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ABSTRACT

MEASUREMENT OF THE BARORECEPTOR SENSITIVITY INDEX (BRSI) IN THE TIME AND FREQUENCY DOMAINS

by
Tanvir Raquib

Time domain analysis for calculating the Baroreceptor Sensitivity Index (BRSI) did not always provide an accurate result. It also had another limitation in that it could not show the influence of the autonomic nervous system for different subjects. The correlation coefficient is a mechanism that was used to either accept or reject the BRSI values in the time domain but the correlation coefficient values changed drastically depending on how many sample points were selected for the calculation.

On the other hand, frequency domain analysis for the BRSI calculation was relatively easier and provided more accurate information compared to the time domain analysis. The modulus was the frequency domain equivalent of the Baroreceptor Sensitivity Index in the time domain. In the low frequency band (0.07Hz-0.14Hz), the baroreceptor response is influenced by the blood pressure control mechanism. Therefore, different modulus values for different subjects showed the influence of the autonomic nervous system in the calculation of modulus. As correlation coefficient was a measure to either accept to reject the BRSI calculation in the time domain, coherence was a measure to either accept or reject the modulus calculation in the frequency domain.

During the analysis the coherence value did not change as drastically as the correlation coefficient differences of several sample points. Frequency domain calculation therefore, proved to be relatively more accurate, stable, and provided more information compared to the time domain analysis.

MEASUREMENT OF THE BARORECEPTOR SENSITIVITY INDEX (BRSI) IN THE TIME AND FREQUENCY DOMAINS

by
Tanvir Raquib

A Thesis
Submitted to the Faculty of
New Jersey Institute of Technology
in Partial Fulfillment of the of the Requirements for the Degree of
Master of Science in Biomedical Engineering

Biomedical Engineering Committee

August 1998

APPROVAL PAGE

MEASUREMENT OF THE BARORECEPTOR SENSITIVITY INDEX (BRSI) IN THE TIME AND FREQUENCY DOMAINS

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This thesis is dedicated to my parents
Mohammed and Hasna Raquib
for all their support and guidance
through my education

ACKNOWLEDGEMENT

The author wished to express his sincere gratitude to his advisor, Dr. Stanley S. Reisman, for his guidance, support, and friendship throughout this research. Special thanks to Dr. David Kristol and Dr. Peter Engler for serving as members of the committee.

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CHAPTER 1

INTRODUCTION

Heart disease, cancer, brain tumors, AIDS, and many more diseases are taking millions of lives every year all over the world. But progress is exploding in the operating rooms through the research in biomedical engineering. Physicians are now able to better understand these fatal illnesses because of the advancement in the biomedical engineering field. Better equipment has resulted into a more comprehensive treatment. To contemplate an end of human sufferings doctors need to discern the relationship between different biological signals. The following document is a small step forward in revealing more clues about these signals.

This thesis will discuss two biological signals, blood pressure and electrocardiogram. It will compare calculations of Baroreceptor Sensitivity Index (BRSI) in time and frequency domains to compare accuracy of two methods. Valsalva is used as a tool to illicit rapid changes in blood pressure and heart rate from which BRSI can be calculated.

1.1 Autonomic Nervous System

The autonomic nervous system is part of the nervous system that controls the visceral functions of the body. Regulation of internal activities such as blood pressure, heart rate, gastrointestianl motility, and body temperature, among many others, is performed by the autonomic nervous system. Autonomic activity is controlled mainly by centers in the spinal cord, brain stem, and hypothalamus. Table 1.1 below summarizes the effects of the autonomic nervous system on selected organs [1].

Table 1.1 Autonomic effects on selected organs of the body. (From Guyton, A. C. *Textbook of Medical Physiology*)

Organ	Effect of SMP Stimulation	Effect of PSMP Stimulation
Heart Muscle	Increased Rate	Slowed Rate
Heart Muscle	Increased Force of Contraction	Decreased Force of Contraction

The autonomic nervous system is divided into two anatomical and functional units with opposite properties. The sympathetic nervous system is generally responsible for creating an increased level of activity in an organism. Anatomically, sympathetic nerves are composed of two neurons: a preganglionic neuron and a postganglionic neuron. These nerves pass from the spinal cord through the white ramus into one of the sympathetic ganglia before reaching their destination (Figure 1.1). Most postganglionic sympathetic nerve endings secrete norepinepherine, a neurotransmitter that activates excitatory receptors, but in some cases can inhibit certain organs. The sympathetic nervous system is also responsible for the alarm or fight-or flight response [1].

The parasympathetic nervous system by contrast, generally lowers the activity of an organism, and is associated with a relaxed state. Anatomically, parasympathetic fibers leave the brain through cranial nerves III, V, VII, IX, and X, and the second and third sacral spinal nerves (Figure 1.2). Cranial nerve X is also called the vagus nerve, and since the vagus innervates much of the thorax and abdomen, especially the heart, for the parasympathetic nervous system, parasympathetic activity is often called vagal activity. All parasympathetic nerve endings secrete acetylcholine. Although acetycloline generally has an excitatory effect, it is also known to have inhibitory effect as well, such as the slowing of the heart by the vagas nerve [2].

Both the sympathetic and parasympathetic nervous systems are continually active. These basal rates of activity are known as sympathetic and parasympathetic

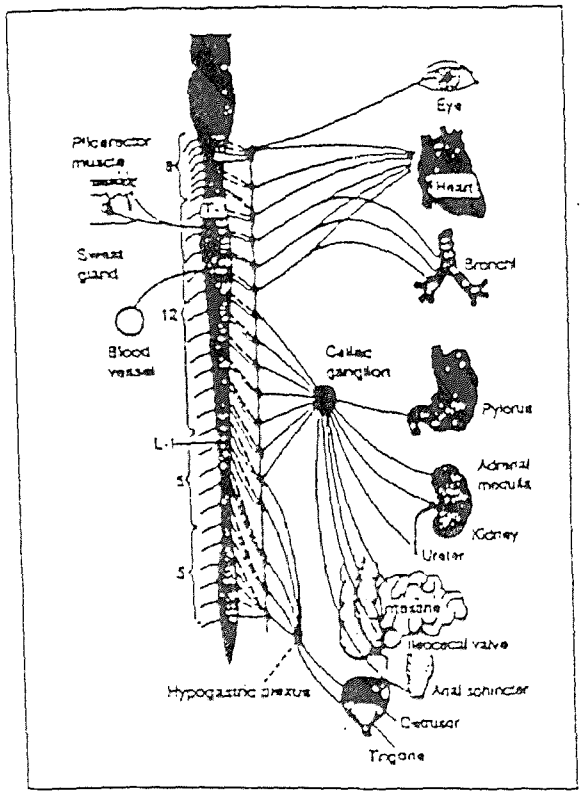

Figure 1.1: The sympathetic nervous System (from Guyton, A. C., *Textbook Of Medical Physiology)*

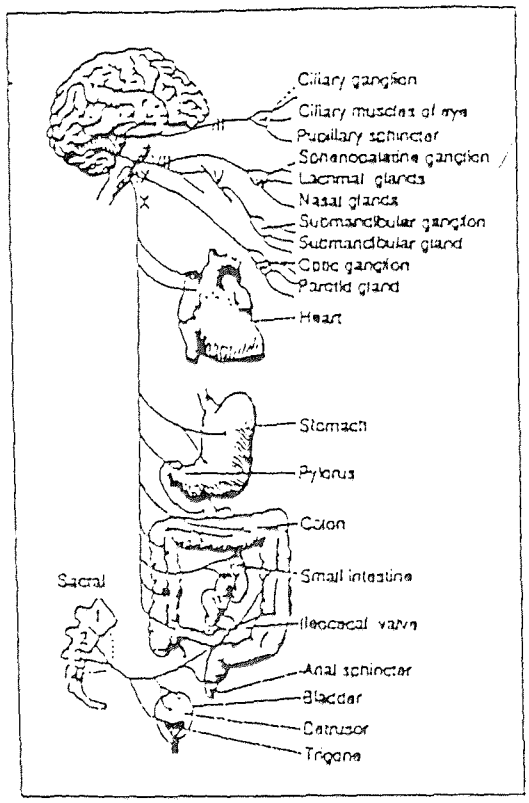

Figure 1.2: The parasympathetic nervous System (from Guyton, A. C., *Textbook Of Medical Physiology)*

tone. The advantage of tone is that it allows a single nervous system to increase or decrease activity in an organ. For instance, normal sympathetic tone keeps the systemic arterioles constricted to approximately half their maximum diameter. By changing the degree of sympathetic tone, the diameter of the arterioles can be increased or decreased. Without tone, the sympathetic nervous system can only cause vasoconstriction, never vasodilation [1].

1.2 Heart Rate and Blood Pressure Variability as a Measure of Autonomic Function

The autonomic nervous system plays the greatest role in the regulation of beat to beat variations in heart rate and changes in the blood pressure. Sympathetic nerve fibers terminate at the sinus node pacemaker, the heart musculature and vasculature. Parasympathetic fibers terminate on the sinoatrial (SA) and atrioventricular (AV) nodes as well as within the cardiac musculature and vasculature [3]. Thus, the autonomic nervous system is made up of two functional divisions: the sympathetic (SMP) division and the parasympathetic (PSMP) division. These two divisions are anatomically, physiologically, and functionally distinct [3]. In general, the PSMP division enhances activities that gain and conserve energy, such as slowing the heart. The SMP division increases energy expenditures and prepares an individual for action by accelerating the heart. When SMP and PSMP nerves innervate the same organ, they usually have antagonistic effects. At rest there is considerably more parasympathetic activity to the heart than sympathetic [4].

The autonomic nervous system characteristically functions as a feedback control system. Although a central command controls overall autonomic behavior, several reflexes provide quick feedback to respond effectively to specific demands on the system. For example, high in the neck, each of two major vessels supplying the head (the common carotid arteries) divides into two smaller arteries. At this division, the wall of the artery is thinner than usual and contains a large number of branching, vinelike nerve endings. This portion is called the carotid sinus. Its

nerve endings are highly sensitive to stretch or distortion. Since the degree of wall stretching is directly related to the pressure within the artery, the carotid sinus serves as a pressure or stretch receptor, called the "baroreceptor" (figure 1.3 and figure 1.4). An area functionally similar to the carotid sinuses is found in the arch of the aorta and is termed the "aortic arch baroreceptor". The carotid sinuses and aortic arch constitute the "arterial baroreceptors". Afferent neurons from them travel to the brain and eventually provide input to the neurons of the cardiovascular control centers.

The large systemic veins, the pulmonary vessels, and the walls of the heart also contain baroreceptors, most of which function in a manner analogous to the arterial baroreceptors. The primary control center for the baroreceptor reflexes is a diffuse network of the highly interconnected neurons in the brainstem medulla called the "medullary cardiovascular center". The neurons in this center receive input from the various baroreceptors. This input determines the outflow from the center along axons that terminate upon the cell bodies and dendrites of the PSMP neurons to the heart and the SMP neurons to the heart, arterioles, and veins. When the arterial baroreceptor increases its rate of discharge, the result is a decrease in sympathetic outflow to the heart, arterioles, and veins, and an increase in parasympathetic outflow to the heart. A decrease in baroreceptor firing rate results in the opposite pattern (figure 1.5). The baroreceptor reflexes are short-term regulators of arterial pressure but adapt to a maintained change in pressure. Thus, in patients who have chronically elevated blood pressure, the baroreceptor continues to oppose minute-to-minute changes in blood pressure, but at a higher level [3].

The main focus of this thesis is to properly calculate Baroreceptor Sensitivity Index (BRSI). Two mathematical parameters, correlation coefficient and coherence, determine the validity of the calculations.

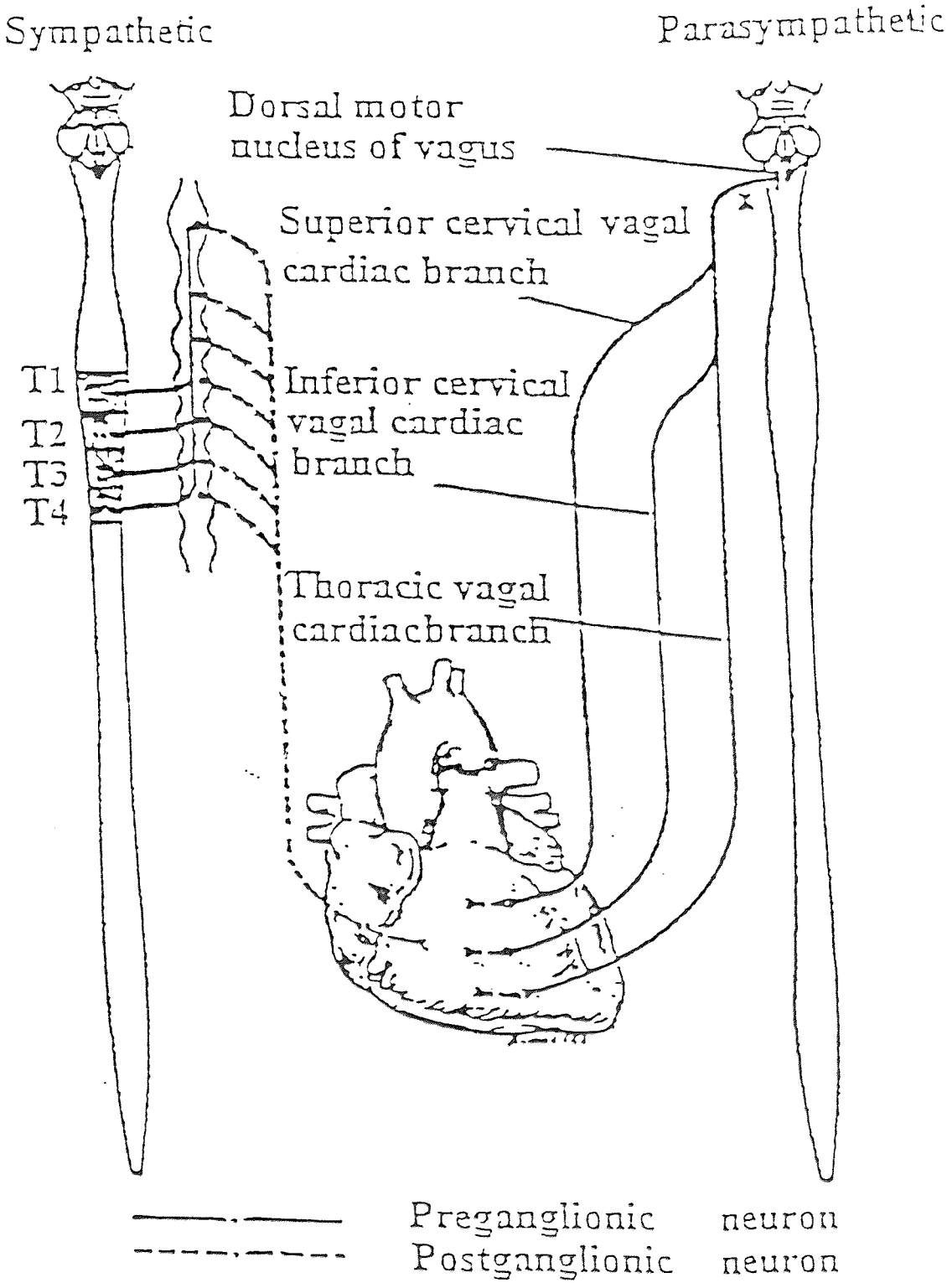

Figure 1.3: Diagram depicting the nerve supply to the heart from both divisions of

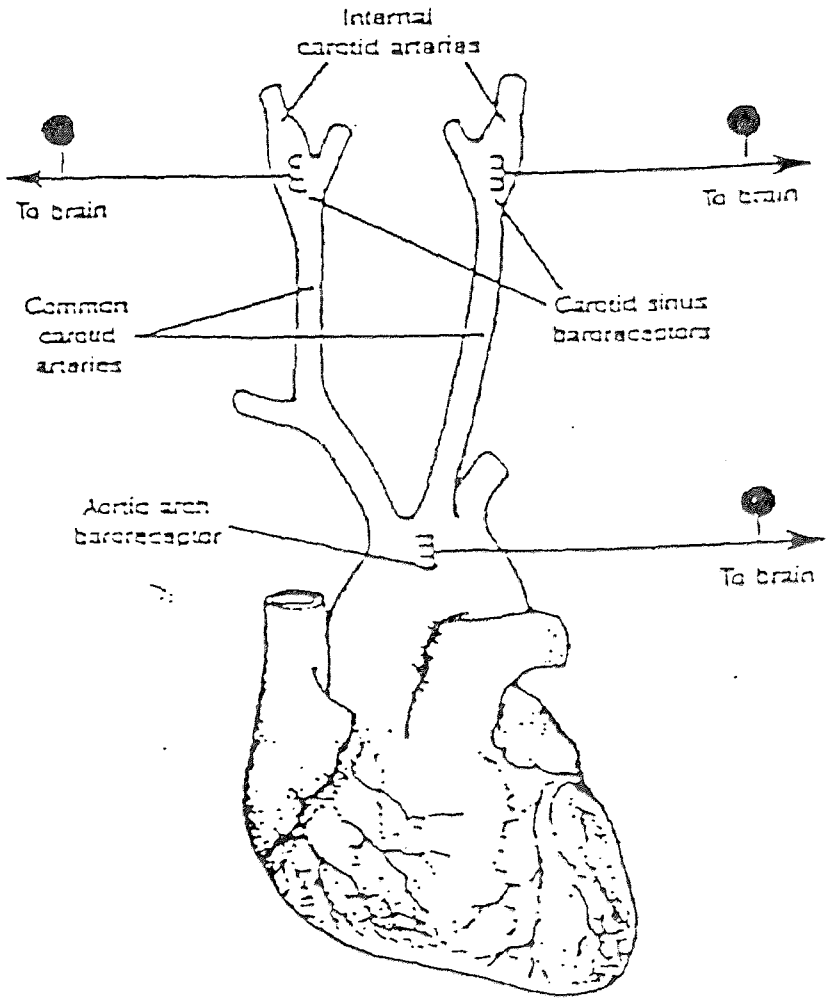

Figure 1.4: Location of arterial baroreceptor

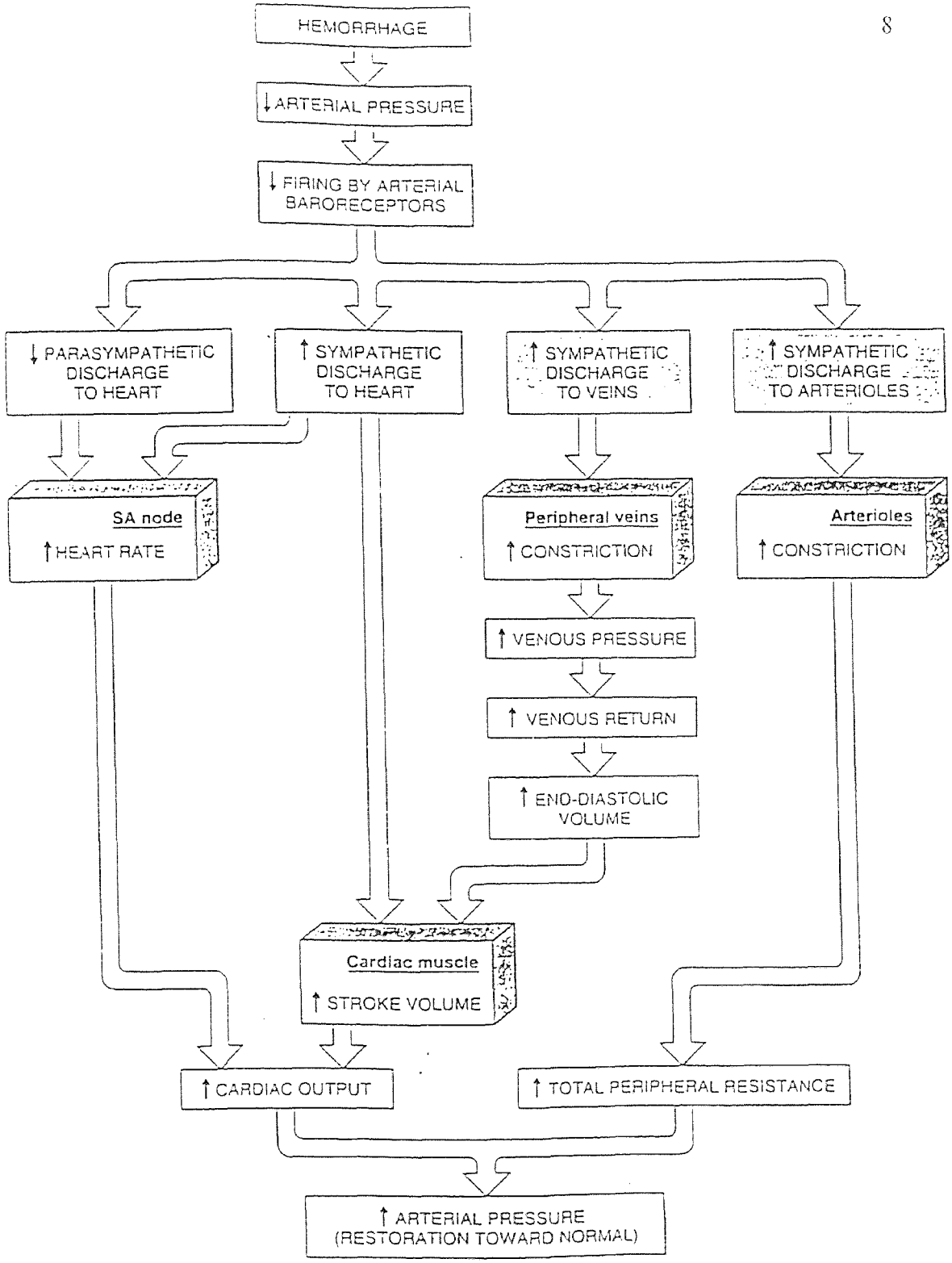

Figure 1.5: Arterial baroreceptor reflex compensation for hemorage. Hemorage causes a decrease in arterial pressure. To restore arterial pressure, discharge rate of the carotid sinus and aortic arch baroreceptors decreases. This induces increased hear rate, increased myocardial contractility, increased arteriolar and venous constriction. The net result is an increased cardiac output, increased total peripheral resistance (arteriolar constriction), and a return of blood pressure toward normal. (From Vander, A. et al. Human Physiology, 1994)

1.3 Heart Rate Variability

Traditionally, the effect of the autonomic nervous system on heart rate has been investigated through two approaches. First, the average heart rate was measured under normal conditions as a reference, and then the average heart rate was measured under different drug treatments – attropine to block the parasympathetic nervous system and propranolol to block the sympathetic nervous system [2]. Recently, a second approach has used power spectrum analysis to decompose a biological rhythm such as heart rate variability, which consists of a time series of successive events, into a number of sinusoidal waves of different amplitudes and frequencies under different drug treatments [2]. Chapter two describes the procedure to calculate the heart rate variability using programs developed by Shin, Reisman, and colleagues [12].

The power spectrum of either systolic blood pressure or heart rate variability yields three major bands (Figure 1.6). The very low frequency variations (<0.07Hz) are related to changes in vasomotor tone, which controls body temperature and adaptation to the task situation. Low frequency (0.07Hz-0.14Hz) variations are due to the blood pressure control system mechanism. High frequency (0.14Hz-0.40Hz) variations are attributed to respiratory activity [9].

Calculating BRSI in the time domain does not give any information about the source of the fluctuation [3]. In this respect, spectral analysis is more informative to show the relation in variations in the heart rate and systolic blood pressure, because spectral analysis can show the variations in any frequency band [3]. Thus, under different noninvasive experimental protocols, spectral analysis in the low frequency band can show the influence of the blood pressure control mechanism on the blood pressure and heart rate variability spectrum.

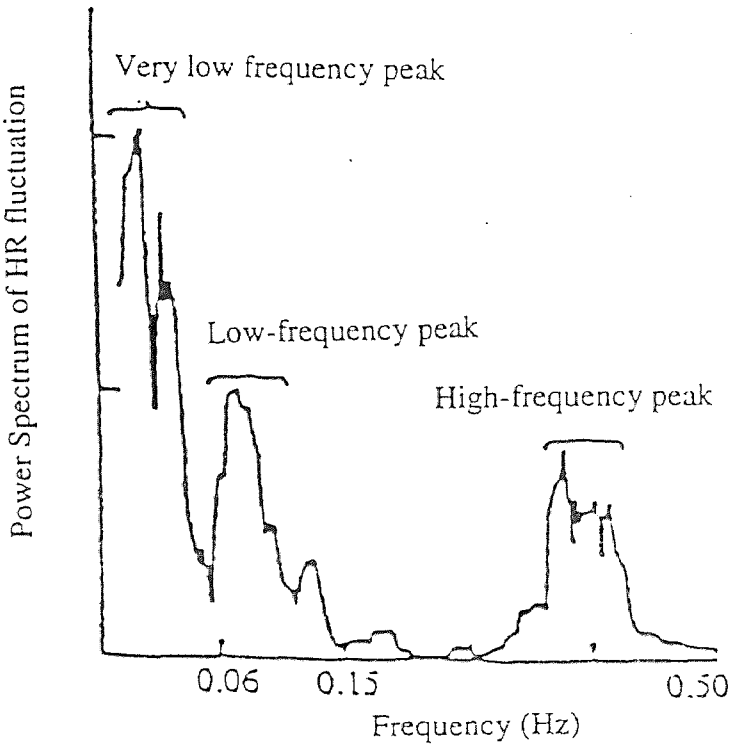

Figure 1.6: Fourier Transform of heart rate fluctuations, indicating very low frequency, Low frequency, and high frequency peaks. (From Akselrod, S. et al. Science, 1981)

1.4 Correlation Coefficient

The correlation coefficient between the corresponding points for two signals X and Y is defined as [14]:

$$r = \frac{SSxy}{\sqrt{SSxx\ SSyy}} \tag{1.1}$$

where, r: Correlation Coefficient

$$SSxx = (\sum Xi)^2 - \frac{(\sum Xi)^2}{n} \tag{1.2}$$

$$SSyy = (\sum Yi)^2 - \frac{(\sum Yi)^2}{n} \tag{1.3}$$

$$SSxy = \sum Xi\ Yi - \frac{(\sum Xi)(\sum Yi)}{n} \tag{1.4}$$

where, i = 1 to n

n = sample size

The correlation coefficient r is scale less and can assume a value between -1 and +1, regardless of the units of X and Y. A value of r near or equal to zero implies little or no linear relationship between X and Y. In contrast, the closer r becomes to 1 or -1, the stronger the linear relationship between X and Y. If r = 1 or r = -1, all the sampling points fall exactly on a straight line. Positive values of r imply a positive linear relationship between X and Y; i.e., X increases as Y increases. Negative values of r imply a negative linear relationship between X and Y, i.e., X decreases as Y increases.

1.5 Coherence

Coherence is a measurement of similarity between two signals [5]. Coherence is calculated in the frequency domain. For two signals X(t) and Y(t) the coherence value can vary between zero and one. Coherence can be viewed as a correlation coefficient in the frequency domain, analogous to the autocorrelation function in the time domain [8]. Coherence is a measure of the linear dependence between a pair of signals, normalized to values between zero and one. The coherence is unity if two signals have the exact same frequency content, in other words if one signal is completely linearly dependent on the other. However for most pairs of real signals, the coherence is less than unity [7]. The coherence function is defined as the ratio between the cross spectral density of X(t) and Y(t) and the product of the individual power spectral density. The coherence function is complex and defined as :

$$Cxy(\omega) = \frac{Gxy(\omega)}{\sqrt{Gxx(\omega)^* \, Gyy(\omega)}} \qquad (1.5)$$

where,

Cxy(ω) : Coherence between x(t) and y(t)

Gxy(ω) : Cross power spectrum at frequency w between x(t) and y(t)

Gxx(ω) : Power spectra (auto spectra) of x(t)

Gyy(ω) : Power spectra (auto spectra) of y(t)

MSC : Magnitude Squared Coherence

$$MSC = \frac{Gxy(\omega)\, Gxy(\omega)^*}{Gxx(\omega)^* Gyy(\omega)} \qquad (1.6)$$

To calculate coherence, data recordings X(t) and Y(t) are first broken up into N segments of equal length. The auto and cross-spectra are estimated on the basis of averages drawn from the individual spectra of the segments [5]. Typically, the individual spectra are obtained by means of the Fast Fourier Transform (FFT). If Xn(ω) and Yn(ω) are the complex FFTs of the nth segment, then

$$Gxx(\omega) = (1/N) \sum_{n=1}^{N} \left| Xn(\omega) \right|^2 \tag{1.7}$$

$$Gyy(\omega) = (1/N) \sum_{n=1}^{N} \left| Yn(\omega) \right|^2 \tag{1.8}$$

$$Gxy(\omega) = (1/N) \sum_{n=1}^{N} \left(Xn(\omega)\, Yn^*(\omega) \right) \tag{1.9}$$

The segments may overlap and the choice of segments and number of overlaps depends on the statistical constraints, which characterizes the data and the required analysis. To attain good spectral resolution in an FFT operation requires fairly long data lengths as the spacing between spectral lines is inversely proportional to the (assumed) time domain repetition period of the data [5]. There is a compromise required in the choice of segment length; it must be long enough to provide adequate frequency resolution but short enough to allow sufficient segments in the average to control bias and variance [5]. In addition each segment must be extracted using a time domain window to control sidelobes in the frequency domain function and thereby limit the bias which arises due to resulting leakage [5].

1.6 Baroreceptor Sensitivity Index

The baroreceptor sensitivity index (BRSI) is a marker of the baroreflexive control of blood pressure. BRSI is used to gauge the functioning levels of the different branches of the autonomic nervous system (ANS) [10]. BRSI is expressed as the slope of a regression coefficient line relating systolic blood pressure (SBP) and the cardiac cycle length during the phase IV of the Valsalva maneuver.

If X and Y are two signals with n data points, say (x1, y1), (x2, y2),.....,(xn, yn), then the equation for the regression line is given by [13]:

$$\hat{y} = \hat{\beta}_0 + \hat{\beta}_1 x \qquad (1.10)$$

where,

$$\hat{\beta}_0 = \frac{\sum y_i}{n} - \hat{\beta}_1 \frac{\sum y_i}{n}$$

$$\hat{\beta}_1 = \frac{SSxy}{SSxx}$$

n = Sample Size

Thus, BRSI can be calculated from the ratio of delta R-R to delta SBP (expressed as msec/mmHg). If the correlation coefficient between the systolic blood pressure peaks and the interpolated interbeat interval of ECG signal is low (< 0.80) then the BRSI value becomes unreliable. The IIBI and the systolic blood pressure signals will be discussed in the next chapter.

The Valsalva maneuver has been shown to be an accurate indicator of baroreceptor reflex sensitivity [9]. The original Valsalva maneuver was described in 1704. It was a technique used for expelling pus from the middle ear. Later in 1851, an "imperceptible pulse" was described by Weber. This pulse can be related to the tachycardiac response that occurred during phase II of the Valsalva maneuver. Today the Valsalva maneuver is clinically used for the assessment of various cardiovascular disorders [9]. The Valsalva maneuver is a simple, non-invasive method of testing BRS since it can elicit significant rapid changes in heart rate, blood pressure, and ECG [9].

The Valsalva maneuver is a simple, non-invasive method of testing baroreflex sensitivity, as it can elicit significant rapid changes in heart rate, blood pressure, and ECG [2]. To obtain ECG and blood pressure signals, diagnostic ECG adhesive silver/silver chloride surface electrodes and the Finapres cuff and transducer have to be attached to the subject. The Finapres measures arterial blood pressure in the finger using a method which is described in section 2.3. The subject will then blow into a sphygmomanometer and maintain an expiratory pressure of 40 mmHg for 15 seconds.

The Valsalva maneuver is divided into four phases (figure 1.7 and Table 1.2) [3]. Phase I, a transient increase in systemic blood pressure with the onset of straining, reflects increased intrathoracic pressure. Phase II, a gradual decrease in pulse pressure and stroke volume due to a decrease in venous return, is often referred to as the active phase of the Valsalva maneuver. During phase III (initial release of straining), the blood pressure transiently decreases further as a result of pooling of the blood in an expanded pulmonary vascular bed due to an abrupt decrease in intrathoracic pressure. This phase is rapidly followed by phase IV, characterized by an "overshoot" of the systemic pressure over baseline values. During phase IV, two periods could be distinguished: a first one in which increments in blood pressure were not followed by changes in cycle length; and a second, in which a progressive slowing of the heart rate followed the increase in pressure. During this second period, starting with a lengthened R-R interval and finishing with the beat with the highest systolic blood pressure, linear regressions can be obtained [10]. Each of these phases is accompanied by a specific reflex change in heart rate that was modulated by baroreceptor mechanisms. In figure 1.6, the vertical variation in the dark horizontal lines represent the interval between consecutive heart beats. This is called the interbeat interval (IBI) [3]. Reflex techycardia occurs during the hypotension of phase II displayed as a decrease in the horizontal dashes showing the decreased distance between heartbeats. Reflex bradycardia is associated with the over shoot (or hypertension) of phase IV. Increased horizontal lines in phase IV shows that the distance between the heart beats was increasing.

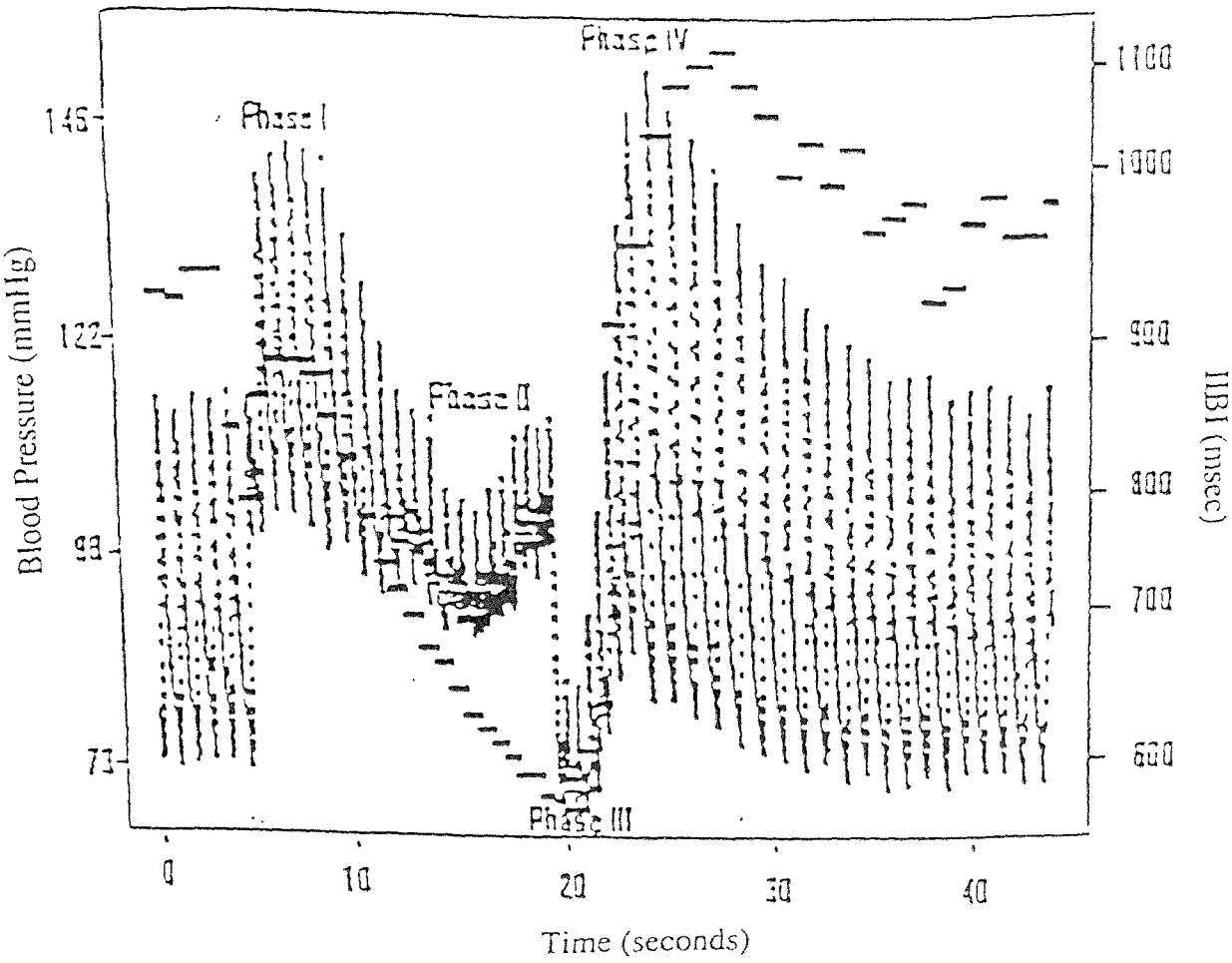

Figure 1.7: Normal response to the Valsalva maneuver.

Table 1.2
Four Phases of the Valsalva Maneuver

Phase	Action	Blood Pressure	Pulse Rate
I	Onset of Straining	Increases	Stable
II	Continued Straining	Decreases	Increases
III	Release of Straining	Decreases	Stable
IV	Continued Release	Increases	Decreases

1.7 Modulus

The modulus, or gain function specifies the ratio between changes in R-R interval time to the changes in Systolic Blood Pressure peaks (SBP) in a specified frequency band. In the low frequency range, the modulus value is controlled by the blood pressure control mechanism [9]. Therefore, the modulus value in the low frequency band is comparable to the regression coefficient (BRSI) in the time domain. The modulus value becomes unreliable if the coherence is low for any two signals [9].

To calculate the modulus, spectral analysis must be performed on the systolic blood pressure peaks and interpolated interbeat interval during the phase IV of the Valsalva maneuver. The modulus is then defined as the square root of the ratio between the Fourier Transform of the IIBI and the Fourier Transform of the SBP.

This technique can be used to calculate the modulus during rest, exercise, and mental activity of a subject. In the low frequency band (0.07Hz - 0.14Hz), the modulus value should be highest during the rest period and lowest during exercise, because during exercise and mental activity, increased sympathetic influence of the autonomic nervous system will cause the heart rate and systolic blood pressure to go up which in turn decreases the modulus value. Because increased heart rate will decrease IIBI and modulus is the ratio between IIBI and SBP. Time domain BRSI calculation should also show similar result but it will not be able to pin point the cause of this fluctuation.

1.8 Scope of Thesis

The aim of this thesis is to properly identify phase IV of the Valsalva maneuver and to calculate the BRSI in the time domain and in the frequency domain. The frequency domain calculation gives us the opportunity to see the modulus value in a specific frequency range (0.07Hz – 0.14Hz). This thesis will prove that the frequency domain calculation is more accurate and informative compared to the time domain analysis.

CHAPTER 2

METHODS

2.1 Data Analysis

The following chapter describes the technique to calculate or detect the interpolated interbeat interval (IIBI), systolic blood pressure peaks (BP), correlation coefficient, baroreceptor sensitivity index (BRSI), coherence, and modulus between IIBI and BP. For this thesis two sets of data were analyzed. One set had 30,000 sampling points and was 1.67 minute long, and the other set was 1 minute long and had 12,000 sampling points. The BP and the ECG data were collected from normal individuals at the Kessler Institute of Rehabilitation, New Jersey by Sanjay Fernando.

2.2 Acquisition of ECG Signal

The electrocardiogram (ECG) is primarily a tool for evaluating the electrical events within the heart (figure 2.1). The first peak, the P wave, corresponds to current flow during atrial depolarization. The second deflection, QRS complex, represents ventricular depolarization. The final deflection, the T wave, is the result of ventricular repolarization [4].

Figure 2.2 shows the standard bipolar limb leads for the ECG signal [2]. In lead I, the negative terminal of the electrocardiograph is connected to the right arm and the positive terminal to the left arm. In lead II, the negative terminal is connected to the right arm and the positive terminal to the left leg. In lead III, the negative terminal is connected to the left arm and the positive terminal to the left leg. The reference point (ground) is connected to the right leg.

Diagnostic ECG adhesive silver/silver chloride surface electrodes (Medtronic, Haverhill MA), connected by wire were placed on each subject to collect the ECG

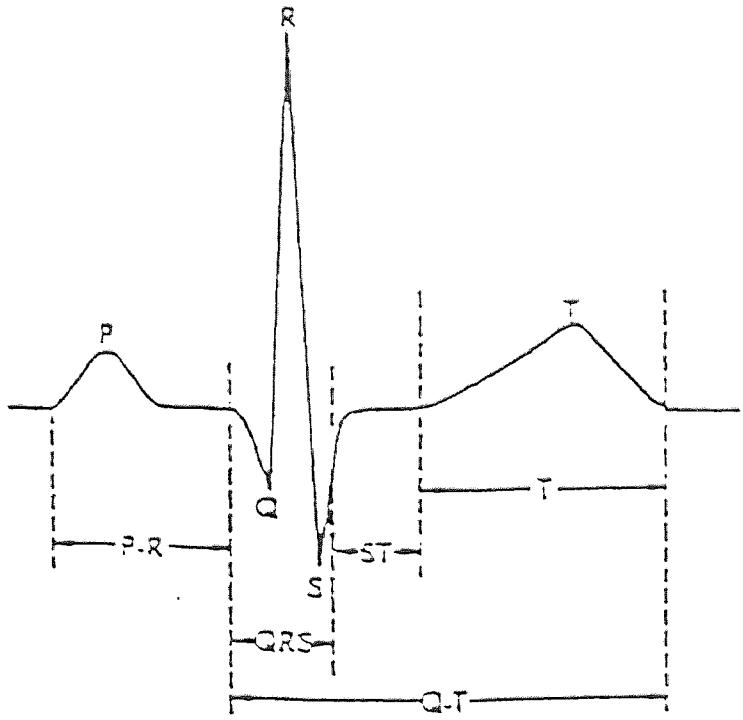

Figure 2.1: ECG Complex

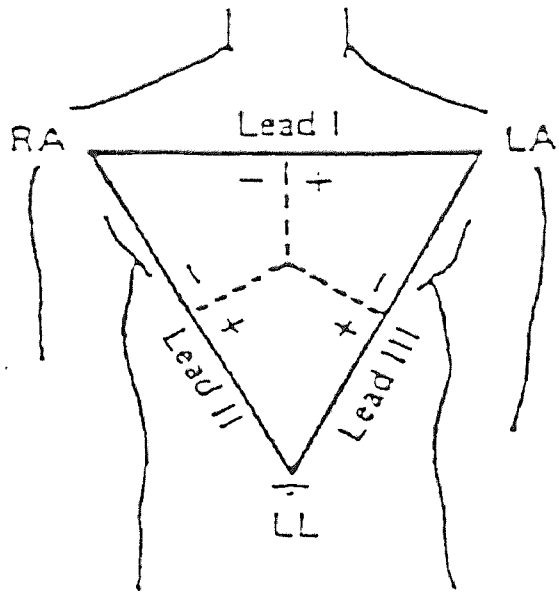

Figure 2.2: Standard bipolar limb leads of electrocardiogram

data. The positive electrode was placed on the torso rather than on the left lower extremity in order to minimize electromyographic noise produced by the leg muscles during exercise. A good, low-resistance electrical connection between the patient and the electrode was essential for clean, interference-free ECG Data. Failure to properly prepare the skin site caused base line shifts and noise from patient motion and respiration. The skin was prepared in the following manner: (1) the site was thoroughly rubbed with an alcohol swab. Then a dry piece of gauze pad was used to rub the site until it became slightly red. This removed the nonconductive outer layer of skin. (2) Application of the electrode to the prepared site was performed by running fingers around the foam pad, smoothing it from the center out. This process was repeated for all the sites.

ECG data collected on the data acquisition computer (Q4000 monitor, Quinton Instrument Co., Seatle, WA) by Streamer was saved in a packed binary format, using 2 bytes per sample. A program called Kunpack1 (a modified version of the unpack utility that Keithley MetraByte/ Asyst provided with the das-1601 A/D board) was utilized to unpack the data, and convert it to ASCII format [2]. The ECG and blood pressure data analysis was performed on an IBM compatible 486/66MHz computer. The data analysis software package used was Matlab v4.0 (The Math Works, Inc. Natick, MA). Ten custom Matlab algorithms were written to calculate IIBI, systolic blood pressure peak, BRSI, correlation coefficient, coherence, and modulus values. Refer to Appendix A and B for details on these calculation procedures and associated Matlab programs.

Figure 2.3a shows the ECG signal (QRS complex). A Q4000 monitor was used to acquire the ECG and detect QRS complexes. A rectangular sync pulse was created each time the QRS complex was detected (figure 2.3b). The interbeat interval (IBI) represents the distance between two consecutive QRS complexes. These IBI samples are not equidistant since they occur whenever a QRS complex is detected. In order to produce a signal with equal spaced samples, all of the interpolated values between a beat time T(m-1) and next beat T(m) was set equal to the time difference between T(m) and T(m-1). For example, in figure 2.3c if a beat occurs at time 2sec

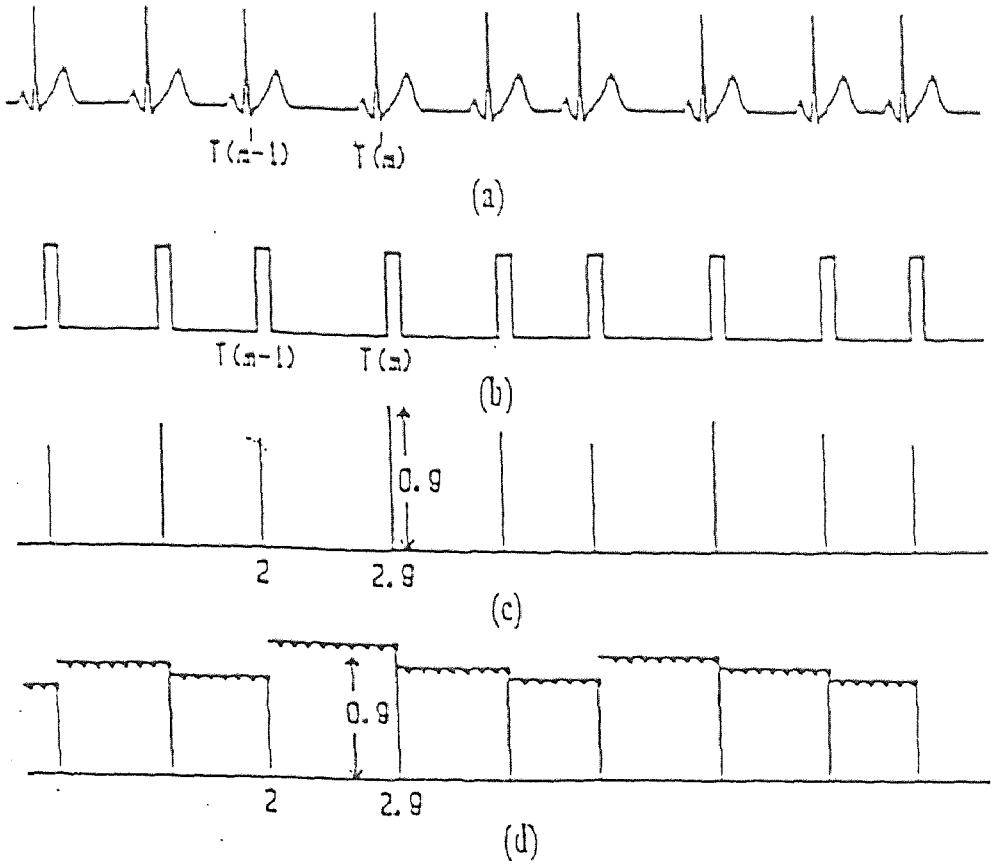

Figure 2.3: (a) ECG Signal, (b) pulse train, (c) IBI values, (d) Interpolated IBI values (From Shin, Shaw-Jyh et al., "Assessment of Autonomic Regulation of Heart Rate Variability by Method of Complex Demodulation," IEEE Transactions on Biomedical Engineering, vol 36. Feb 1989)

and the next beat occurs at time 2.9sec, the interpolated values between those two is 0.9sec (figure 2.3d) [2].

The interbeat interval signal (IBI) was calculated from the ECG sync pulse produced by the Quinton Q4000 Monitor and represented the distance between two successive R-R intervals. Any misdetection (either additional beats or missed beats) was removed by hand.

2.3 Acquisition of Blood Pressure

Real-time pulse blood pressure data was collected as an analog signal using a Finapres Model 2300 Blood Pressure Monitor (Ohmeda, Englewood CO). Analog data was fed into a DAS-16 analog to digital converter (Keithley MetraByte/Asyst, Natick MA). The converted digital data was then stored on an IBM-compatible 286 computer with 2MB RAM and 170MB hard drive, using Streamer v.3.25 data acquisition software (Keithley MetraByte/Asyst, Natwick MA).

The Finapres measures arterial blood pressure in the finger using a method originally devised by Dr. Jan Penaz [2]. The 2300 Finapres monitor provided continuous measurement of finger arterial blood pressure displaying the pressure waveform, digital values of systolic, diastolic, and mean pressure as well as pulse rate and a time annotated trend display. To provide the dynamic response required to accurately measure the arterial pressure waveform, the cuff's pressure servo valve and the pressure transducer are located in the subject interface module (figure 2.4).

First, the external pressure on the finger cuff was brought in equilibrium with the arterial pressure. At this stage, the transmural pressure was zero. With this technique the arterial walls would not change in size. The blood volume in these arteries would not change, resulting in no change in the photoplethysmogram. A finger cuff containing photoelectric components for measuring blood plethysmography and a bladder for applying pressure to the finger was wrapped around the subject's finger and connected to the interface module. The blood volume

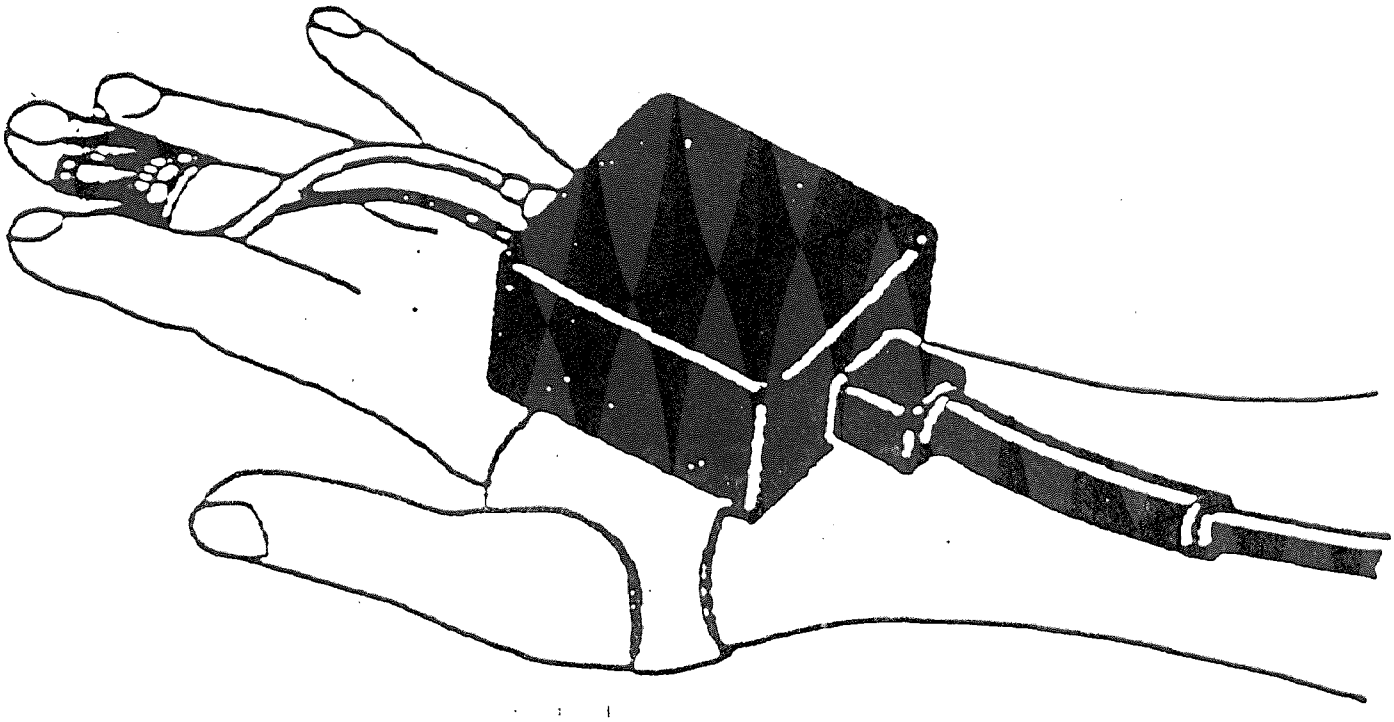

Figure 2.4: Cuff and the interface module mounted on the hand (From 2300 Finapres Blood Pressure Monitor Operation Manual, Ohmeda CO. 1991)

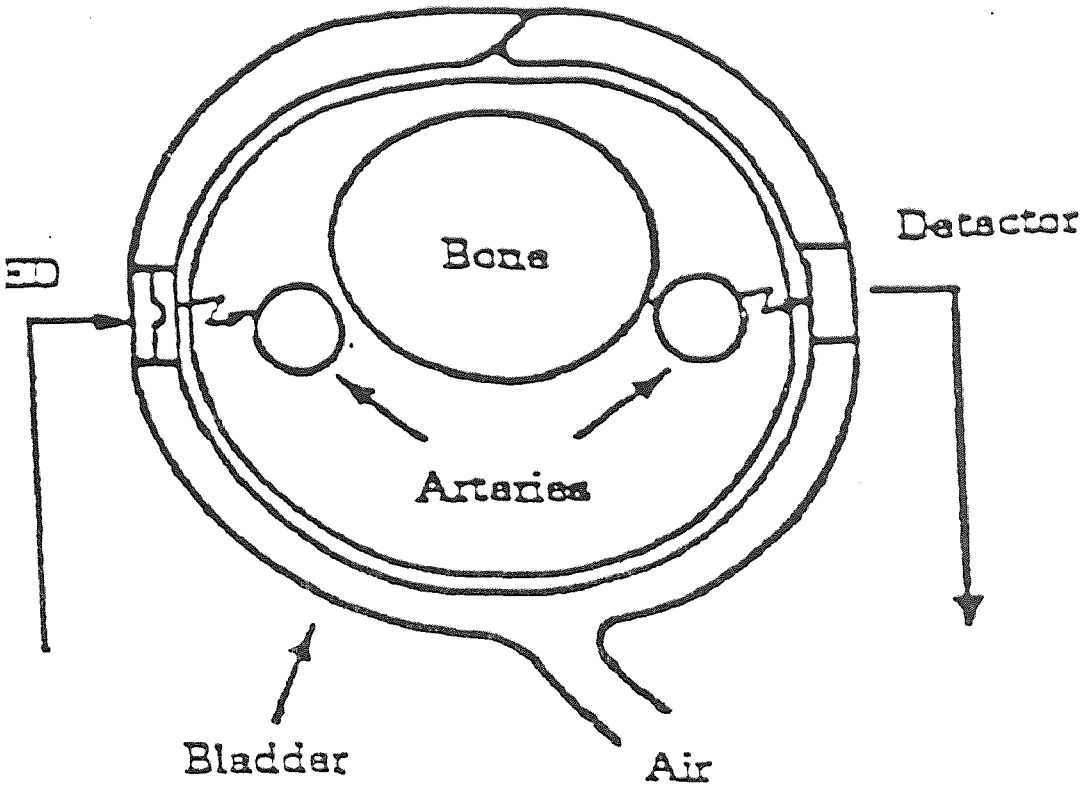

Figure 2.5: Finger cross-section view illustratingoptoelectronic components and bladder (From 2300 Finapres Blood Pressure Monitor Operation Manual. Ohmeda CO. 1991)

was measured by a small photoplethysmograph located in the finger cuff (figure 2.5). When the Penaz method used a constant pressure to "zero transmural pressure", the Finapres applied the reverse of this concept. The photoplethysmogram varied from the set point. A servo-valve caused a decrease or increase in the cuff pressure. This in return allowed for the photoplethysmogram to maintain a set point. The cuff pressure can be measured with can electric pressure transducer and the resulting signal displayed as arterial pressure. It was important to note that the manufacturer of the Finapres stated that the finger arterial pressure measurement may not always reflect or correlate with the central arterial pressure [2]. However, it has been reported that the blood pressure values obtained in this manner are comparable (+/- 4mmHg) to those obtained using intra-arterial cannulas [2].

To optimize the Finapres measurements the following steps were followed: (1) the hand should be as relaxed as possible. (2) For the best results, fingers with good circulation were used, since poor circulation would produce low blood pressure values and dampened (rounded) waveforms. (3) Fingers were positioned at the heart level.

After the data collection, systolic blood pressure peaks were detected. First, a customized Matlab program, getsap.m, detected the systolic blood pressure peaks. Any misdetection was corrected manually by using customized Matlab programs (undetect.m and mdetect.m). These programs also calculated the interpolated systolic blood pressure (PRSP) by measuring the distance between two consecutive SBP peaks.

Figure 2.6 is an example of the IIBI plot for a normal subject (m1902va). It has 1200 sampling points and four phases. Phase IV is between 600 and 720 sampling points shown in figure 2.7. Similar plots for the BP are shown in figure 2.8 and figure 2.9.

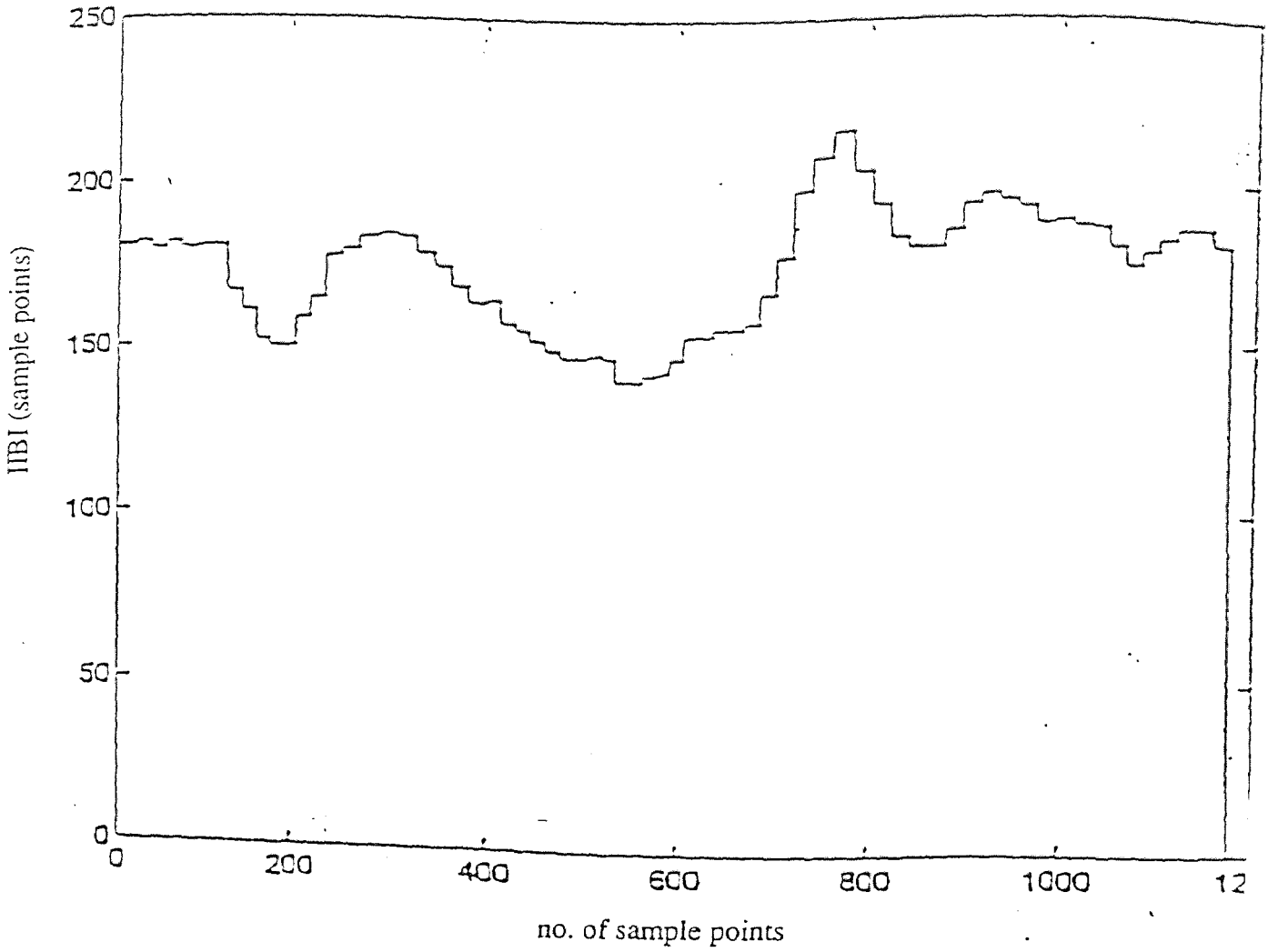

Figure 2.6: IIBI plot of a Valsalva file (m1902va). It has phase I, II, III, and IV. M1902va is a one minute long file or has 1200 sampling points. The vertical axis represents sample points which can be converted into seconds by dividing by 200 (the sampling rate).

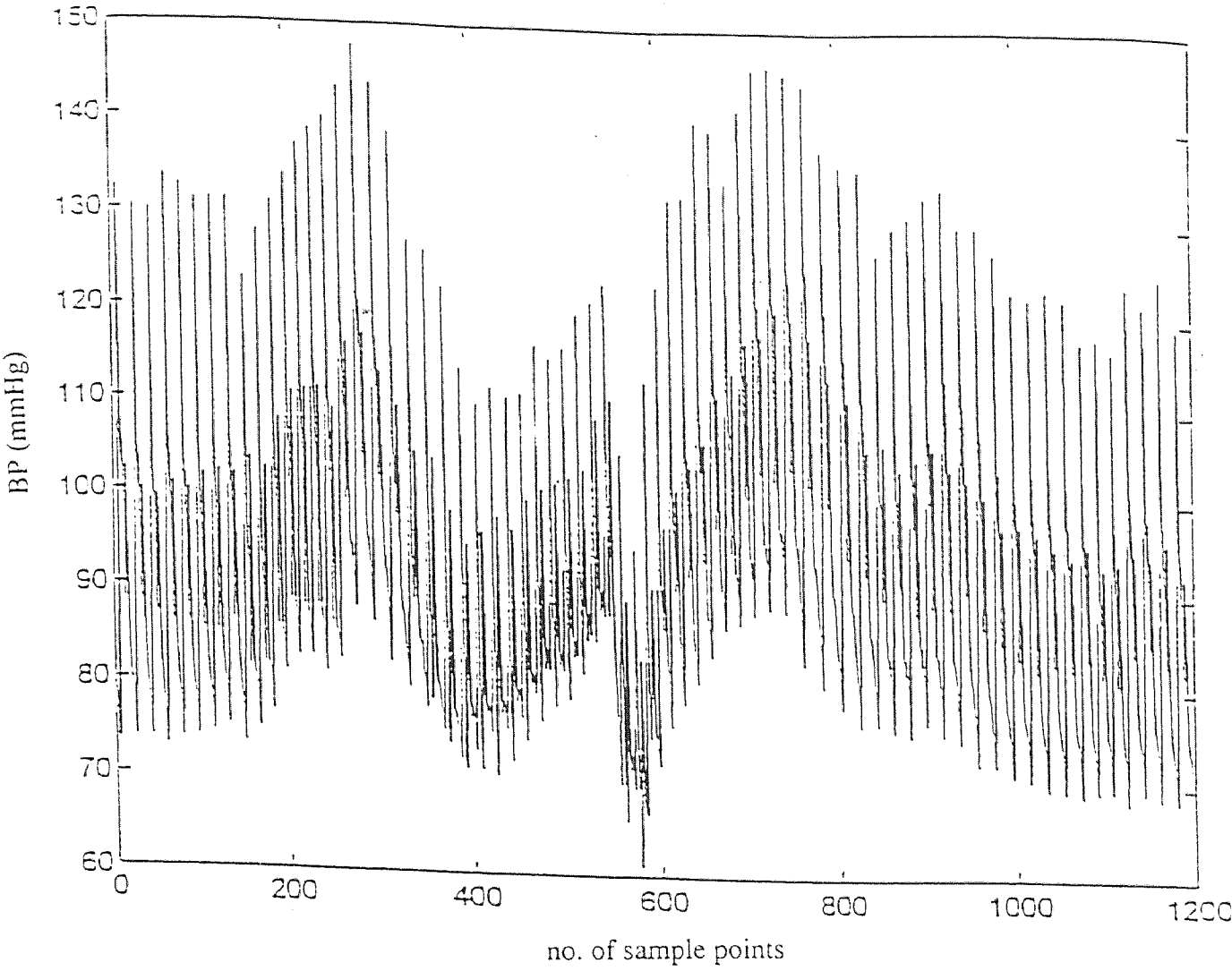

Figure 2.8: BP plot of a Valsalva file (m1902va). It has phase I, II, III, and IV. M1902va is a one minute long file or has 1200 sampling points.

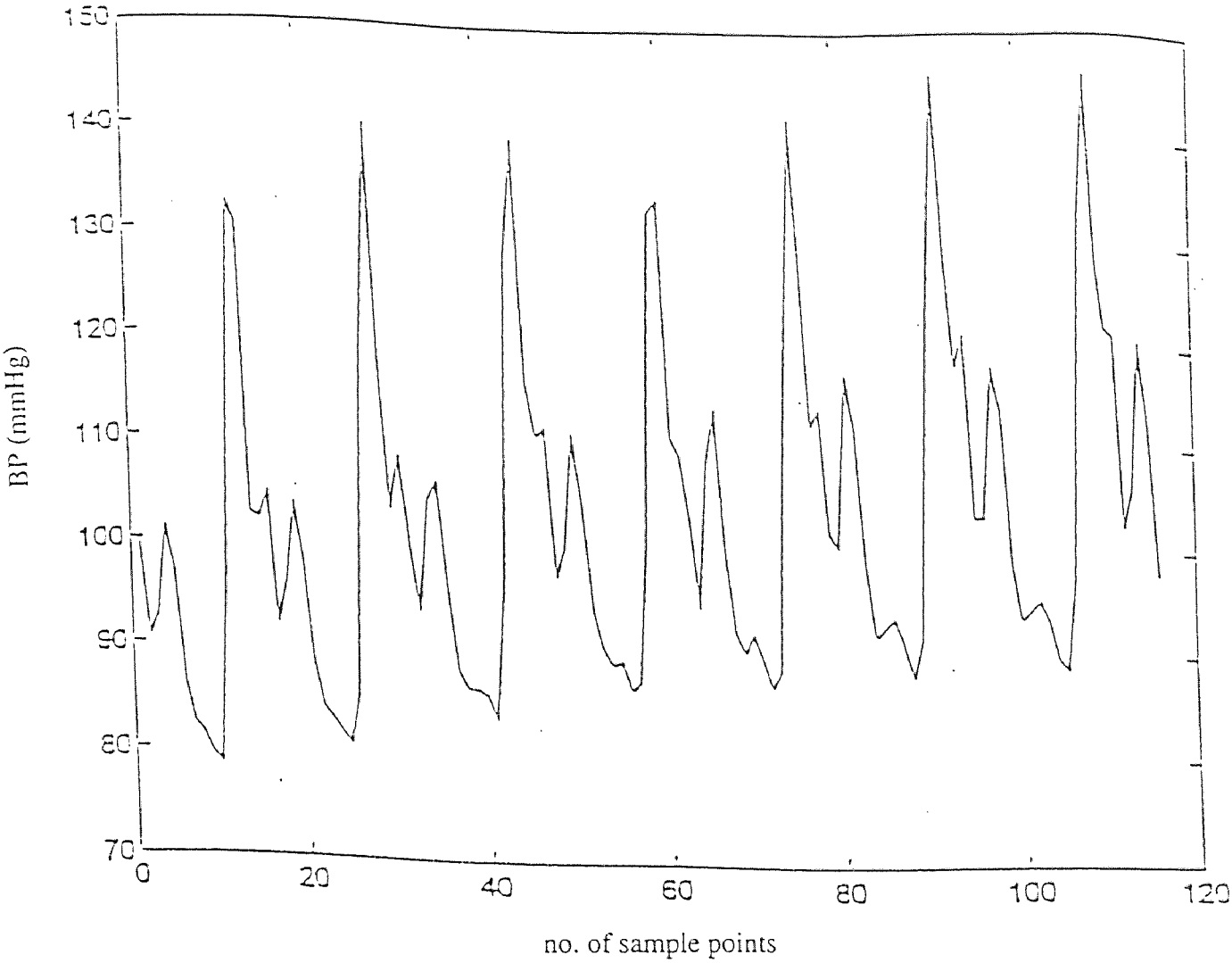

Figure 2.9: Phase IV plot of a Valsalva file (m1902va). This file is six second long or has 120 sampling points. For m1902va initial phase IV BP value is 131 mmHg and the final phase IV BP value is 145 mmHg

2.4 Calculating BRSI

To Calculate BRSI, ECG data was analyzed for the detection of QRS complexes followed by calculating the IIBI. The next step was to detect systolic blood pressure peaks followed by calculating interpolated blood pressure (PRSP). Systolic blood pressure and R-R intervals were calculated as increments to baseline measurements. Then the R-R intervals of the phase IV of Valsalva maneuver were plotted against the corresponding interpolated systolic blood pressure (PRSP). This plot had a minimum of five points to a maximum of seven points. Linear regression analysis of the plot calculated the BRSI and correlation coefficient. The slope of the line represented the baroreceptor sensitivity index (BRSI). A correlation coefficient of 0.80 was the threshold value for the acceptance of the BRSI result.

As an example, seven systolic BP peaks are plotted against the corresponding IIBI values in figure 2.10 to calculate the BRSI and correlation coefficient during the phase IV of the Valsalva maneuver. A customized Matlab program called rmsline.m estimated a straight line through those seven points. The slope of that line (BRSI) was 18.74. For this particular subject the correlation coefficient was 0.80.

2.5 Calculating Modulus

The modulus is the frequency domain equivalent of the BRSI during phase IV of the Valsalva maneuver. For the frequency domain calculation, previously calculated time domain BP and IIBI signals were used. An 8192 point FFT (Fast Fourier Transform) of BP and IIBI gave the corresponding power spectrum density. A customized Matlab program mod_prsp.m calculated the modulus by taking the squared root ratio of the IIBI and BP power spectra. In the low frequency band (0.07Hz – 0.14Hz), the modulus value was independent of the numbered points in the FFT. However, to maintain consistency, an 8192 point FFT was used to analyze all the files.

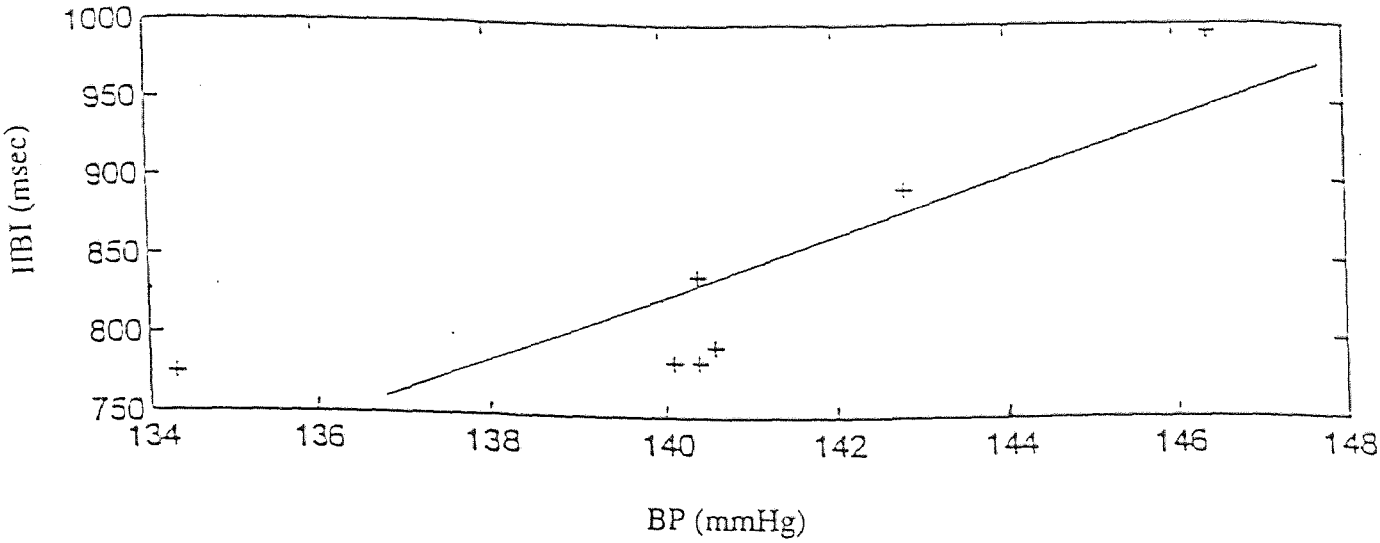

Figure 2.10: BRSI plot of a Valsalva file (m1902va). This plot shows eight Systolic Blood Pressure peaks and corresponding IIBI values during the Phase IV of the Valsalva maneuver. A straight line was estimated by Regression analysis for those eight points. For this file slope of the straight line (BRSI) was 18.74 and correlation coefficient 0.80.

Figure 2.11 is the modulus plot for m1902va. In the low frequency band (0.07Hz – 0.14Hz), the modulus value was 6.2 msec/mmHg.

2.6 Calculating Coherence

The coherence of a normal rest file is the measure in the frequency domain to either accept or reject the modulus value for the subject's phase IV Valsalva file [9]. In the low frequency band (0.07Hz – 0.14Hz), the threshold value of coherence was 0.8. Coherence > 0.8 in the low frequency band, meant that the modulus value is acceptable. A customized Matlab program called coherebp.m was used to calculate the coherence between BP and IIBI. These two signals were given as input arguments to the program.

To calculate the coherence, two input signals, BP and IIBI were first divided into short epochs of 256 samples. The cross spectrum of each epoch was computed using an ensemble of ten overlapping data segments. As a result, each epoch was divided into a number of 256 points sections, each of which overlapped by 10 points. Each section was windowed with a hanning window algorithm, an 8192 point FFT was taken, and then accumulated with a running sum of the previous sections. Welch first outlined this method of calculation in 1967. He states that if x(n), n=0,....., N-1 is a stationary second order stochastic random process, then the sequence can be divided into K sections of length L, that may overlap. To estimate the power spectrum, the sequence x(n) is multiplied by a window w(n), then the Fourier transforms (8192 point FFT) of the K sequences are calculated. From the Fourier transforms, K periodograms (magnitude squared function) are calculated, then averaged to produce the power spectrum [11]. Once the power and cross spectra are computed, the squared coherence spectrum for each epoch was calculated.

Figure 2.12 and figure 2.13 are the BP and IIBI plot for the same subject (m1902ba), during the rest period. In the low frequency band (0.07Hz – 0.14Hz), this subject had a high coherence value (0.9). Figure 2.14 is the coherence plot for m1902ba.

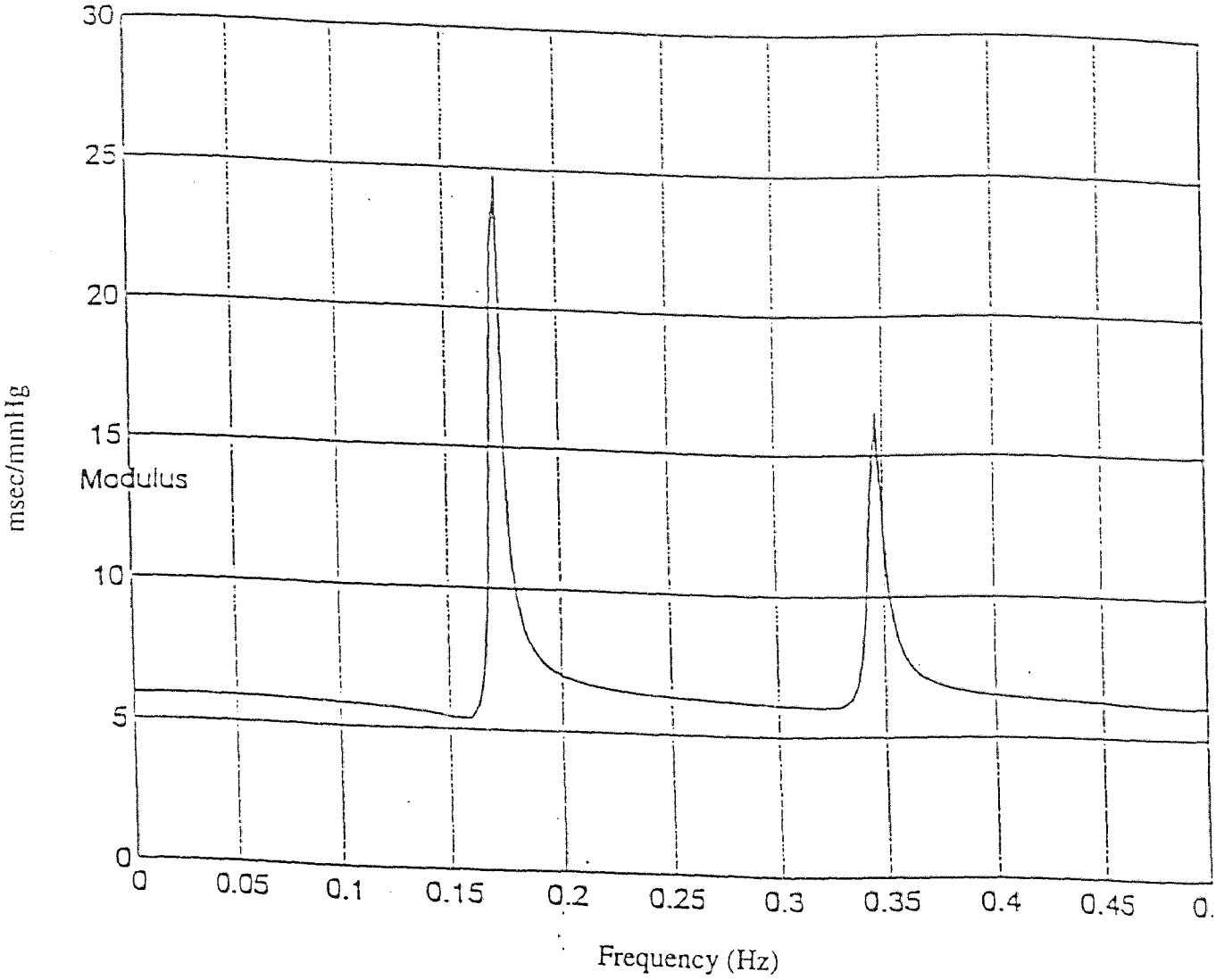

Figure 2.11: Modulus (msec/mmHg) plot of a Valsalva file (m1902va). In the low frequency range (0.07-0.14)Hz, modulus for m1902va is 6.1 msec/mmHg.

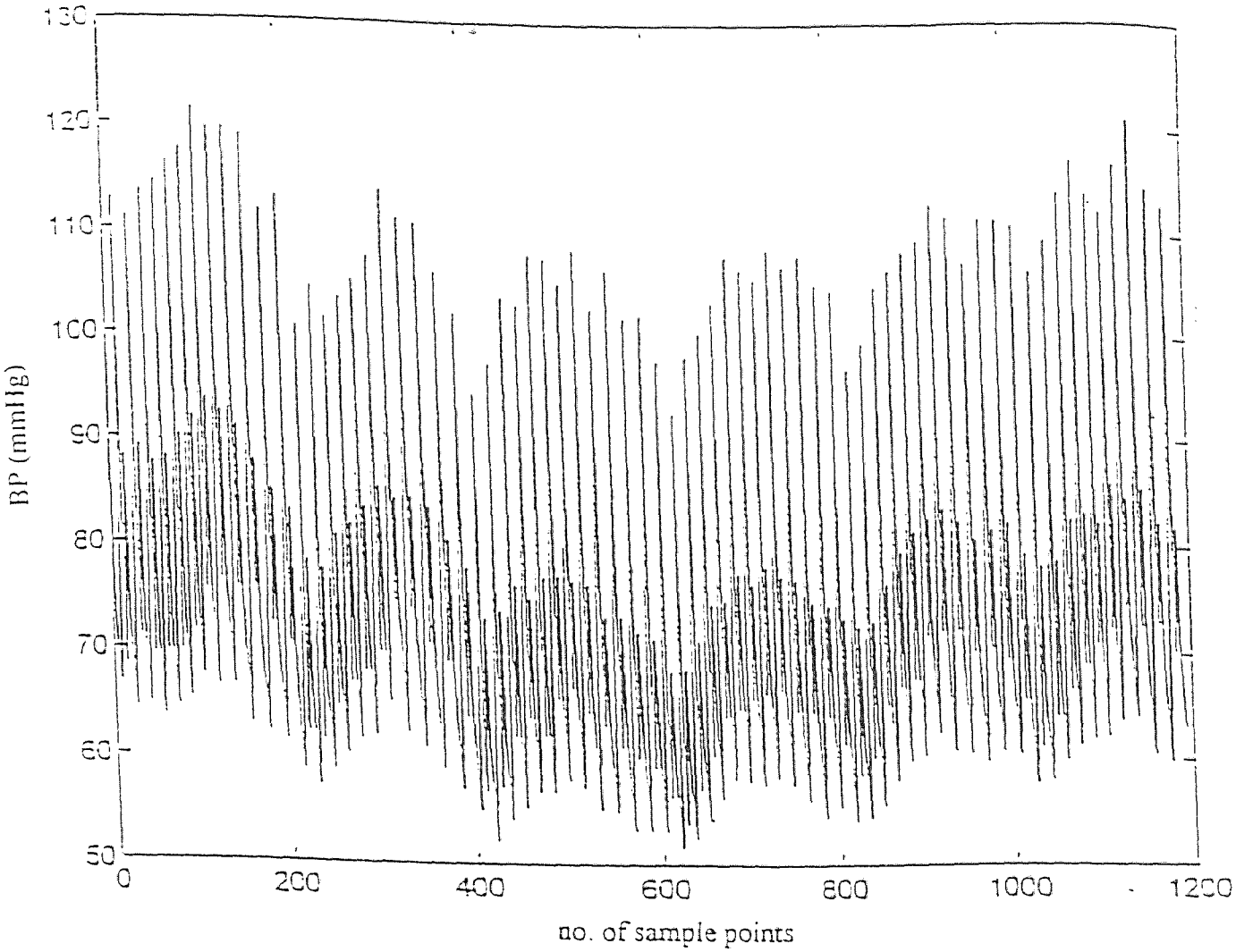

Figure 2.12: BP plot of a normal subject (m1902ba) during the rest period. This file is one minute long or has 1200 sampling points.

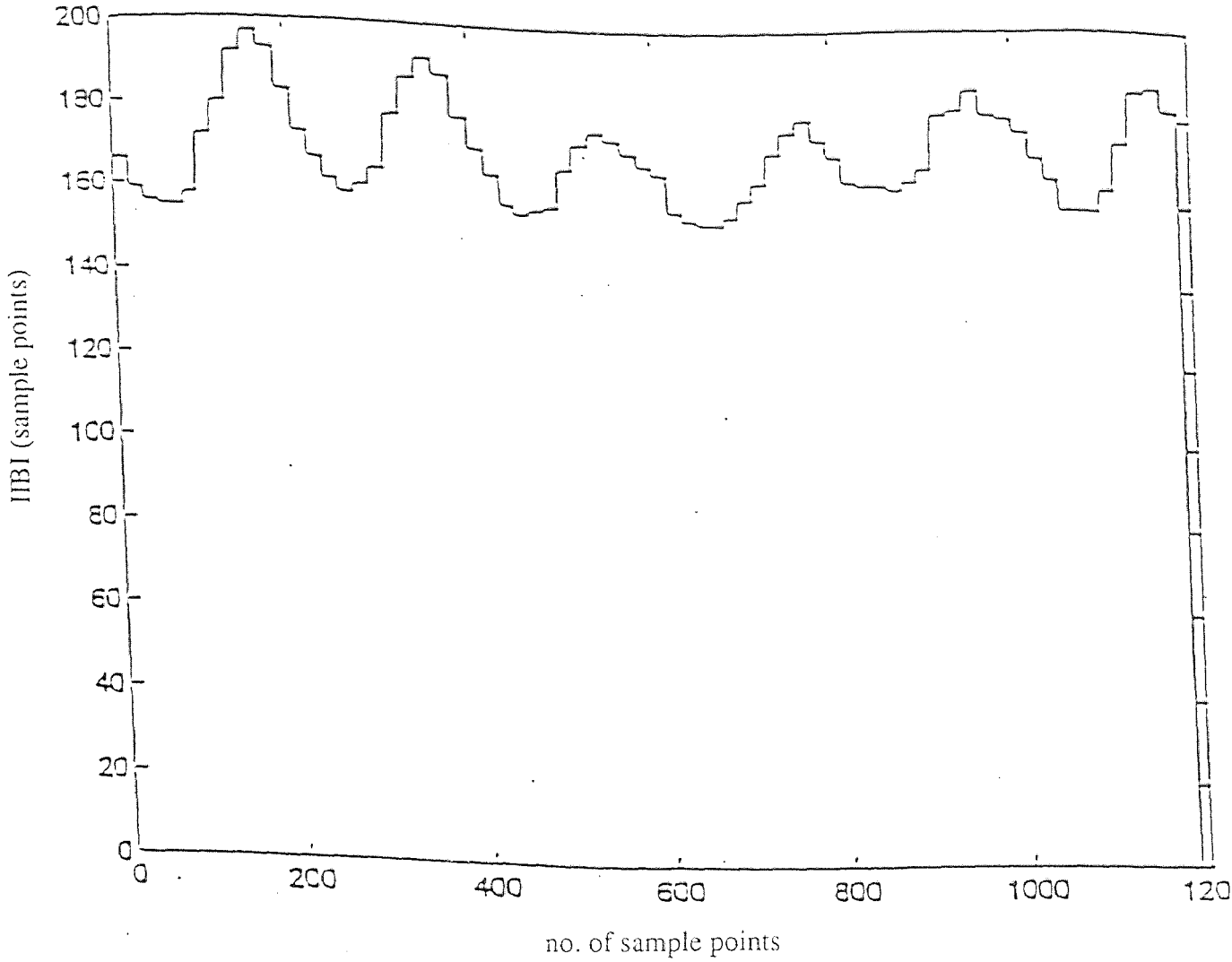

Figure 2.13: IIBI plot of a normal subject (m1902ba) during the rest period. This file is one minute long or has 1200 sampling points. The vertical axis represents sample points which can be converted into seconds by dividing by 200 (the sampling rate).

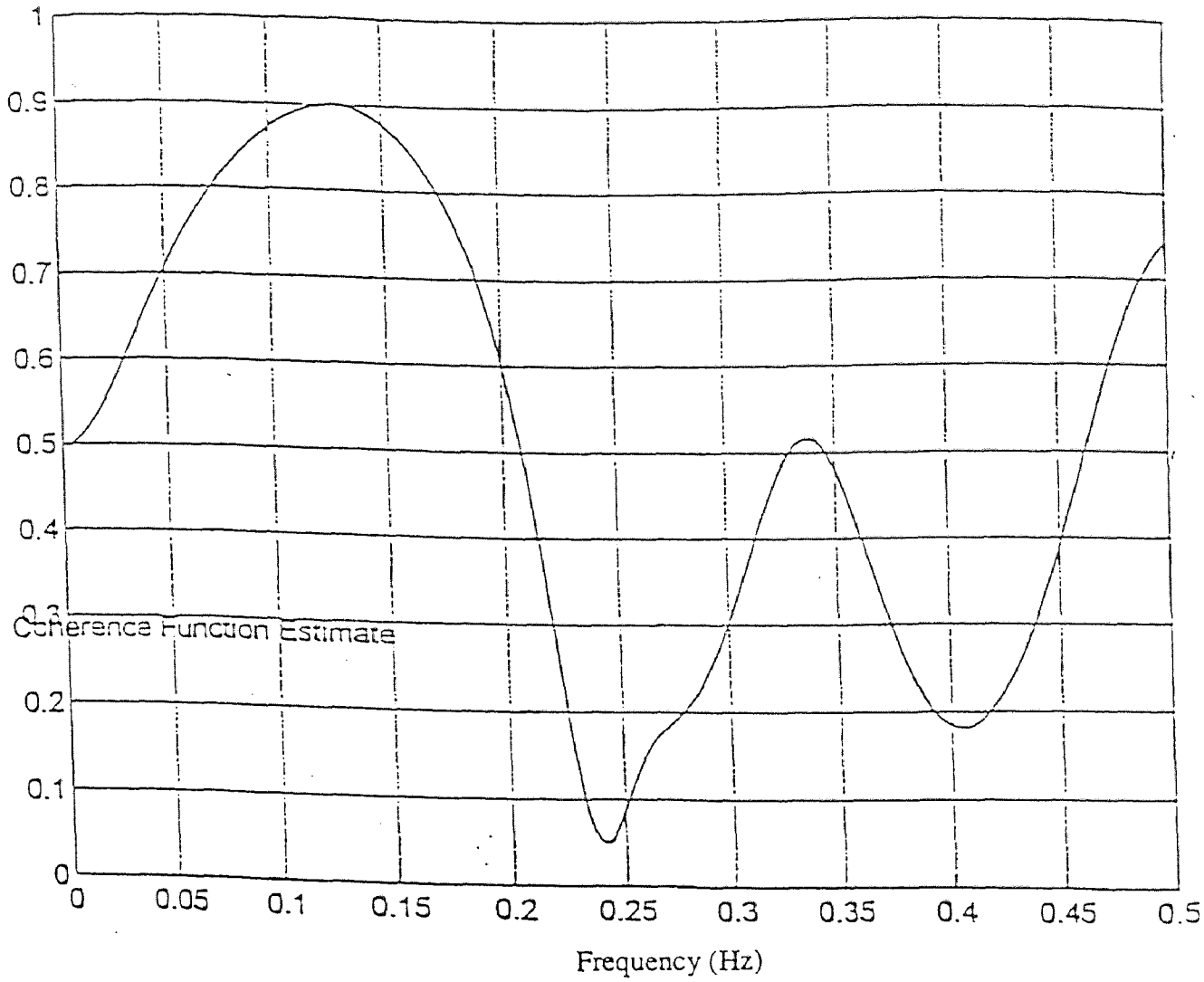

Figure 2.14: Coherence plot of m1902ba. In the low frequency range (0.07-0.14)Hz, this file had a Coherence value of 0.9.

For the calculation of modulus and coherence, the sampling frequency was reduced from 200 to 20 because the IIBI and BP signals were decimated by a factor of ten. The IIBI, BP, and PRSP signals were decimated to get a smaller file for faster calculation. Window size, number of overlaps, and number of point FFT did not affect the coherence or modulus value for any of the files.

CHAPTER 3

3.1 RESULTS AND DISCUSSION

The following chapter details the progression of research in measuring the Baroreceptor Sensitivity Index (BRSI) in both the time and frequency domains. Two different sets of files were used, one set had Valsalva and rest data and other set had only Valsalva data. The first set of data had files of two minutes in length and the second set had files of one minute length. Subjects for these data were normal individuals.

Figure 3.1 is a normal response to the Valsalva maneuver for a normal healthy subject. During phase IV of the Valsalva maneuver, the subject began to increase systolic blood pressure rapidly from a low of 100 mmHg to a high of 150mmHg. This range can vary for different subjects. In general, during phase IV, a low BP can start at 80mmHg and will stop at a high of 155 mmHg. For the normal subjects, as the heart rate began to decrease during continued release of air, the IIBIs increased rapidly. Table 3.1 and Table 3.2 present BRSI, correlation coefficient, coherence, and modulus values for the normal subjects.

For the first set of data (files starting with the letter 'm') the average BRSI was 14.84 msec/mmHg, with a high of 20.7 msec/mmHg and a low of 8.02 msec/mmHg. In the low frequency range (0.07Hz-0.14Hz), these sets of files had an average modulus value of 6.2 msec/mmHg, with a high of 6.25 msec/mmHg and a low of 6.1 msec/mmHg.

For the second set of data (files starting with the letter 'r' and 'q') the average BRSI was 7.5 msec/mmHg, with a high of 11.88 msec/mmHg and a low of 6.71 msec/mmHg. In the low frequency range (0.07Hz-0.14Hz), these sets of files had an average modulus value of 7.48 msec/mmHg, with a high of 12.0 msec/mmHg and a low of 3.8 msec/mmHg.

Files starting with the letter 'm' did not have a clear phase IV (Figure 3.1). It was not easy to correctly point to phase IV for one file and be consistent for all other

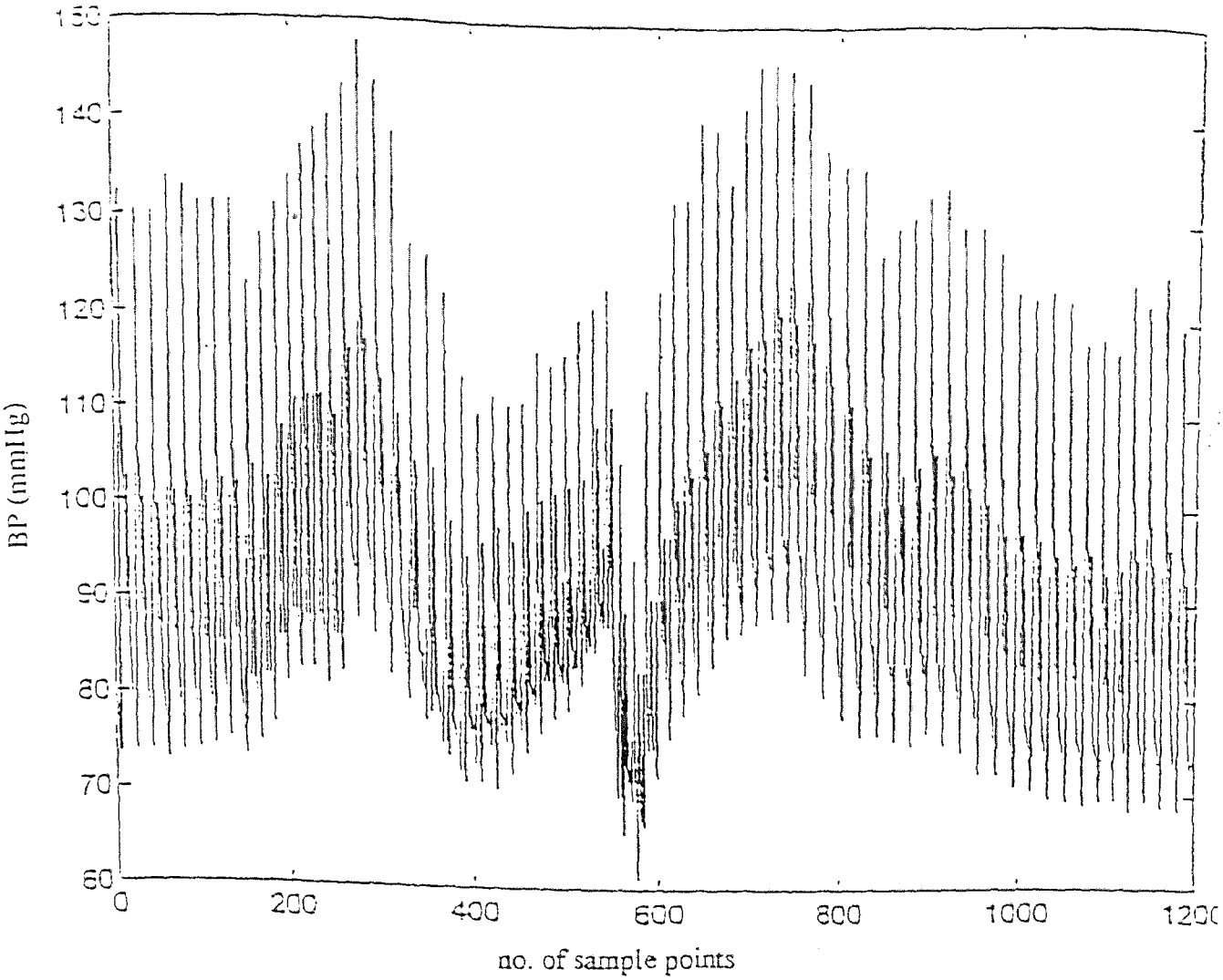

Figure 3.1: BP plot of a normal subject (m1902va) during the Valsalva maneuver. This file is one minute long or has 1200 sampling points. M1902va does not have a clear phase IV.

Table 3.1: Correlation Coefficient, BRSI, and Modulus value

File Name	Correlation Coefficient	BRSI msec/mmHg	Modulus msec/mmHg
m1b02va	0.87	8.02	6.20
m1b02vb	0.90	17.53	6.20
m1902va	0.80	18.74	6.10
m1902vb	0.79	11.49	6.10
m16002va	0.85	13.82	6.20
m16002vb	1.00	15.73	6.25
m13002va	0.90	20.7	7.10
m13002vb	0.96	12.71	6.25
r0378	0.92	7.81	7.20
r0379	0.69	6.71	6.90
r03710	0.91	11.88	12.00
q22310	0.93	3.63	3.80

Table 3.2: Coherence values for normal rest files

File Name	Frequency Range	Coherence
m16002bb	0.07Hz-0.14Hz	0.88
m1302ba	0.07Hz-0.14Hz	0.70
m1302bb	0.07Hz-0.14Hz	0.70
m1902ba	0.07Hz-0.14Hz	0.90
m1902bb	0.07Hz-0.14Hz	0.70
m1b02ba	0.07Hz-0.14Hz	0.92
m1b02bb	0.07Hz-0.14Hz	0.80

files. The modulus value for these files did not vary in the low frequency region several reasons. First, these files were collected from four similar subjects. Each subject provided two Valsalva data files and two rest data files. Files with the same number but a different extension meant they were from the same subject, but were taken at different times (m1902va and m1902vb). A logical conclusion from this statement is that these files should have a close BRSI value, similar correlation coefficient, and almost an exact modulus value. From Table 3.1, we can see that these types of files had similar modulus and correlation coefficients, but totally different BRSI values. Other files, starting with the letter 'm', were also from similar normal subjects. Their modulus values were almost the same, correlation coefficient within reasonable variance ($r > 0.8$), but their BRSI values were completely different. This means that the time domain calculation for these files was not accurate.

For the second set of files (file name stating with the letter 'r' and 'q') BRSI and modulus values in the low frequency range were almost the same, and had a high correlation coefficient. These files had a clear phase IV, therefore, maintaining a consistent approach for the data analysis was not difficult (Figure 3.2).

In comparing these two sets of data it appears like the time domain calculations may not be accurate under certain circumstances. For example, if the phase IV is not well defined, calculations could be in error. The present results indicate that BRSI can be estimated by means of spectral analysis and this would be more reliable in comparison to the time domain calculations.

As the correlation coefficient was a measure to either accept or reject the BRSI calculation in the time domain, coherence was the measure for modulus in the frequency domain. Methods described in chapter 1 and chapter 2 were utilized to calculate the coherence. A normal (rest) file with 0.8 coherence in the low frequency band meant that the modulus value in phase IV of the Valsalva file was acceptable. Figure 3.3 and figure 3.4 are the coherence plot and the modulus plot for m1902va. These two files are from the same subject; m1902va is the Valsalva file, and m1902ba has the rest data.

From the above discussion, it is clear that frequency domain calculations or

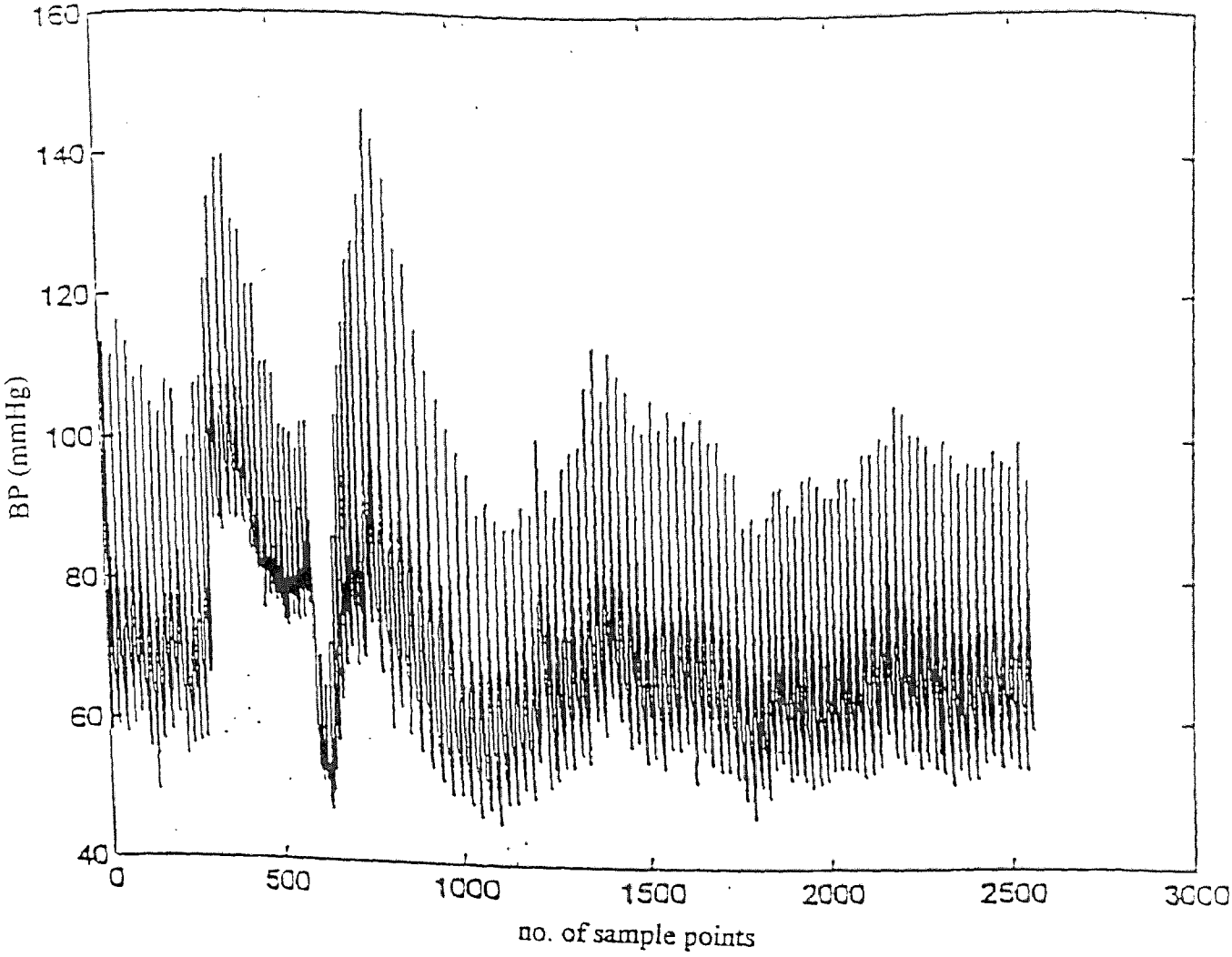

Figure 3.2: BP plot of a normal subject (r0378) during the Valsalva maneuver. This file is 2.5 minute long or has 3000 sampling points. R0378 has a clear phase IV.

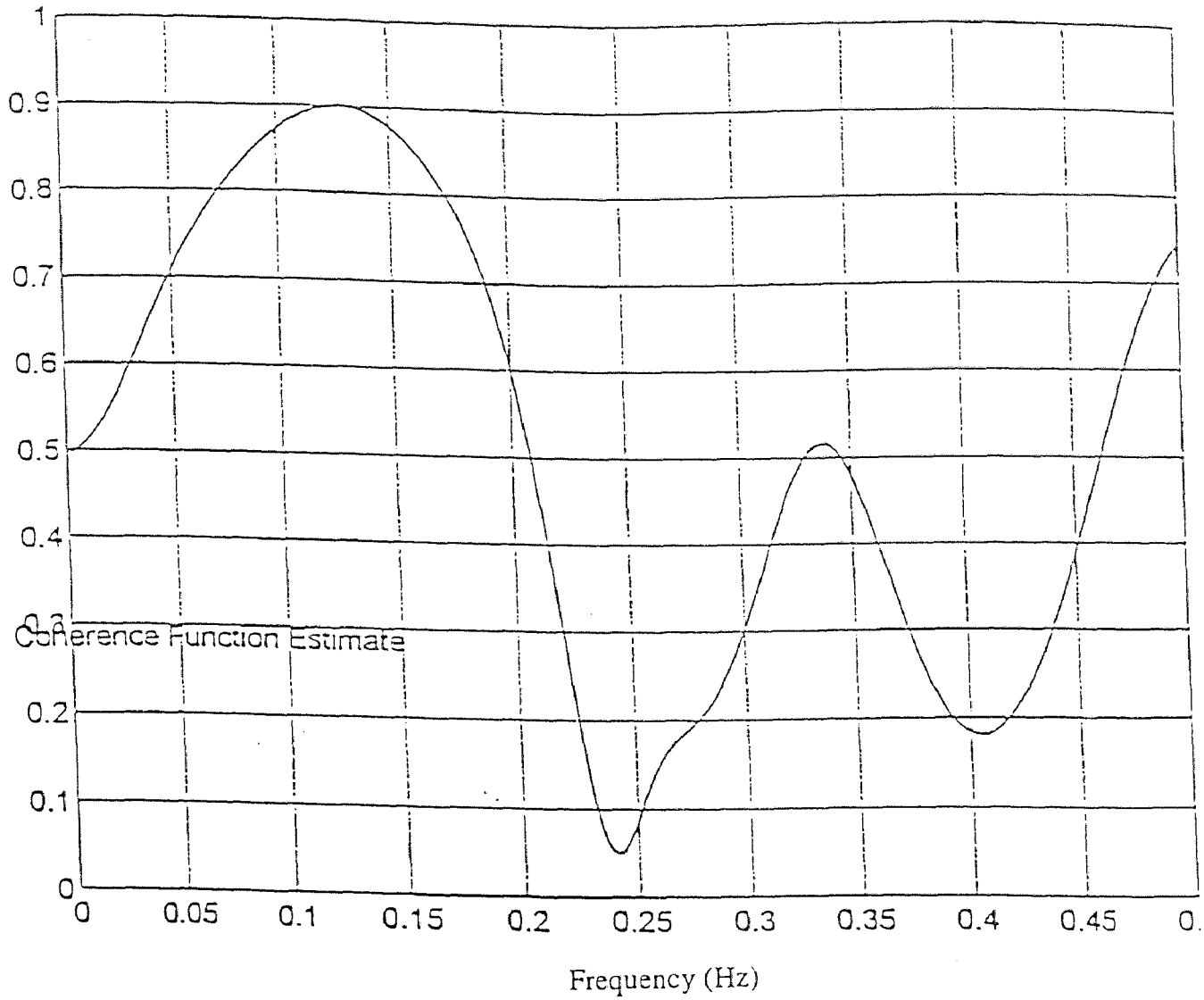

Figure 3.3: Coherence plot of m1902ba. In the low frequency range (0.07-0.14)Hz, this file had a Coherence value of 0.9.

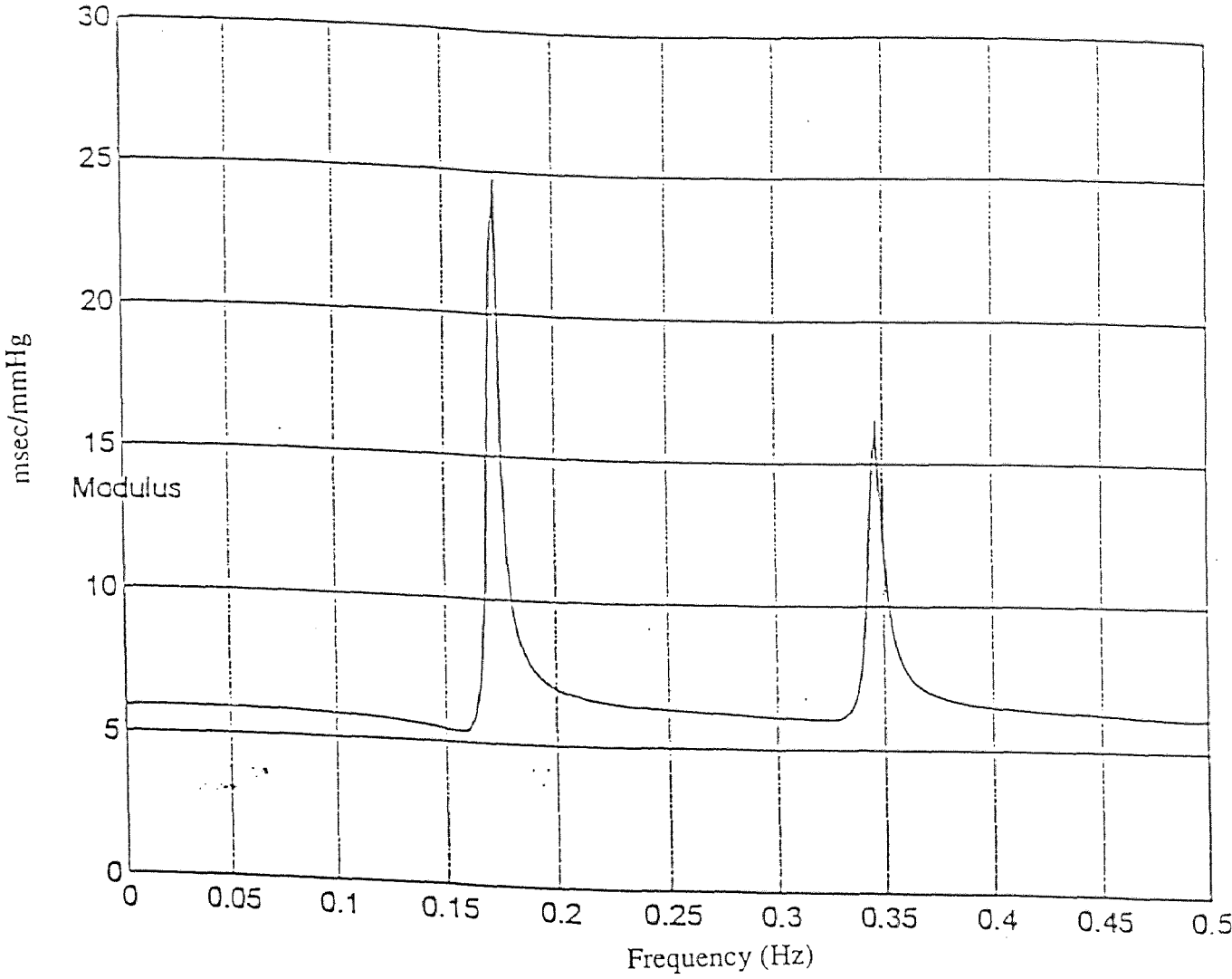

Figure 3.4: Modulus (msec/mmHg) plot of a Valsalva file (m1902va). In the low frequency range (0.07-0.14)Hz, modulus for m1902va is 6.1 msec/mmHg.

spectral analysis is more accurate than time domain calculations and more informative. Variations in the low frequency band are believed to originate from the characteristics of the blood pressure control system itself. Therefore, estimation of modulus and coherence in the low frequency range will give us an insight in figuring out the root cause of different values for different subjects. It can also show spontaneous fluctuations in blood pressure and the corresponding changes in R-R interval time.

CHAPTER 4

4.1 CONCLUSION

Frequency domain calculations are a better way to calculate the Baroreceptor Sensitivity Index (BRSI). If the coherence of BP and IIBI signals is high (>0.80) during the rest period, the modulus (BRSI) value during the phase IV of the Valsalva maneuver will be acceptable. The modulus, or gain function specifies the ratio between changes in systolic blood pressure (msec/mmHg) in a specified frequency band (0.07Hz-0.14Hz). This frequency band is associated with the baroreceptor mediated blood pressure control mechanism.

The modulus function in the frequency domain is analogous to the regression coefficient in the time domain. The modulus value becomes unreliable if the coherence is low. This can be compared to the regression coefficient (BRSI) in regression analysis becoming unreliable if the correlation coefficient is low.

Time domain analysis can often deliver the wrong result. If the phase IV of the Valsalva maneuver is not clearly defined, it suggests from the previous discussions that the time domain calculation for BRSI can be unreliable. In those situations, modulus or frequency domain calculations are relatively more accurate.

4.2 Future Work

Accurate data is extremely important for the BRSI or modulus calculations. All files should have a clear phase IV and at least a one minute long rest file.

For future work, three kinds of data can be collected. Data from normal subjects, spinal cord injured patients, and subjects under the influence of a prescription drug. In the low frequency band (0.07Hz – 0.14Hz), these types of data may show some insight to the sympathetic and parasympathetic influence on the blood pressure control mechanism under different circumstances. During the Valsalva maneuver, each type of subject may have a specific range of modulus values, different from one another. Thus, their average modulus value and the coherence in the low frequency band would be different too. This means, even under the same experimental protocol, the baroreceptor response can vary for different type of subjects due to the physiological constraints.

From this thesis we have developed an accurate technique to properly calculate the modulus and the coherence in any frequency band. This method can be further utilized for other physiological parameters, such as heart rate, respiration, and blood pressure. We can perform similar analysis on the heart rate and respiration or on the blood pressure and respiration to see how any one of these signals responds to the changes on the other one.

APPENDIX A

```
IIBI
clear
clc

global signal peaks RESPs

FirstStep=250 ;
[ECGs,RESPs] = getdata ;          % get ECG signal
[signal,peaks] = getpeaks(ECGs,FirstStep) ;

clear ECGs
control ;
display ;

function [ECGsig,RESPsig] =  getdata

% GETDATA reads an ascii file with three columns with the ECG signal in the
% third column and the respiration in the first one. It returns
% these two signals in ECGsig and RESPsig variables respectively


[fname,pname]=uigetfile('*.*','Open Data File "ASCII" ');

if isstr(fname) == 0
    disp(' Cannot find file')
    dbquit
end

Filename = [pname fname];

load(Filename) ;              % load file
fname = strtok(fname,'.');          % drop extension
k=eval(fname);                      % evaluate fname


ECGsig=k(:,4);              % ECG signal (old file, r0378)
RESPsig=k(:,1);             % Respiration signal (old file r0378)

%ECGsig=k(:,1);             % ECG signal (new file, m1302 etc)
%RESPsig=k(:,3);            % Respiration signal (new file m1302)
```

```
clear fname pname Filename k

function [signal,peaks] = getpeaks(signal,FirstStep)


    signal=signal(:);                       % vertical column
    V = mean(signal(2:length(signal)));
          sig=rot90(signal);                                % horizental row

    sig(1) = V ;     % modify first point

%%%%%%%%%%%%%%%% high-pass filter  %%%%%%%%%%%%%%%%


A=[V V sig V V];
B=[V V V V sig];          % shift right by 2
C=[sig V V V V];          % shift left by 2
m= 2*A - B - C;
m=m(3:length(m)-2);               % remove added 4 points

clear A B C V

%%%%%%%%%%%%%%%%  low-pass filter
%%%%%%%%%%%%%%%%%%%%%%

V = mean(m);
A = [V m V];
B = [V V m];
C = [m V V];
s = A + B + C ;
s=s(2:length(s) - 1)/4;
clear A B C V

%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
%%%%%%%%%%%%%%%%

LENGTH=length(s);
TOP=max(s);
[MAX,k]=max(s(1:FirstStep));
peaks=zeros(1,LENGTH);
peaks(k)=TOP;
```

```
%%%%%%%%      testing for the peaks    %%%%%%%%%%

N1 = 200 ;                    % to be used for interval threshold

n=fix(0.2*(k + N1));                % initial count of points per cycle
i=k+n ;

THERMOMETER = bar(0,' Detecting the Peaks ');

while i < LENGTH
   i=i+1;            % increment count
   n=n+1;
   if s(i) >= 0.25*MAX + 0.2*TOP                % check for threshold
           [MAX,T] = max(s(i:min(i+10,LENGTH)));
           N=n+T-1;                      % update current interval
           peaks(i+T-1)=TOP;             % a peak
           n=fix(0.2 *(N + N1));
           i=i+T+n-1;                    % Jump foreward
           N1 = N ;                      % previous interval
           bar(i/LENGTH)                         % update THERMOMETER

   end

end
close(THERMOMETER) ;

signal=sig - min(sig)+TOP;

clear m s MAX TOP k n N LENGTH


% This function gets the file to be analyzed from the users and
% Processes the data by calling several functions and terminates
% by plotting 3 plots required for our study. The variables
% available for use and for further processing are IBI, IIBI,
% respiration, and frequency and spectrum of both IIBI
% and respiration.
% pi and fi are the power and the frequency of iibi respectively.
% pr and fr are the power and the frequency of respiration respectively.

global peaks RESPs
clear g ibi rsp rpd iibi
close(gcf) % close current figure
```

```
tit_le = ' ' ;

peaks=peaks(:) ;
peaks=rot90(peaks) ;        % row matrix


[g,ibi,rpd]=grep(peaks,RESPs);

clear peaks

x=iibi(g,ibi);

clear g

[iibi,rsp]=seq(x,rpd);

    clear x rpd

    [d_iibi,d_rsp]=sqdt(iibi,rsp);

    [pi,pr,fi,fr] =graph(iibi,rsp,ibi,d_iibi,d_rsp,tit_le);

    clear d_iibi d_rsp

    stdgraff(pi,fi,pr,fr,tit_le);

    toc

% This function detects Interbeat interval(ibi) and extracts
% respiration signal (rpd).

function [g,ibi,rpd]= grep(file1,file2)

jks=file1;
g=diff(jks) ;
j=0;
for i = 1:1:length(g)

    if(g(i) > 0)
            j=j+1;
            ibi(j)=i;
    end
end
ibi=diff(ibi);
```

```
% respiration
rpd = file2;

clear jks j I

% Generation of Interpolated Interbeat intervals

function x = iibi(g,ibi)

j=0;
s=length(g)-max(size(ibi))-2;
x(s)=0;

h=bar(0,'finding iibi....');
for i=1:1:length(ibi)

    n=round(ibi(i));
    for k =1:1:n
        j=j+1;
    x(j)=ibi(i);
    end
    bar(i/length(ibi));
end         %keyboard
close(h);
clear j t s n

% This program converts the unit of IIBI into msec

for K =  1 : length (ibi)
cibi(K) = 0;
end;
cibi=ibi*5;
clear K

for P= 1: length(iibi);
ciibi(P) =0;
end;
ciibi=iibi*5;
clear P

% This function plots the Interbeat interval and Respiration plots.
% Here the function spectrak is called to get the power spectrum
%  values. The parameter 0 passed is noverlap (number of overlaping
% section),the 20 is the decimated sampling frequency, 8192 is
% the best number-point FFT.
```

```
function[p_ii,p_r,f_ii,f_r] = graph(iibi,rsp,ibi,d_iibi,d_rsp,tit_le)

[p_ii,f_ii]=rspect(iibi-d_iibi,8192,0,hanning(length(d_iibi)),20);

[p_r,f_r]=rspect(rsp-d_rsp,8192,0,hanning(length(d_rsp)),20);

figure('Name','IBI : IIBI : RSP')

z=1:length(iibi);

subplot(311)
    plot(ibi/200,'.b');
    xlabel('Beat Number'), ylabel('IBI'),
    title('Inter beat interval');

subplot(312)
    plot(z,iibi/200,'b',z,d_iibi/200,'g:');
    xlabel('Time'), ylabel('IIBI'),
    title('IIBI');

subplot(313)
    plot(rsp,'b');
    xlabel('Time'), ylabel('RSP'), title('RSP');

figure('Name',' Power spectrum Vs Frequency')

subplot(211)
    plot(f_ii,p_ii/200,'r');  % Power spectrum of IIBI
    xlabel('Frequency')
    ylabel('IIBI Power');
    title(tit_le);

subplot(212)
    plot(f_r,p_r/200,'g:');
    xlabel('Frequency')              % Power spectrum of Respiration.
    ylabel('RSP Power');
```

BP

```
function [bp,prsp]=getsap(bp,thr,hr)

% This program detects the systolic peaks given a blood pressure signal.
% Compare is then automatically run to check detection accuracy.
% Syntax: prsp=getsap(bp,thr,hr)
%   (Where usual values are: thr=20 hr=70)
```

```
bp=bp*500/2048;  %old file (r0378 etc)

%bp=bp*100; % Convert into mm Hg(new file, m1302).

disp('Detecting systolic peaks...')

prsp=presap(bp,thr,hr);                % Detect systolic peaks

disp('Check detections now...')

compare(prsp,bp)

function compare(prsp,bp)
function prsp=presap(bp,thr,hr)

% This function takes the blood pressure waveform and returns
% the pre-interpolated systolic arterial blood pressure signal.
% Pre-interpolated refers to the interpolated signal but with
% a string of zeros until the first systolic peak was detected.
% Syntax: prsp=presap(bp,thr,hr)

winsize=12000/hr;
wincomp=-winsize;
bpdiff=diff(bp);

bpmax=max(bp(1:400));                  % Height of first peak

% This function plots the prsp signal on top of the blood
% pressure signal for purposes of viewing the accuracy of
% the detection algorithm.
% It plots 1000 points at a time so to see the next 1000
% points, hit the return key. To exit, hit Ctrl-C.
% Syntax: compare(prsp,bp)

lenbp=length(bp);
lenprsp=length(prsp);
i=0;

while lenbp > i+1000
    plot(bp(i+1:i+1000),'b')
    hold on
    plot(prsp(i+1:i+1000),'r')
    hold off
    pause
    i=i+1000;
```

```
end
plot(bp(i+1:lenbp),'b')
hold on
plot(prsp(i+1:lenprsp),'r')
hold off
break

function prsp=undetect(prsp,bp)

% This program uses the mouse to remove unwanted detections.
% Simply click the mouse on both sides of an incorrect detection.
% Syntax: >> prsp=undetect(prsp,bp)

disp('Click on both sides of an incorrect detection.')
disp('(Left to right only)')
disp('Press return when done')

lenbp=length(bp);
lenprsp=length(prsp);
i=0;

while lenbp > i+1000
    plot(bp(i+1:i+1000),'b')
    hold on
    plot(prsp(i+1:i+1000),'r')
    hold off
    [x,y]=ginput;
    x=round(x);

x=sort(x);
    if size(x) ~= 0
            n=i.*ones(size(x));
            x=n+x;
            prsp=undet(x,bp,prsp);
            plot(bp(i+1:i+1000),'b')
            hold on
            plot(prsp(i+1:i+1000),'r')
            hold off
            pause
    end
    i=i+1000;
end

plot(bp(i+1:lenbp),'b')
hold on
```

```
plot(prsp(i+1:lenprsp),'r')
hold off
[x,y]=ginput;
x=round(x);
x=sort(x);
    if size(x) ~= 0
        n=i.*ones(size(x));
        x=n+x;
        prsp=undet(x,bp,prsp);
        plot(bp(i+1:lenbp),'b')
        hold on

plot(prsp(i+1:lenprsp),'r')
        hold off
    pause
    end

function prsp=undet(x,bp,prsp)

xpos=1;

for j=1:1:length(x)/2
    for n=x(xpos+1):1:length(prsp)-1
        if prsp(n) == prsp(n+1)
            ending = 1;
        else
            ending = 0;
            break
        end
    end

if ending == 0
        z=0;
        while prsp(x(xpos+1)) == prsp(z+x(xpos+1))
            z=z+1;
        end
        last=z+x(xpos+1)-1;
        for j=x(xpos):1:last
            prsp(j) = prsp(x(xpos)-1);
        end
    else
        for k=x(xpos):1:length(prsp)
            prsp(k) = prsp(x(xpos)-1);
        end
    end
```

```
xpos=xpos+2;
end

function prsp=mdetect(prsp,bp)

% This program uses the mouse to create a manual
%  detection. Simply click the mouse on both sides
%  of a peak where a detection should be.
% Syntax: >> prsp=mdetect(bp,prsp)

disp('Click on both sides of a peak that requires a detection.')
disp('(Left to right only)')
disp('Press return when done')

lenbp=length(bp);
lenprsp=length(prsp);
i=0;
while lenbp > i+1000
    plot(bp(i+1:i+1000),'b')
    hold on
    plot(prsp(i+1:i+1000),'r')
    hold off
    [x,y]=ginput;
    x=round(x);
    x=sort(x);
    if size(x) ~= 0
            n=i.*ones(size(x));
            x=n+x;

prsp=mdet(x,bp,prsp);
            plot(bp(i+1:i+1000),'b')
            hold on
            plot(prsp(i+1:i+1000),'r')
            hold off
            pause
    end
    i=i+1000;
end
plot(bp(i+1:lenbp),'b')
hold on
plot(prsp(i+1:lenprsp),'r')
hold off
[x,y]=ginput;
x=round(x);
x=sort(x);
```

```
if size(x) ~= 0
            n=i.*ones(size(x));
            x=n+x;
            prsp=mdet(x,bp,prsp);
            plot(bp(i+1:lenbp),'b')
            hold on
            plot(prsp(i+1:lenprsp),'r')

hold off
            pause
    end

function prsp=mdet(x,bp,prsp)
xpos=1;

for i=1:1:length(x)/2
    for j=x(xpos+1):1:length(prsp)-1
            if prsp(j) == prsp(j+1)
                    ending = 1;
            else
                    ending = 0;
                    break
            end
    end
    seg=bp(x(xpos):x(xpos+1));
    bpmax=max(seg);
    locmax=find(seg==max(seg))+x(xpos)-1;
    if length(locmax) ~= 1

locmax = locmax(length(locmax));
    end
    if ending == 0
            z=0;
            while prsp(x(xpos+1)) == prsp(z+x(xpos+1))
                    z=z+1;
            end
            last=z+x(xpos+1)-1;
            for k=x(xpos):1:locmax-1
                    prsp(k) = prsp(x(xpos)-1);
            end
            for l=locmax:1:last
                    prsp(l) = bpmax;
            end
    else
            for m=locmax:1:length(prsp)
```

```
prsp(m) = bpmax;

end
    end
    xpos=xpos+2;
    end
```

BRSI

```
test=diff(prsp);

scroll=0;
size_peak= max(size (test));
for j=1:1:size_peak,
    if test(j) ~= 0,
      scroll=scroll + 1;
       hold(scroll) = j;
     end
end

poi_iibi=ciibi(hold);
poi_bp=prsp(hold);

%function P=rmsline(x,plotfitfilename,SecondsPerBlock)
% rmsline.M
% Creates a new vector based on linear regression
% and plots data with best-fit line, slope, intercept,
% and correlation coefficient.
% USES data in workspace: x
% USES data in workspace: plotfitfilename
% CREATES 1x3 vector P=[slope, intercept,coeff]
% CALLS Function LineFit for regression calculations
%last=length(x)
%P=linefit(x(1:last))
P=linefit(poi_iibi,poi_bp);
newx=1:max(size(poi_bp));
newpfity=P(2)+P(1).*newx;

figure
subplot (2,1,1)
%plot(newx,x(1:last),'w+',newx,x(1:last),'g-')

plot(poi_bp,poi_iibi, 'r+')
%hold
```

```
subplot(2,1,2)
plot(newpfity,'g')
%hold off

tstring1=sprintf('slope = %4.3f',P(1));
tstring2=sprintf('y int = %4.3f',P(2));
tstring3=sprintf('r val = %1.3f',P(3));

text(10,min(newpfity(1:last))+1.*(max(newpfity(1:last))-
     min(newpfity(1:last))),tstring1)
text(10,min(newpfity(1:last))+.95*(max(newpfity(1:last))-
     min(newpfity(1:last))),tstring2)
text(10,min(newpfity(1:last))+.90*(max(newpfity(1:last))-
     min(newpfity(1:last))),tstring3)

%title(sprintf('%s sequential %d sec. intervals',plotfitfilename,SecondsPerBlock))
%xlabel(' interval number')
%ylabel('Root  Mean Square   ')
%print

%clean up
clear newx
clear newpfity
clear tstring1
clear tstring2
clear tstring3
clear P
```

Coherence

```
function [Cxy, f] = coherebp(P1, P2, P3, P4, P5, P6, P7)

% Coherence between IIBI and BP
% % Syntax [Cxy,f]=coherebp(x,y,nfft,Fs,window,noverlap)

error(nargchk(2,7,nargin))
if (length(P1)~=length(P2)),
   error('X and Y must be the same length.')
end
[msg,x,y,nfft,Fs,window,noverlap,p,dflag]=eval(optargs('psdchk',nargin,''));
error(msg)
```

```
% compute PSD and CSD
x = x(:);              % Make sure x is a column vector
y = y(:);              % Make sure y is a column vector
window = window(:);
n = length(x);                % Number of data points
nwind = length(window); % length of window
k = fix((n-noverlap)/(nwind-noverlap));   % Number of windows
                                          % (k = fix(n/nwind) for noverlap=0)
index = 1:nwind;

Pxx = zeros(nfft,1); Pxx2 = zeros(nfft,1);
Pyy = zeros(nfft,1); Pyy2 = zeros(nfft,1);
Pxy = zeros(nfft,1); Pxy2 = zeros(nfft,1);
for i=1:k
   if strcmp(dflag,'linear')
      xw = window.*detrend(x(index));
      yw = window.*detrend(y(index));
   elseif strcmp(dflag,'mean')
      xw = window.*detrend(x(index),0);
      yw = window.*detrend(y(index),0);
   else
      xw = window.*x(index);
      yw = window.*y(index);
   end
   index = index + (nwind - noverlap);
   Xx = fft(xw,nfft);
   Yy = fft(yw,nfft);
   Xx2 = abs(Xx).^2;
   Yy2 = abs(Yy).^2;

Xy2 = Yy.*conj(Xx);
   Pxx = Pxx + Xx2;
   Pxx2 = Pxx2 + abs(Xx2).^2;
   Pyy = Pyy + Yy2;
   Pyy2 = Pyy2 + abs(Yy2).^2;
   Pxy = Pxy + Xy2;
   Pxy2 = Pxy2 + Xy2.*conj(Xy2);
end
% Select first half
if ~any(any(imag([x y])~=0)),   % if x and y are not complex
   if rem(nfft,2),    % nfft odd
      select = [1:(nfft+1)/2];
   else
      select = [1:nfft/2+1];   % include DC AND Nyquist
   end
```

```
Pxx = Pxx(select);
   Pxx2 = Pxx2(select);
   Pyy = Pyy(select);
   Pyy2 = Pyy2(select);
   Pxy = Pxy(select);
   Pxy2 = Pxy2(select);

else
   select = 1:nfft;
end

Coh = (abs(Pxy).^2)./(Pxx.*Pyy);          % coherence function estimate
freq_vector = (select - 1)'*Fs/nfft;

if (nargout == 2),
  Cxy = Coh;
  f = freq_vector;

elseif (nargout == 1),
  Cxy = Coh;
elseif (nargout == 0),   % do a plot
  newplot;

figure(1)

plot(freq_vector,Coh), grid
xlabel('frequency'),ylabel('Coherence Function Estimate');
end
```

Modulus

```
% This program calculates modulus value between IIBI and BP

x=iibi;
y=prsp;
z=iibi*5;              % Converts IIBI unit into msec.
A=fft(z,8192)./fft(y,8192);

MOD=(A.*conj(A)).^(0.5);
select=1:8192;
freq_vector=(select -1)'*(20/8192);
newplot;
plot(freq_vector, MOD ), grid;
xlabel ('Frequency'), ylabel ('Modulus');
end
```

APPENDIX B

1.) **kunpack1 filename.dat,filename.asc,0-###/b/das16**
(76799)
Converts any file into ASCII format

2.) The ASCII blood pressure data is first loaded into matlab as follows:
load filename.asc

3.) The Systolic peaks are detected:
[bp,prsp]=getsap(filename (:,3),20,70)

4.) False detections are eliminated by:
prsp=undetect(prsp,bp)
then clicking the cursor on both sides of the false detection.

5.) Manual detections are created by:
prsp=mdetect(prsp,bp)
then clicking the cursor on both sides of a missed detection.

6.) Calculating IIBI:
ps1, then select the **file name** (enter)

7.) **Corr_ibi**
This converts IIBI unit into msec

8.) **Findpeak**
Detects systolic blood pressure peaks and corresponding IIBI values in phase IV of the Valsalva maneuver.

9.) **Rmsline**
Draws a straight line from the detected IIBI and BP peak values

10.) **COHEREBP(bp,iibi,8192,20,hanning(256),10);**
Calculates coherence

11.) **Mod_prsp**
Calculates modulus

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