
NN50 = [L(:,2) L(:,4) L(:,6) L(:,8) L(:,10)];
pNN50 = [M(:,2) M(:,4) M(:,6) M(:,8) M(:,10)];
Tri = [N(:,2) N(:,4) N(:,6) N(:,8) N(:,10)];
TINN = [O(:,2) O(:,4) O(:,6) O(:,8) O(:,10)];
VLF_fft =[P(:,2) P(:,4) P(:,6) P(:,8) P(:,10)];
LF_fft =[Q(:,2) Q(:,4) Q(:,6) Q(:,8) Q(:,10)];
HF_fft = [R(:,2) R(:,4) R(:,6) R(:,8) R(:,10)];
LF_HF_fft = [S(:,2) S(:,4) S(:,6) S(:,8) S(:,10)];
LF_ar =[T(:,2) T(:,4) T(:,6) T(:,8) T(:,10)];
HF_ar = [U(:,2) U(:,4) U(:,6) U(:,8) U(:,10)];
LF_HF_ar = [V(:,2) V(:,4) V(:,6) V(:,8) V(:,10)];
SD1 = [W(:,2) W(:,4) W(:,6) W(:,8) W(:,10)];
SD2 = [X(:,2) X(:,4) X(:,6) X(:,8) X(:,10)];
```

```
ApEn = [Y(:,2) Y(:,4) Y(:,6) Y(:,8) Y(:,10)];

label = {'70-80';'81-90';'91-100';'101-130';'131+'};

subplot(3, 2, 1);
boxplot(Average,1)
set(gca, 'XTicklabel', label);
xlabel('Blood/Sugar Levels (mg/dL)');
ylabel('Average RR Intervals');

subplot(3,2,2);
boxplot(RMS,1)
set(gca, 'XTicklabel', label);
xlabel('Blood/Sugar Levels (mg/dL)');
ylabel('RMS');

subplot(3,2,3)
boxplot(SD,1)
set(gca, 'XTicklabel', label);
xlabel('Blood/Sugar Levels (mg/dL)');
ylabel('Standard Deviation');

subplot(3,2,4);
boxplot(Var,1)
set(gca, 'XTicklabel', label);
xlabel('Blood/Sugar Levels (mg/dL)');
ylabel('Variance');

subplot(3,2,5);
boxplot(Kurt,1)
set(gca, 'XTicklabel', label);
xlabel('Blood/Sugar Levels (mg/dL)');
ylabel('Kurtosis');

subplot(3,2,6);
boxplot(Med,1)
set(gca, 'XTicklabel', label);
xlabel('Blood/Sugar Levels (mg/dL)');
ylabel('Median');
set(gcf, 'PaperPosition', [.05 .05 8 10]);

figure, subplot(3,2,1);
boxplot(Mode,1)
set(gca, 'XTicklabel', label);
xlabel('Blood/Sugar Levels (mg/dL)');
ylabel('Mode');
```

```
subplot(3,2,2);
boxplot(Skew,1)
set(gca, 'XTicklabel', label);
xlabel('Blood/Sugar Levels (mg/dL)');
ylabel('Skewness');

subplot(3,2,3);
boxplot(Max,1)
set(gca, 'XTicklabel', label);
xlabel('Blood/Sugar Levels (mg/dL)');
ylabel('Maximum');

subplot(3,2,4);
boxplot(Min,1)
set(gca, 'XTicklabel', label);
xlabel('Blood/Sugar Levels (mg/dL)');
ylabel('Minimum');

subplot(3,2,5);
boxplot(RMSSD,1)
set(gca, 'XTicklabel', label);
xlabel('Blood/Sugar Levels (mg/dL)');
ylabel('RMSSD');

subplot(3,2,6);
boxplot(NN50,1)
set(gca, 'XTicklabel', label);
xlabel('Blood/Sugar Levels (mg/dL)');
ylabel('NN50');
set(gcf, 'PaperPosition', [.05 .05 8 10]);

figure, subplot(3,2,1);
boxplot(pNN50,1)
set(gca, 'XTicklabel', label);
xlabel('Blood/Sugar Levels (mg/dL)');
ylabel('pNN50');

subplot(3,2,2);
boxplot(Tri,1)
set(gca, 'XTicklabel', label);
xlabel('Blood/Sugar Levels (mg/dL)');
ylabel('RR Triangular Index');

subplot(3,2,3);
boxplot(TINN,1)
```

```
set(gca, 'XTicklabel', label);
xlabel('Blood/Sugar Levels (mg/dL)');
ylabel('TINN');

subplot(3,2,4);
boxplot(VLF_fft,1)
set(gca, 'XTicklabel', label);
xlabel('Blood/Sugar Levels (mg/dL)');
ylabel('VLF (fft)');

subplot(3,2,5);
boxplot(LF_fft,1)
set(gca, 'XTicklabel', label);
xlabel('Blood/Sugar Levels (mg/dL)');
ylabel('LF (fft)');

subplot(3,2,6);
boxplot(HF_fft,1)
set(gca, 'XTicklabel', label);
xlabel('Blood/Sugar Levels (mg/dL)');
ylabel('HF (fft)');
set(gcf, 'PaperPosition', [.05 .05 8 10]);

figure, subplot(3,2,1);
boxplot(LF_HF_fft,1)
set(gca, 'XTicklabel', label);
xlabel('Blood/Sugar Levels (mg/dL)');
ylabel('LF/HF (fft)');

subplot(3,2,2);
boxplot(LF_ar,1)
set(gca, 'XTicklabel', label);
xlabel('Blood/Sugar Levels (mg/dL)');
ylabel('LF (ar)');

subplot(3,2,3);
boxplot(HF_ar,1)
set(gca, 'XTicklabel', label);
xlabel('Blood/Sugar Levels (mg/dL)');
ylabel('HF (ar)');

subplot(3,2,4);
boxplot(SD1,1)
set(gca, 'XTicklabel', label);
xlabel('Blood/Sugar Levels (mg/dL)');
ylabel('SD1');
```

```
subplot(3,2,5);
boxplot(SD2,1)
set(gca, 'XTicklabel', label);
xlabel('Blood/Sugar Levels (mg/dL)');
ylabel('SD2');

subplot(3,2,6);
boxplot(ApEn,1)
set(gca, 'XTicklabel', label);
xlabel('Blood/Sugar Levels (mg/dL)');
ylabel('ApEn');

set(gcf, 'PaperPosition', [.05 .05 8 10]);
```

C.3 Poincare' plot program

```
[A] = textread('HRV file.txt','%f');

t=0:0.2:2*pi;
rotation=pi/4;

xm=A;
xp=A;
xm(end)=[];
xp(1)=[];
plot(xm,xp,'r.')
hold
M1= mean(xm);
M2= mean(xp);
SD1=std(xp-xm)/sqrt(2);
SD2=std(xp+xm)/sqrt(2);
y = SD1 * cos(t);
x = SD2 * sin(t);
nx = x*cos(rotation)-y*sin(rotation)+M1;
ny = x*sin(rotation)+y*cos(rotation)+M2;

plot(nx,ny,'b');

axis([.55  1.1  .55  1.1])
title('Sugar = 111 mg/dL','FontSize',12)
xlabel('RRn (DDn)(seconds)')
ylabel('RRn-1 (DDn-1)(seconds)')
```

Appendix D : IRB and Consent Forms

THE UNIVERSITY OF TEXAS AT EL PASO

MEMORANDUM

Vice Provost
for Research

TO: H. Nazeran, Associate Professor, Electrical Engineering
Emily Haltiwanger, Assistant Professor, Occupational Therapy
Chantal Vella, Assistant Professor, Kinesiology
Marcos Bolanos, MS Student, Electrical Engineering
Principal Investigator(s)

FROM: Karen Hoover
Institutional Coordinator for Research Review

DATE: August 1, 2006

SUBJ: Research Protocol #2341: "A Correlation of Glucose Levels in the Blood with Changes in Heart Rate Variations"
PROTOCOL PERIOD: August 1, 2006 through July 31, 2007

This research protocol, has been reviewed and approved by The University of Texas at El Paso Institutional Review Board and is in accord with University policy. The review indicates that the project is meritorious, that your safeguards against risks to human subjects are adequate, and that the proposed consent forms are appropriate.

You have passed an IRB compliance test, in accordance with the recommendations of the Office for Human Research Protections.

You have the responsibility to protect the rights and welfare of human research subjects, including the requirements to provide each subject with an IRB-approved informed consent document, and to promptly report any injuries or unexpected risks to this office. If your research significantly changes or you involve human subjects in activities not described in the protocol, you should submit an amended research protocol to this office. Please provide an email progress report on your research activities before the expiration date listed above. A copy of the informed consent documents is attached.

Attachment

El Paso, Texas
79968-0587
(915) 747-5680/5689
FAX: (915) 747-6474

#2341

A Correlation of Glucose Levels in the Blood with Changes in Heart Rate Variations

M Bolanos, H Nazeran, E Haltiwanger, C Vella

April, 2006

INSTITUTIONAL REVIEW BOARD

RESEARCH PROTOCOL FOR PROJECTS INVOLVING HUMAN SUBJECTS

Please refer to the Procedures for Review and Approval of Research Using Human Subjects including the University Assurance of Compliance statement (available from the Office of Research and Sponsored Projects, ORSP) in completing all parts of this form. Sign completed form and return to ORSP.

To be completed by ORSP. This research project involves humans as subjects in research. ORSP has determined initially that the research proposed (check one) ____ is ✓ is not exempt from coverage under CFR 46.101. The project is exempt under category _____. Expedited X or full __ committee review.

Title: A Correlation of Glucose Levels in the Blood with Changes in Heart Rate Variations.

1. **Describe the proposed research, including statement of the problem, rationale, whom the subjects will be, how they will be solicited and venue, methods and data analysis strategies.**

This is a biomedical engineering project involving two faculty from Health Sciences: Emily Haltiwanger OTD, Chantal Vella PhD; one faculty and one MS student from Electrical and Computer Engineering (ECE): Homer Nazeran PhD and Marcos Bolaños (a Bridge to the Doctorate Fellow). Data collection from type I diabetic subjects will involve Ms Sara Choi a nurse practitioner from Del Sol Medical Center. This is a pilot study focusing on establishing correlations between spectral features of Heart Rate Variability Signal (HRV) and glucose levels in non-diabetic and diabetic subjects.

Statement of the Problem: Rationale - Heart rate variability is the beat-to-beat changes in the heart rate. It is a reflection of sympathetic and parasympathetic activity of the autonomic nervous system in controlling the heart rate. The parasympathetic nervous system is responsible for slowing down the heart rate, lowering blood pressure, and controlling other relaxing activities. The sympathetic nervous system has a balancing and opposing effect, thereby increasing the heart rate and blood pressure.

The specialized literature in the field shows that there is a correlation between heart rate variability (as an indicator of autonomic regulation of the heart rate) and glucose levels in the blood (Bianchi et al., 1990). A study of abnormal cardiovascular autonomic function leads to the observation that glycemia is inversely related to the spectral components of the HRV signal (Bellavere, 1992). It has been observed that the ratio of the low frequency (LF) and high frequency (HF) components (LF/HF) in the HRV signal reduced significantly in diabetics compared to non-diabetics. Another study of cardiovascular autonomic function demonstrated that the total HRV power spectrum was sensitive to changes in glucose levels (Makimattila, 2000). This study is focused on establishing quantitative relationships between derived parameters from the HRV signal and glucose levels in normal and diabetic subjects.

Therefore, the specific aims of this research are to test the following hypotheses:

H1: Spectral and nonlinear dynamic features of HRV signal are correlated with glucose levels in normal subjects.

H2: Spectral and nonlinear dynamic features of HRV signal are correlated with glucose levels in Type 1 diabetics.

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Subjects: Six volunteer type I diabetics wearing an insulin pump and ten volunteer non-diabetics of both genders, 18-65 years from UTEP students, faculty and the community will be recruited to participate in this pilot study.

Data to be gathered from diabetic volunteer subjects include demographic information, ECG data from 24-hour Holter monitoring, sugar level data from 24-hour continuous glucose monitoring, and temperature. Data to be collected from non-diabetic volunteers include demographic information, ECG data, photoplethysmographic (PPG) recording of blood pressure, temperature, and blood glucose samples. Holter monitoring is a very well-established, noninvasive method and does not pose any potential risks. Continuous blood sugar monitoring is also an established clinical procedure. It may be uncomfortable while wearing this monitoring device due to insertion of a plastic catheter to continuously measure sugar levels but type 1 diabetics wearing an insulin pump are accustomed to this procedure and this does not pose any additional potential risks to them. Photoplethysmographic (PPG) recording of blood pressure is totally noninvasive and very convenient as it only involves placing an infrared light probe on one finger and does not pose any potential risks. Temperature monitoring simply requires a small sensor to be placed under the arm of the patient. Both the photoplethysmographic and temperature sensors are controlled and monitored with the use of a Personal Digital Assistant (PDA).

Informed consent will be obtained from all volunteers in providing information appropriate to their linguistic skills and educational level. Subjects will be recruited by Marcos Bolaños (in consultation with Emily Haltiwanger OTD, Chantal Vella PhD and Sara Choi RN) who will be available to answer questions about the study and screen potential participants for eligibility.

Venues:

1. Non-diabetic data collection: Photoplethysmographic, temperature, and blood glucose sampling before exercise (baseline), after mild exercise, and after a high sugar drink will be carried out in the Exercise Physiology Lab in Memorial Gym 109 under supervision of Chantal Vella PhD. Data will be analyzed at Electrical and Computer Engineering at UTEP.
2. Diabetic data collection: Holter, temperature, and continuous glucose level monitoring devices will be fitted onto type 1 diabetic subjects at Del Sol Medical Center under the supervision of nurse practitioner Sara Choi at 10301 Gateway West. Data collected from these subjects will be provided to Marcos Bolaños and Homer Nazeran PhD in electronic form for signal processing and analysis at ECE.

Methods:

Non-diabetics: After giving informed consents, **10** non-diabetic students will be recruited for this pilot study. All efforts will be made to include equal gender. Marcos Bolaños (in consultation with Emily Haltiwanger OTD and Chantal Vella PhD) will coordinate the data collection process with the volunteers to be carried out on pre-arranged dates at the Memorial Gym. Photoplethysmographic data, temperature, and blood samples will be collected before exercise (baseline), after mild exercise (i.e., on a bicycle), and after drinking a high sugar drink. The data collection from these volunteers will be performed by Marcos Bolaños under supervision of Chantal Vella PhD. A baseline blood sample will be taken from a finger on the non-dominant hand. The finger will be cleaned with alcohol and blood will be collected from a finger stick using a Lancet pen and disposable pen needle. The Lancet pen and disposable needle will be used to

puncture the skin and one drop of blood will be placed on a glucose strip and placed in a portable One Touch® Ultra glucose monitor for determination of blood glucose. Following the baseline blood sample, subjects will begin to exercise on a bicycle at a mild intensity (50 Watts) or treadmill at 3.5 to 4.0 mph. Total exercise time will not exceed 25 minutes. Three blood glucose measurements will be taken by the finger stick method on each subject (baseline – end of Interval1, after exercise - end of interval 2, and after high sugar drink – end of interval 5). The testing procedure and duration can be seen in table 1. Tests refer to data collected via Photoplethysmograph, temperature, and blood sampling. Subjects will be monitored during exercise and will be allowed to stop exercise at any time. Universal precautions will be used for all blood sampling. Approximately 3 drops of blood will be taken per subject (< 4 micro liters).

Interval #	1	2	3	4	5	6
Event	Test 1	Exercise	Rest	Test 2	Sugar Drink	Test 3
Duration	5 min	25 min	5 min	5 min	15 min	5 min

Table 1: Testing Procedure Over 60 Minutes

Type I Diabetics: After giving informed consent, **6** type 1 diabetic subjects from UTEP and the community will be recruited. Recruitment will be performed by Marcos Bolaños (in consultation with Sara Choi RN). ECG (Holter) and temperature sensor attachment will be carried out by Marcos Bolaños under supervision of Sara Choi RN. Continuous blood glucose monitoring protocols and fitting of devices will be performed by the patients on themselves and supervised by Sara Choi. ECG, temperature, sugar level data will be collected over a period of 24 hours.

Signal Processing and Data Analysis:
Data collected from diabetic subjects will be in the form of ECG signals (acquired by Holter monitoring), temperature values, and blood sugar levels by means of continuous glucose monitoring following standard procedures. Data collected from non-diabetics will be in the form of photoplethysmographic (PPG) signals, temperature values, and One Touch® Ultra data entries from a written log kept by Marcos Bolaños. A program developed in LABVIEW software environment will perform all signal acquisition for photoplethysmograhic and temperature data and processing/analysis functions necessary to correlate HRV signal parameters with blood sugar levels.

Universal Precautions. The investigators will collaborate with the University Safety Officer on a protocol for safe handling and disposal of blood sampling and temperature sensors used in measurement of sugar levels and thermometry procedures in non-diabetics. Gloves will be used when handling these sensors. All used sensors will be placed into plastic yellow bags and will be transferred on a regular basis to large yellow plastic bags. After double bagging and sealing, these large bags (after temporary secure storage) will be collected for technical disposal by incineration using the University system for disposal of clinical waste. All investigators will be trained in Universal Precautions. The nurse practitioner will follow standard procedures to dispose of ECG electrodes and plastic catheters used in Holter monitoring of diabetics subjects.

All blood sampling procedures (fingering lancing) will be performed using aseptic techniques. Universal precautions for the handling of body fluids will be followed during

all collection and analysis procedures. Gloves will be used when taking blood samples and the disposable lancets will be disposed of in a sharps container. Chantal Vella PhD, who is trained in finger stick blood sampling and Universal Precautions will supervise and train Marcos Bolaños in the proper techniques for finger stick blood sampling. Approximately 3 drops of blood will be taken per subject (< 4 micro liters).

2. **Explain whether and how women, minorities and children under 21 will be included as subjects in this study.**

College of Health Sciences at UTEP is comprised of faculty and students with a variety of ethnic backgrounds, including Caucasian(Non-Hispanic) and Hispanic, both of whom will be recruited for the study described in this application. The ethnic (Hispanic, non-Hispanic) and health status (diabetic, non-diabetic) of the subjects is determined by routine data that requests self identification of the subjects. Due to the large proportion of Hispanic females, inclusion of sufficient number of Hispanic women in this pilot study will be accomplished. A large number of UTEP students are under age of 25 so this part of the population will be well represented in this pilot study.

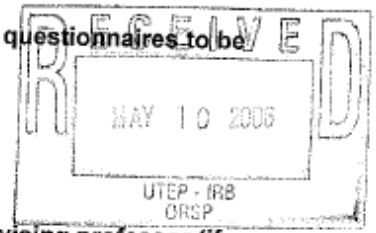
3. **Describe provisions to adequately protect the rights and welfare of prospective research subjects.**

Research materials will be coded and stored with an identification number. A list matching identifying information with code number will be kept separate from all other research materials and only available to the investigators.

4. **Describe provisions to insure that pertinent laws and regulations are observed.**

Marcos Bolaños involved in data collection from human subjects, and the nurse practitioner will provide evidence of completion of training and copies of certificates will be on file. For example, http://cme.cancer.gov/clinicaltrials/learning/humanparticipants-protections.asp?action=sendLoginPass&course=protection or the ORSP compliance & testing modules available from the UTEP website will be accessed.
Procedures present no risk to welfare or health of subjects. Study procedures that have a possibility of discomfort (manual blood sampling and continuous monitoring of sugar levels) will be conducted by Marcos Bolaños after adequate training by Chantal Vella PhD and Sara Choi RN. The letter of informed consent will be presented to participants in their preferred language form for signature and witnessed by their classmates or friends. Subjects are free to drop out of the study at any time without consequences.

5. **Attach samples of proposed informed consent forms and questionnaires to be used in research projects.**



6. **Proposed Research Period:** 4/15/06 to 11/15/06

7. **Funding Source:** NSF: Bridge to Doctorate Fellowship

This entire research protocol has been reviewed by the supervising professor (if applicable) & the department head (or equivalent) for ethical considerations and merit.

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April, 2006

Department Chairperson (Signature) — 4/26/06 Date

B. Flores
Department Chairperson (printed name)

Supervising Professor (Signature) — 4/20/06 Date

H. Nazeran
Supervising Professor (printed name)

Emily Haltiwanger
Co Supervising Professor (Signature) — 4/20/06 Date

Emily Haltiwanger,
Co Supervising Professor (printed name)

Chantal Vella
Co Supervising Professor (Signature) — 4/21/06 Date

Chantal Vella
Co Supervising Professor (printed name)

Principal Investigator (Signature) — 4/20/06 Date

Marcos Bolaños
Principal Investigator (printed name) — MS student Title

Electrical Engineering
Department — mbolanos@utep.edu email address

500 W. University Ave. Engineering A325
Address — (915) 242-8810 Telephone

I certify, as the Principal Investigator of this research project, that by implementing standard Universal Precautions procedures for handling of blood and hazardous agents, there will be no risks to the health or welfare of subjects, research assistants or bystanders during the approved protocol period. I will abide by all requirements of the Departmental Safety Officer and the University Office of Environmental Health & Safety regarding the use and disposal of blood products & hazardous agents.

Principal Investigator — 4/20/06 Date

Appendix B
Informed Consent Form
(Non- Diabetics)

TITLE OF THE STUDY: A Correlation of Glucose Levels in the Blood with Changes in Heart Rate Variations

I am being asked to participate in a research study designed to determine if there is a correlation between glucose levels in the blood and heart rate variations in Type 1 diabetics.

Prior to my enrollment in this study, the principle investigator will explain in detail, the purpose of the project, the procedures to be used, and the potential benefits and possible risks of operation. I may ask the principle investigator any questions at any time to help better understand the nature of this study and my role in it. A written explanation of the project has been provided below. I will read this explanation and discuss with the researcher any questions that I might have.

If I decide to participate in this project, my signature on this form validates that I have not been diagnosed with Type I diabetes. I will sign my name below in the presence of the principal investigator. I will be given the information about this study to keep, as well as a copy of this consent form.

I understand that at the end of this experiment, I will be given any additional information I desire about the research.

1. **Nature and Purpose of the Project:** Heart rate variations are suspected to be effected by the glucose levels in the blood. Type 1 diabetics are prone to noticeable changes in glucose levels and thus are the primary subjects of this study. Hence the purpose of the study is to determine a correlation between fluctuating glucose levels and heart rate variation.

2. **Explanation of the Procedures:** Procedures for the acquisition of heart rate variation will be as follows. An infrared finger probe will be attached to the forefinger of the right or left hand in order to obtain the photoplethysmographic (PPG) signal. A small temperature sensor will be placed on the underside of the right arm. PPG signals and body temperature values will be interfaced to a Personal Digital Assistant (PDA). PPG and temperature data will be collected continuously for duration of the test. The principle investigator, Marcos Bolaños, while under the supervision of Sara Choi, a Registered Nurse, and Chantal Vella PhD, will obtain blood samples (< 4 micro liters) from the finger tip to determine the current glucose levels in the blood via a One Touch® Ultra glucose monitor at the end of each interval (intervals 1 to 6 shown in Table 1). All data will be collected prior to exercising on a stationary bicycle (baseline), after exercising,

and after drinking a high sugar drink. The testing period will not exceed 60 minutes. The procedure is outlined in Table 1 below.

Interval #	1	2	3	4	5	6
Event	Test 1	Exercise	Rest	Test 2	Sugar Drink	Test 3
Duration	5 min	25 min	5 min	5 min	15 min	5 min

Table 1: Testing Procedure Over 60 Minutes

3. **Discomfort and Risks:** Risk associated with this type of testing is minimal. Possible discomfort to the participant may include slight pressure to the forefinger due to the infrared finger probe. Other risks associated with this type of testing include expected minimal pain on the finger tips from the One Touch® Ultra glucose monitor lancets.

4. **Benefits:** Each participant will benefit from the knowledge that their participation will help in the possible development of a non-invasive glucose monitoring system that can be used as supplemental monitoring equipment in daily glucose management of diabetics.

5. **Confidentiality:** All information collected in this study will remain confidential. The principle investigator and faculty sponsor will be the only two people to have access to any information pertaining to the participants. The risk of loss of confidentiality will be minimized through the use of subject identification codes rather than name identifiers. Once data is collected, all information will be stored under lock and key in Dr. Homer Nazeran's office in the Engineering Annex.

6. **Refusal/Withdrawal:**
   I understand that participation in this study is entirely voluntary. I understand that anyone who agrees to participate has the right to withdraw from the study at any time with no penalty to him/her. I understand that I must be 18 years of age to participate in this study.

I have read the following information and understand what is being asked of me. For more information, I can contact Marcos Bolaños, (915) 747-8810 or contact Dr. Homer Nazeran, Ph.D. in the Electrical Engineering Department at The University of Texas at El Paso (915) 747-6955.

If I have any questions regarding my rights as a participant in this research, I may contact Karen Hoover, Institutional Coordinator for Research Review (UTEP) at (915) 747-5680.

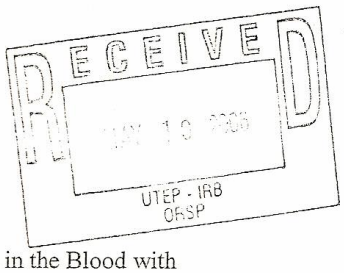
Thank you for your time and cooperation in this research project.

_____ _____ _____ _____

Participant's Signature Date Witness's Signature Date

_____ _____

Participant's Printed Name Witness's Printed Name



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Appendix B

Informed Consent Form
(Type 1 Diabetics)

TITLE OF THE STUDY: A Correlation of Glucose Levels in the Blood with Changes in Heart Rate Variations

I am being asked to participate in a research study designed to determine if there is a correlation between glucose levels in the blood and heart rate variations in Type 1 diabetics.

Prior to my enrollment in this study, the principle investigator will explain in detail, the purpose of the project, the procedures to be used, and the potential benefits and possible risks of operation. I may ask the principle investigator any questions at any time to help better understand the nature of this study and my role in it. A written explanation of the project has been provided below. I will read this explanation and discuss with the researcher any questions that I might have.

If I decide to participate in this project, my signature validates that I am accustomed to self-inserting a catheter for purposes of glucose measurement in my abdomen. I will sign my name below in the presence of the person who explained the project to me. I will be given the information about this study to keep, as well as a copy of this consent form.

I understand that at the end of this experiment, I will be given any additional information I desire about the research.

1. **Nature and Purpose of the Project:** Heart rate variations are suspected to be effected by the glucose levels in the blood. Type 1 diabetics are prone to noticeable changes in glucose levels and thus are the primary subjects of this study. Hence the purpose of the study is to determine a correlation between fluctuating glucose levels and heart rate variation.

2. **Explanation of the Procedures:** Procedures for the acquisition of heart rate variations and continuous sugar levels in the blood will be as follows. Electrocardiogram signals will be obtained by attaching 3 small disposable electrodes to the right and left inner shoulders and the navel (reference electrode) using a wearable Holter monitor. I will fit a narrow plastic catheter similar to the catheters used in insulin pumps in my abdominal region to sense sugar levels in the blood by a small glucose monitor. A small temperature sensor will be placed on the underside of the right arm to acquire temperature using a wearable digital thermometer. The principle investigator, Marcos Bolaños, will attach the electrodes and temperature sensor. Sara Choi, a Registered Nurse, will supervise the entire process assuring all standard clinical procedures are followed. The data will continuously be collected over a 24 hour period.

3. **Discomfort and Risks:** Risk associated with this type of testing is minimal. It may be uncomfortable while wearing the continuous glucose monitoring device due to insertion of a catheter to continuously measure sugar levels but type 1 diabetics wearing an insulin pump are accustomed to this procedure and this does not pose any additional potential risks to them. Disposable ECG electrodes used for Holter monitoring are applied to the surface of the skin and may cause a minor skin irritation in some subjects after several hours. In that case they will be instructed to use fresh electrodes provided to them.

4. **Benefits:** Each participant will benefit from the knowledge that their participation will help in the possible development of a non-invasive glucose monitoring system that can be used as supplemental monitoring equipment in their daily glucose management.

5. **Confidentiality:** All information collected in this study will remain confidential. The principle investigator and faculty sponsor will be the only two people to have access to any information pertaining to the participants. The risk of loss of confidentiality will be minimized through the use of subject identification codes rather than name identifiers. Once data is collected, all information will be stored under lock and key in Dr. Homer Nazeran's office in the Engineering Annex Room 317.

6. **Refusal/Withdrawal:**
   I understand that participation in this study is entirely voluntary. I understand that anyone who agrees to participate has the right to withdraw from the study at any time with no penalty to him/her. I understand that I must be 18 years of age to participate in this study.

I have read the following information and understand what is being asked of me. For more information, I can contact Marcos Bolaños, (915) 747-8810 or contact Dr. Homer Nazeran, Ph.D. in the Electrical Engineering Department at The University of Texas at El Paso (915) 747-6955.

If I have any questions regarding my rights as a participant in this research, I may contact Karen Hoover, Institutional Coordinator for Research Review (UTEP) at (915) 747-5680.

Curriculum Vitae

Marcos Bolaños was born in El Paso, Texas. He is the oldest son of Ofelia and Arturo Bolaños and sibling to two brothers, Andres and Efren. He graduated high school in 2000 from Bethel Temple Christian as valedictorian. Marcos enrolled in the electrical engineering program at The University of Texas at El Paso in the Fall and gained an interest in a research orientated career after taking part in the National Science Foundation's (NSF) Research Experience for Undergraduates (REU) program. He gained a particular interest in biomedical applications in engineering his senior year. His senior project team, Team Evolution, won the award for Best Senior Project in the Spring 2004 for developing a PDA-based electrocardiogram/blood pressure telemonitor for telemedicine. The team was made up of Christopher Martinez, Izaac Gonzales, and Marcos' oldest cousin Rick Parra who graduated along side him. Marcos immediately enrolled in the graduate school at The University of Texas at El Paso in the fall and was awarded the NSF Bridge to the Doctorate fellowship. He continued research in the biomedical areas of electrical engineering and went on to present a conference paper at the IEEE EMBS conference in New York, New York on the "Comparison of heart rate variability signal features derived from electrocardiography and photoplethysmography in healthy individuals". Marcos was an officer of the Institute of Electrical and Electronic Engineers professional organization at The University of Texas at El Paso for six years and served as President for two of those years. He graduated with his masters of science in electrical engineering in summer 2007 and will begin his doctoral program in electrical engineering at Michigan State University with a full academic fellowship.

Permanent Address: P.O. Box 220493
El Paso, TX 79913