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ABSTRACT

Clinical evidence exists to suggest that an individual's level of stress contributes to the state of many physiological and psychological disorders. The autonomic nervous system, by adjusting parasympathetic and sympathetic activity, is attributed with the control over an individual's level of neural stress. Therefore, it is desired to develop a better and quantitative understanding of the stress/ autonomic system mechanism.

Previous work has been done to gain a partial understanding of such activity. The primary objective for this study is to complement and advance the previous work by determining whether there is other physiological data which could reveal more about the correlation between autonomic neurological activity and illness or disease.

The work in this study was designed to identify a valid procedure for quantifying relative stress levels. Furthermore, it includes the objective to be useful for clinical and commercial application. This requires that the equipment be inexpensive, and the method simple to implement, non-invasive, straightforward to interpret, and yield accurate results.

A method which uses a Photoplethysmograph to measure blood volume in the fingertip was selected. A lap-top computer with LabVIEW software was used to acquire, display, store and process that data. An experimental protocol which was designed to change the stress level in test subjects was executed.

DEVELOPMENT OF A PRACTICAL AND EFFECTIVE TECHNIQUE TO DETERMINE THE COMPLETE LEVEL OF AUTONOMIC NEURAL ACTIVTY DURING STRESS

by
Vikki Hazelwood

A Thesis
Submitted to the Faculty of
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APPROVAL PAGE

DEVELOPMENT OF A PRACTICAL AND EFFECTIVE TECHNIQUE TO DETERMINE THE COMPLETE LEVEL OF AUTONOMIC NEURAL ACTIVTY DURING STRESS

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CHAPTER 1

INTRODUCTION

This study had been developed to follow and augment earlier works which have been done to obtain measurable, non-invasive physiological data useful for the understanding of autonomic neurological activity in an individual as it relates to disease or illness. The present difficulty in stress evaluation and control resides in the fact that although there are various conventional and alternative holistic techniques, which have demonstrated qualitative effectiveness, the results cannot be directly measured or quantified. With quantitative results, it is hoped that evaluation and treatment could be more accurately monitored, evaluated, and prescribed, leading to a more efficient and effective result.

"Heart Rate Variability" (HRV) is an example of one recent and successful study in this area.[1] In the evaluation of HRV, through the measurement of heart rate and respiration, abnormal parasympathetic activity can be detected. A valid correlation between such abnormal parasympathetic activity and an individual's risk or likelihood to suffer a stroke or heart attack has been developed.

To date, this study—and those like it—have contributed only partially to an ultimate goal. Due to complex interactions within the neurological system, it is difficult for a study such as HRV to isolate a value which strictly represents sympathetic activity; the interpretation of which is not always direct. An independent measurement of sympathetic activity would be needed to provide a total picture of the autonomic nervous system.

The development of a more advanced and simplified method may create opportunities for broader application. It is possible that in addition to heart attack or stroke, other cardiac and autonomic disorders may be evaluated. Furthermore, the interpretation of results could be refined to turn this technique into an effective diagnostic tool. Finally, it could be applied to control or develop a cure for illnesses which are influenced by the autonomic system.

Therefore, to be more useful and practical, many advancements are needed. A more direct correlation between measured data and autonomic activity is required. Clinical and interpretive methods must be simplified. More comprehensive information about the autonomic nervous system is needed; i.e. information about sympathetic activity is needed to accompany the information about parasympathetic activity. This study addresses these needs for advancement.

1.1 Basis

With regard to the need for non-invasive physiological measurements, earlier work [2]suggests that there are at least three types of measurements which can be made and which may provide data directly related to autonomic activity. They are: EEG, skin conduction, and peripheral blood volume. [2 ,3, 8] Based upon the results from early studies, it is reasonable to hypothesize that each may produce relevant and measurable data. This is discussed in greater detail in section 2.2.

The need for simplified clinical and interpretive methods is further addressed by the original work in this project. The original work resides in three parts: (1) the design of an experimental system, (2)the execution of experiments in which blood flow in the fingertip of test subjects is measured during "changes, i.e. rest, relaxation, and stress, and (3) interpretation of the results.

1.2 Selection of a Measuring Technique

The use of EEG for this purpose deserves serious consideration. The method for potential application of EEG is discussed in greater detail in section 2.2.1. However, access to EEG equipment is very limited. Furthermore, the application of EEG is relatively elaborate and costly. As such, the use of EEG does not lend itself to broad practical application. If possible, a more accessible and simpler measuring technique is desirable.

Other non-invasive techniques have also been considered; they include peripheral skin conductivity, peripheral skin temperature , and peripheral blood volume. None, however, have been developed enough to provide a direct correlation to autonomic neurological activity. The progress of each, to date, is summarized in section 2.2. Based upon the results from the previous work, the method selected for use in this study is direct measurement of blood volume in the fingertip.

The need for a direct correlation to autonomic neural activity is addressed by the type of measurement selected. The autonomic nervous system controls the dilation and constriction of blood vessels in the periphery in order to regulate the blood flow through those vessels. As the level of sympathetic activity increases, the blood flow to the body extremities decreases. At the fingertip, this effect is particularly pronounced. Furthermore, there is no parasympathetic activity in this area.[4]

It is plausible to suggest that the relative size of the blood vessel may be determined from the measurement of blood flow in the vessel. This "relative size" of the blood vessel would indicate its degree of constriction or dilation and therefore the degree of sympathetic autonomic nervous activity in the individual.

1.3 Experimental Design

This work involves some unique and fundamental differences from the research which has been done prior to it. The first important difference is the design of the experimental system. Until this project, data had been acquired and recorded using a desktop PC. That equipment was located in the NJIT lab. With the availability of a relatively powerful and portable lap-top computer, and some appropriate hardware and software, the technology used to execute this project offers significant improvements.

Accuracy, cost, practicality and the clinical or commercial usefulness of this work are very substantial benefits of this new design. This new approach is expected to offer many advantages over the earlier experiments. Advantages can be anticipated due to these features: Environment, Computer, Portability.

1.3.1 Environment

A more comfortable environment for test subjects provides a better opportunity to obtain more natural data. The subject is more likely to rest and relax as instructed. This improves the chance to produce more accurate results, creating a more realistic picture of the subject's blood volume response to the changes he experiences.

1.3.2 Data Acquisition, Storage, and Processing

The results from this project can be stored and processed in the computer. The software package, LabVIEW was selected so that sophisticated manipulation of the data can be done directly in the computer and it can be executed with relative ease. The data can be stored on a disk and submitted for future projects and analysis.

This method has significant clinical/commercial implications as well. This type of approach is used across many industries; equipment, software and support are readily available and reasonably priced. Probably, too, clinics, physicians and the like would be able to make a complete diagnosis more readily because of the ease with which the data can be acquired stored and processed. Furthermore, it is far more probable that data interpretation can be made "on-line" with this method. Such immediate feed back would be necessary to effectively implement and evaluate any control or remedy which might be required.

1.3.3 Portability

For the purposes of this project, the portable "set-up" makes it far more convenient to obtain data from different types of subjects, not just from students and faculty who are available to the campus lab location. This will facilitate future population studies and clinical application as well.

1.4 The Tasks

The design goals for the system and methods—simple, non-invasive, and practical to apply—are not trivial. Once achieved, however, the design, alone, is not useful if the experimental protocol is not effective. Therefore, after outlining a plausible design concept, experiments must be conducted and evaluated. This includes test and layout of the equipment, protocol trials, selection and evaluation of subjects, execution of experiments and analysis of the results. During each step of experimental design and execution, extreme care must be taken to ensure the accuracy of the results.

Due to the introduction of a lap top computer and LabVIEW software into this type of work, the most complex step is to develop the application of the software and the lap-top. The remaining original work of this project, therefore, will focus on the development of an effective method by which the lap-top computer can be used to acquire, store and process necessary data.

The specific major tasks which will be discussed in this project can be outlined as follows:

1. Become familiar with the selected software, LabVIEW, program for lap-top computer.
2. Write programs, in LabVIEW, which will acquire, display and store raw data.
3. Conduct a study with a test population; record data.
4. Develop data analysis features which can be used to interpret raw data.
5. Evaluate the data to determine whether a useful correlation between blood flow at the fingertip and "a change" can be identified.

Subjects will be evaluated under three imposed conditions: "Rest", "Relaxation", and "Stress"; after which a recovery period will be included. The collected data will be subsequently evaluated and interpreted to determine whether a useful correlation can be identified between blood flow measurement and autonomic activity in an individual.

If successful, the device and methods developed in this study will be characterized as an effective means for correlating fingertip blood flow behavior and autonomic sympathetic neural activity in test subjects. Future work would be required in three directions: (1) improving and fine tuning the device and methods, (2) comparison to data from other methods which provides information about an individual's stress level and (3) population studies. After such work, the system can be calibrated and commercialized.

CHAPTER 2

BACKGROUND

A good command of the pertinent physiological systems is necessary to appropriately design, perform and evaluate the proposed study. In addition, an understanding of previous work with similar objectives is needed. This enables streamlining and focusing of this work so that it produces the most meaningful results in the most efficient manner. A summary of the key physiological systems and issues from previous works are included in this section.

2.1 Physiological Systems

It is desired to establish a method by which "stress" can be measured. The method which is selected must be supported by good physiological rationale. Furthermore, to meet the additional objectives of this study, it must be simple and practical. From a physiological standpoint, this means it should give accurate results with the least amount of harm, discomfort, or inconvenience to the subject. The dynamic interaction between the cardiovascular and the neural system provides an opportunity for establishing a reasonable method based upon these criteria. Therefore, these two major physiological systems are reviewed in this study.

2.1.1 Blood Flow in the Cardiovascular System

Measurement of blood flow in the fingertip has been chosen for a very specific reason. Blood flow in this area is regulated in the absence of parasympathetic activity. [4] It therefore offers the opportunity to potentially isolate sympathetic activity and the possibility to develop a direct correlation between blood flow and the level of sympathetic activity.

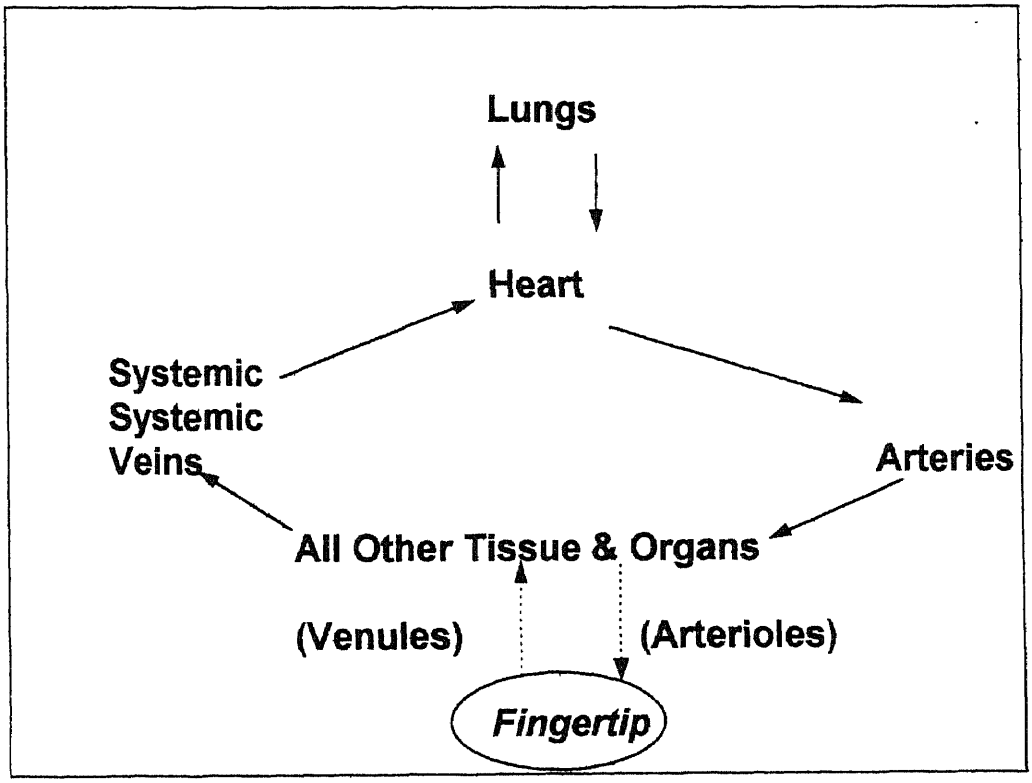


Figure 2.1 Blood Flow in the Cardiovascular System

In order to interpret the data acquired, however, all the factors which affect the blood flow patterns in the fingertip must be understood. It is therefore necessary to develop a basic understanding of the cardiovascular system as it relates to the control of blood flow in the fingertip. This requires review of the control of the heart, the heart's control of cardiac output, and the systemic regulation of blood flow.

2.1.1.1 The Heart: The heart is the main and most significant controller of blood flow since it acts as the primary pump for the circulatory system. There are other minor pumping mechanisms, skeletal muscle and respiratory pumps, but they are discounted in the context of this discussion. As outlined in figure 2.1, the heart pumps oxygenated blood into major arteries and which then branch into smaller arterioles and are finally distributed into capillaries.

The heart can be divided into four major chambers. Nutrient depleted blood flows into the heart via the Right Atrium from the periphery. Then, via the triscuspid valve, it enters the Right Ventricle whereupon it exits through the pulmonary valve to the lungs. The lungs oxygenate the blood and then return it to the Left Atrium. The blood is then released into the Left Ventricle through the mitral valve, where it is expelled into the aorta through the aortic valve. [4]

From the aorta, blood is distributed into arteries.[4] The volume of blood pumped by either ventricle is referred to a the cardiac output, CO. Normal CO is about 5.0 liters/min. CO is a function of the heart rate (HR) and the stroke volume (SV) and can be expressed as:

$$CO = HR \times SV \quad [4] \tag{2.1}$$

Heart rate is function of a coordinated triggering of heart muscle contractions. The presence of gap junctions between myocardial cells allows the transfer of excitation from one cell to the next. Thus, from an initial excitation to one cell, all other cells can be excited. The sequence of triggering is controlled by a firing path which begins with the SA (sinoatrial) node. This is normally the pacemaker for the entire heart. [4]

Heart rate is controlled from the cardiac center which is located in the medulla in the brain. [4] The SA node is affected both by parasympathetic and sympathetic nerves. The cardio-inhibitory center in the left side of the medulla connects to the heart via the vagus nerve, which is a parasympathetic fiber. The cardio-accelaratory center, in the right side of the medulla, reaches the heart via sympathetic fibers referred to as the "cardiac nerve". With sympathetic and parasympathetic activity removed, the SA node will pulse at ~100 beats per minute; this implies there is more parasympathetic activity than sympathetic for a normal resting heart rate of 60 - 70 beats per minute. [4]

The result is a cardiac cycle of contraction and relaxation which pulses blood flow out to the lungs, systemic vessels, and organs. This cycle is divided into two phases, systole and diastole. Systole is the period of ventricular contraction and ejection; the stroke volume (SV) is the volume of blood ejected from the ventricle during this period. Diastole is the period of relaxation where the ventricle fills with blood.

Stroke volume is a function of the force of each contraction. This is controlled predominately by two factors, end diastolic volume and amount of sympathetic nervous system input. End diastolic volume can be described by Starling's Law, which states that the stroke volume will increase in response to higher filling volume. Sympathetic nerves increase the contractility of the ventricle regardless of the end diastolic volume.[4]

Sympathetic nerves are distributed to all cardiac muscle. Increased sympathetic activity causes a more powerful contraction and results in a higher percent of ventricular volume ejection. It also causes contraction and relaxation to occur more quickly, increasing the heart rate, as mentioned earlier. With more rapid cycles, the time allowed for filling is decreased, however, the more powerful contraction compensates for this effect by allowing a larger percentage of the ventricle to be available for filling. [4]

2.1.1.2 The Electrocardiogram: The electrocardiogram, EKG, describes the electrical events within the heart; it measures the currents in the extracellular fluid generated by changes occurring in many cells. It is used extensively, both directly and indirectly to evaluate the health condition of an individual. Significant to this study is its use in the application of Heart Rate Variability (see section 2.2.2).A typical EKG recording for a normal heart is shown in figure 2.2.

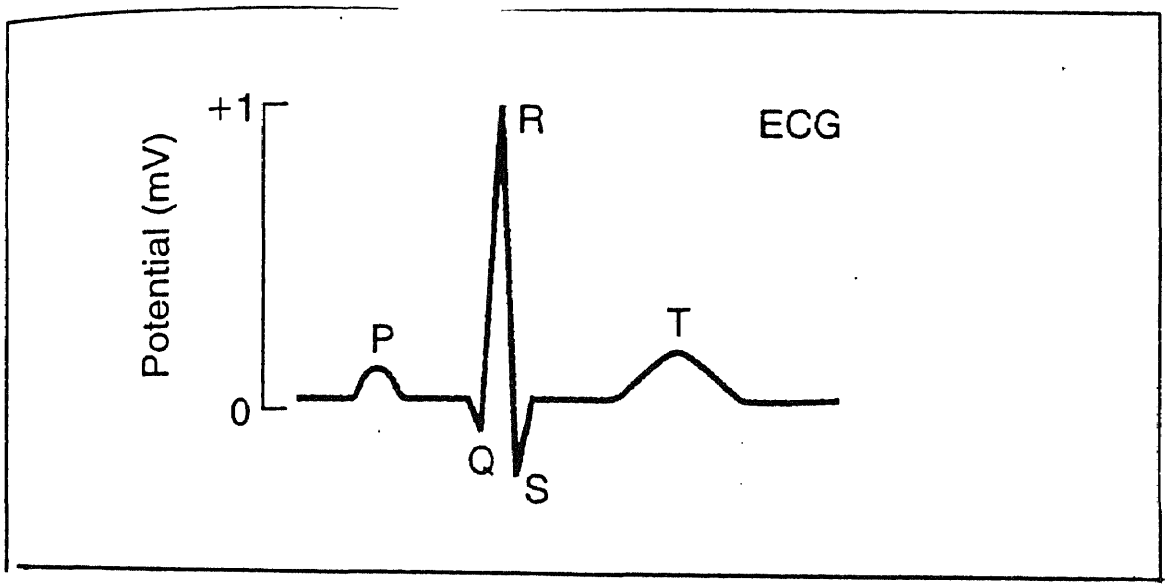


Figure 2.2: Significant components of a typical EKG signal [4]

In this figure, P represents atria depolarization, QRS are frequently grouped into the QRS complex, representing ventricular depolarization, and T represents ventricular re-polarization. The re-polarization of the atria occurs during the same time as the QRS complex and is not seen independently.[4]

2.1.1.3 Systemic Blood Flow: It can be seen from section 2.1.1.1 that blood flow to the vessels is initially controlled by the heart and its resultant cardiac output. That cardiac output is affected by sympathetic and parasympathetic activity, in addition to other physiological effects. Blood flows into the fingertip via arteries and then arterioles. All regulation of blood flow to cells is via the arterioles. [4] At this point, the oxygen and nutrient rich blood is distributed into capillaries and then diffuses into other cells in the fingertip, while the "depleted" blood returns via the capillaries and flows into the venules. That depleted blood then flows from the venules into the veins and returns to the heart to be pumped into the lungs to be replenished.

Regulation of blood flow to the fingertip, however, is not simply a function of the heart stroke volume and rate. Blood vessels are elastic, possessing the property to dilate or constrict, depending upon how much blood the body commands to flow into that area. The size of the blood vessels, too, contribute to the overall blood flow in the fingertip.

In fact, the arterioles have two major roles in controlling blood flow. First, they are the main factor for determining mean arterial pressure, MAP. Secondly, and most significant to this study, the arterioles are responsible for determining the relative blood flow to the individual organs in which they reside. Since MAP is identical throughout the body, the difference in flow between organs is determined entirely by the relative resistance presented by the arterioles in each organ.[4] Likewise, for a given constant mean arterial pressure, any change in flow to a given organ is due to a change in resistance of the arterioles in that organ.

Arterioles are made of smooth muscle which can either relax to cause vasodilation where the vessel radius increases, or vasoconstriction, where the vessel radius decreases. [4] There are many causes for arteriolar smooth muscle activity. First, there is myogenic tone, which is spontaneous contractile activity. This occurs independently from any neural, or hormonal, input and is referred to as basal, setting a baseline from which the level of contraction can be changed by external signals. [4]

The external signals which cause increases or decreases in the contractile forces of myogenic tone are grouped into two categories: local controls and extrinsic controls. Extrinsic controls refer to those which have mechanisms involving nerves or hormones. Local controls have mechanisms which are independent of either of these, and are listed in the right-hand box in figure 2.3. [4]

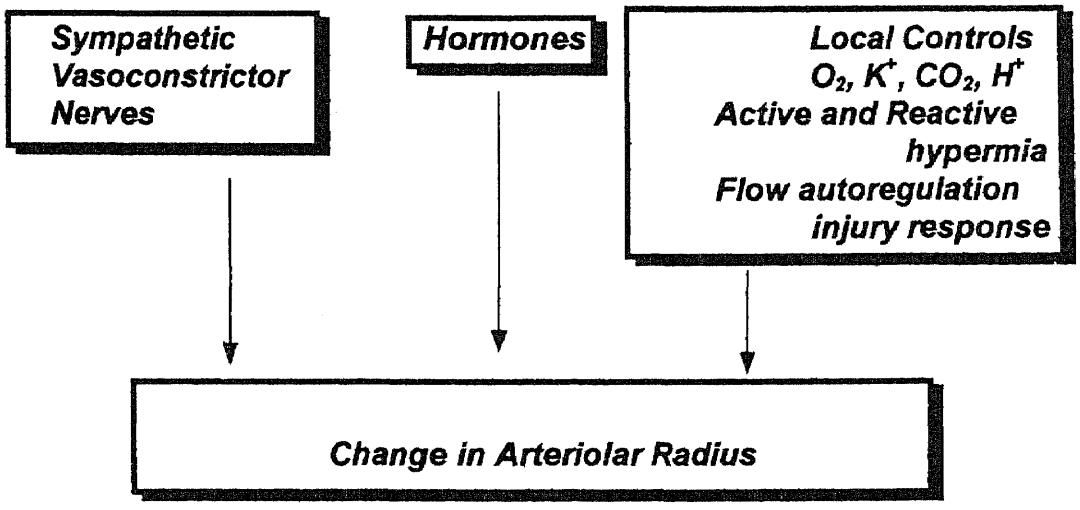


Figure 2.3: Factors Affecting Arteriolar Radius [4]

Since blood flow in the fingertip is being measured, the performance of the arterioles in the cutaneous tissue at this location is essentially being measured. Therefore, it is important to know which of these factors may contribute to a change in blood flow at this location.

The most significant external signal is that supplied by the sympathetic nerves. Sympathetic nerves can cause both vasoconstriction and vasodilation. To cause vasoconstriction, sympathetic, postganglionic nerve fibers release norepinephrine which triggers alpha-adrenergic receptors on the smooth muscle wall of the arteriole.[4] Vasodilation, on the other hand, may be achieved by decreasing the rate of sympathetic activity below the basal level.

Sympathetic activity in blood vessels is more a reaction to conditions of stress, whereas other controls are more concerned with metabolic needs of the organ. A sympathetic response to stress is generally, but not always, considered to occur without conscious control. When this occurs it is referred to as the "fight or flight" response, which is used to describe the "involuntary" reaction an animal has when confronted with a potential danger, that is to run away or rise to the challenge. [4]

This activity is particularly pronounced at the skin. Since, at room temperature, there is a moderate level of sympathetic activity, a "stress" stimulus reflexively causes more sympathetic discharge, resulting in vasoconstriction. Conversely, an increase in body temperature reflexively inhibits sympathetic activity, permitting vasodilation which allows the skin to flush or liberate heat.[4]

2.1.2 Neurological Physiology

It is important to briefly review the functionality of the sympathetic division of the autonomic nervous system and how that division fits into the overall scheme of the nervous system. Nerve fibers in the peripheral nervous system transmit signals between the central nervous system and all other parts of the body. These fibers are grouped into efferent or afferent divisions. The efferent division is further divide into somatic or autonomic nervous systems. The efferent innervation of all tissues other than skeletal muscles is via the autonomic nervous system. [4]

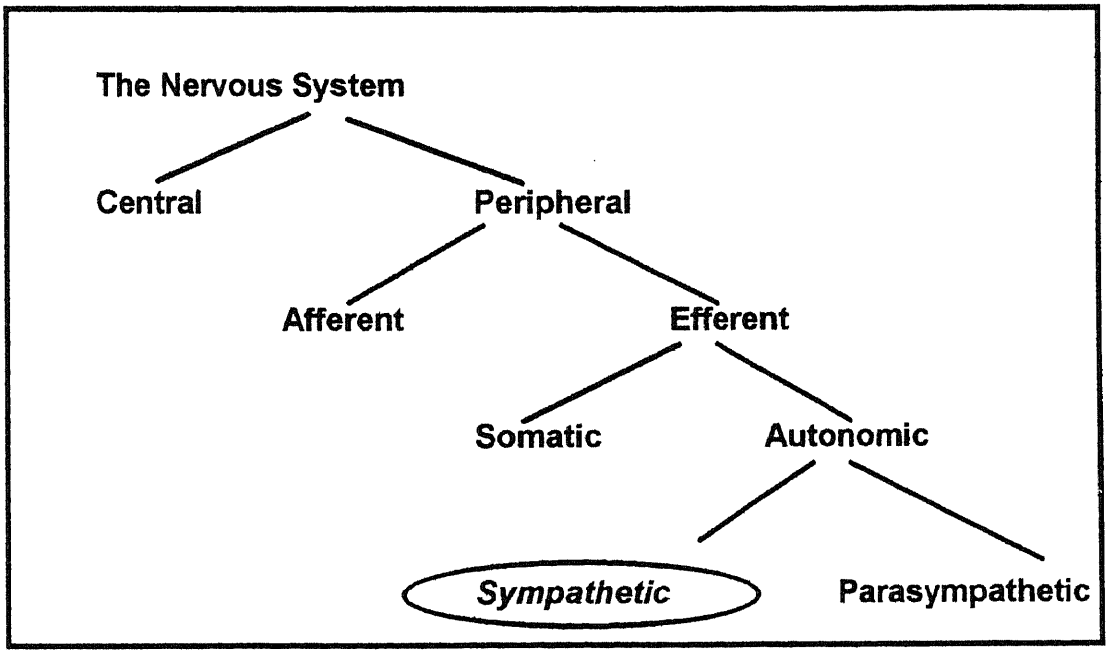


Figure 2.4 Divisions of the Nervous System.

The autonomic nervous system is, in lay-terms, considered the part of the nervous system which is considered to be that part over which one has "no conscious control". Although not entirely correct it is "frequently accurate" and a reasonable distinction in comparison to the function of the somatic nervous system. [4] It is indeed a useful distinction within the context of this study, since it is designed to evaluate "uncontrolled" physiologic response after changes are imparted to the neurological state.

This study evaluates the functionality of the autonomic nervous system, more specifically, the sympathetic division of the autonomic nervous system. The "change" which is imparted to the neurological states is designed to alter the stress level of the individual. The sympathetic system is generally considered to increase its response under stress conditions. In fact, strongest sympathetic response is more commonly known as the fight-or-flight response, based upon "animal instincts" which either confronts danger or runs away from it. [4]

In contrast, the activity of the parasympathetic division of the autonomic nervous system increases with "vegetative" functions. Many organs, glands, or smooth muscle receive dual innervation. Usually, the sympathetic and the parasympathetic have opposite effects to provide a fine degree of control over the effector organ.[4]

2.1.3 Physiology at the Skin

It is actually the behavior of blood flow in the skin at the fingertip which is being evaluated. At rest, 9% of total systemic blood flow is to the skin. One square centimeter of skin contains 1 yd. of blood vessels, 4 yards of nerves, 100 sweat glands, as well as 3000 sensory cells at the end of nerve fibers, which include special apparatuses to sense heat, cold, pressure, and to record pain. [5] In addition to its protective and sensory functions, it is also plays a key role in the regulation of body temperature.

Heat loss from the body is controlled by radiation, conduction, and evaporation through the skin. The skin's effectiveness as an insulator is determined primarily by the blood flow to it. Change in skin blood flow can regulate body temperature by altering heat loss in the thermoneutral zone, i.e., over a range of 75° to 86°F. Above this range, sweating plays a major role in the ability to lose heat. Heat is also lost from evaporation via insensible water losses, namely from respiration and diffusion through the skin.[4]

Production of sweat is stimulated by sympathetic nerves. The firing rate of vasoconstrictor sympathetic nerves is increased in response to cold and decreased in response to heat. There is also a sympathetic response associated with sweating, causing active vasodilation. Since certain areas are affected more significantly than others by these mechanisms, skin temperature will vary with location. [6]

2.2 Previous Work

2.2.1 Use of Electroencephalogram

The Electroencephalograph, or EEG, is a device which measures and records fluctuating electrical activity in the cerebral cortex. The frequency spectrum of the EEG can be broken down into 4 groups, two of which are mostly used to register activity in wakeful individuals; the other two identify activity during sleep.

Of those two groups, or bands, the alpha activity is the one which can best identify one's "state". The alpha band is most easily seen when an individual is relaxing, i.e. eye's closed, physical relaxation, mental inactivity; conversely, it is less easily seen when eye's are open and during mental activity. By evaluating the rhythm, frequency, amplitude, and other characteristics of the signal, it can be used to identify the waking mental state of an individual. [7]

One additional phenomenon which can be observed is the phenomenon of coherence. Normally, during wakeful mental activity and even during simple rest and relaxation, the alpha waves in different parts of the brain are doing different things. However, during extremely deep states of relaxation, e.g. that which is experienced during deep meditation, the alpha waves in different parts of the brain become coherent. [8].This phenomenon, too, may be observed using EEG, and used to identify one's mental state.

Dr. Richard Frenkel is a practicing psychiatrist in Scarsdale, NY. He has developed a therapy to treat patients with what are believed to be stress related disorders using colored light therapy. Such disorders include Attention Deficit Disorder (ADD), Dyslexia, Phobia, and "Rage Control". His technique includes the evaluation of an individual for his "good colors" and "bad colors", then he tells his patient to wear a colored lens, which is matched to the patient's good color. This is supposed to help the individual to perform with more normal conduct. [8]

He has not conducted significant population studies with his approach; however, he has conducted case studies. He claims the result of his case studies show improved behavior when they wear their colored lens. He recognizes that his method is controversial within the medical community, and has attempted to develop methods by which the effects of such applied therapy may be measured. [8]

This particular evaluation identifies the need for developing a measuring technique as proposed in this study. Dr. Frenkel explained that it is difficult to prove his therapeutic methods using conventional techniques of controlled, duration population studies. The availability of qualified subjects is very limited and the effects of the applied therapy would be extremely difficult to monitor in a controlled environment. Furthermore, it is likely that several years would be required before any interpretation of the results may be made.

Dr. Frenkel chose to measure the EEG of a patient whom he had identified as being deeply affected/enraged by the color red. The patient was also aware of the fact that she had been identified as being affected by this color. He measured her EEG both while exposed to the color red and in the absence of that color. The results showed dramatically different EEG's in each case. Though not a well controlled experiment, since the patient knew she was supposed to respond differently to the color red, the results are still noteworthy.[8] Whether the results are attributable to the color exposure or due to the placebo effect is indeterminable. Also, it is not clear from his data what the difference in EEG is between stress and relaxation; this would have to be determined in a scientific study.

Although the application of EEG for the evaluation of ones affectation by a change in circumstances may be useful for identifying some aspect or degree of that effect, it is indeed a difficult method to implement. The availability and cost of equipment, availability of subjects, naturalness of surroundings and comfort to the subject are all minimal. It would be more useful if other physiological effects, which are easier to monitor, be first considered.

2.2.2 Heart Rate Variability

Heart Rate Variability is a non-invasive method for measuring autonomic neural activity which has proven successful in the determination of one's predisposition to certain illnesses. This technique involves monitoring of the electrocardiogram and respiration rate under steady state conditions. It, however, only isolates the parasympathetic activity; the sympathetic activity is obtained only in conjunction with the parasympathetic activity and cannot be isolated.

As described in section 2.1.1.1, heart rate is regulated by autonomic activity. In fact, it has been determined that this activity plays the most significant role in controlling the "beat to beat" variations in heart rate. A correlation has been developed between autonomic activity and inter-beat intervals, IBI, which is a summary of the intervals between R-waves of the EKG. [1]

The IBI are studied using spectral analysis, and three peaks are obtained. The high frequency peak, ~0.15Hz to 0.4Hz, provides independent information about parasympathetic activity; this is only true when the respiration frequency remains above the lower limit of this range, i.e. ~9 breaths per minute. When this condition is met, the information from the high frequency peak can be used to determine one's likelihood of having a heart attack or a stroke.

In general, the less the variability, the greater the likelihood of the individual to become ill. However, there are many other factors which must be considered in such interpretation, including age and gender. [1]

The IBI are processed using power spectral analysis. The power spectrum yields three major bands as illustrated in figure 2.5. The high frequency peak, as noted above, represents parasympathetic activity; the low frequency peak, ~0.06 to 0.15 Hz, describes a mixture of sympathetic and parasympathetic activity. Note that to date, the sympathetic activity cannot be isolated independently from this signal. The very low frequency peak is believed to be associated with vasomotor control and/or temperature control; it is not considered useful in this context. [1]

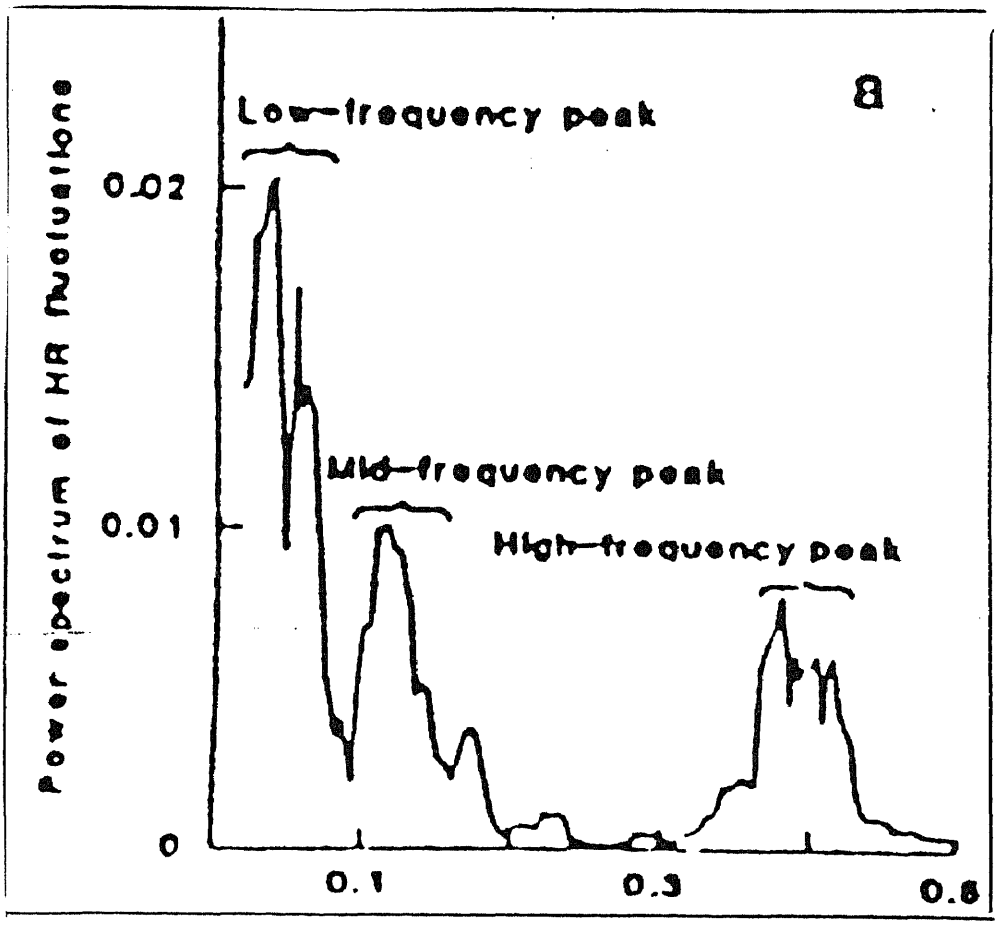
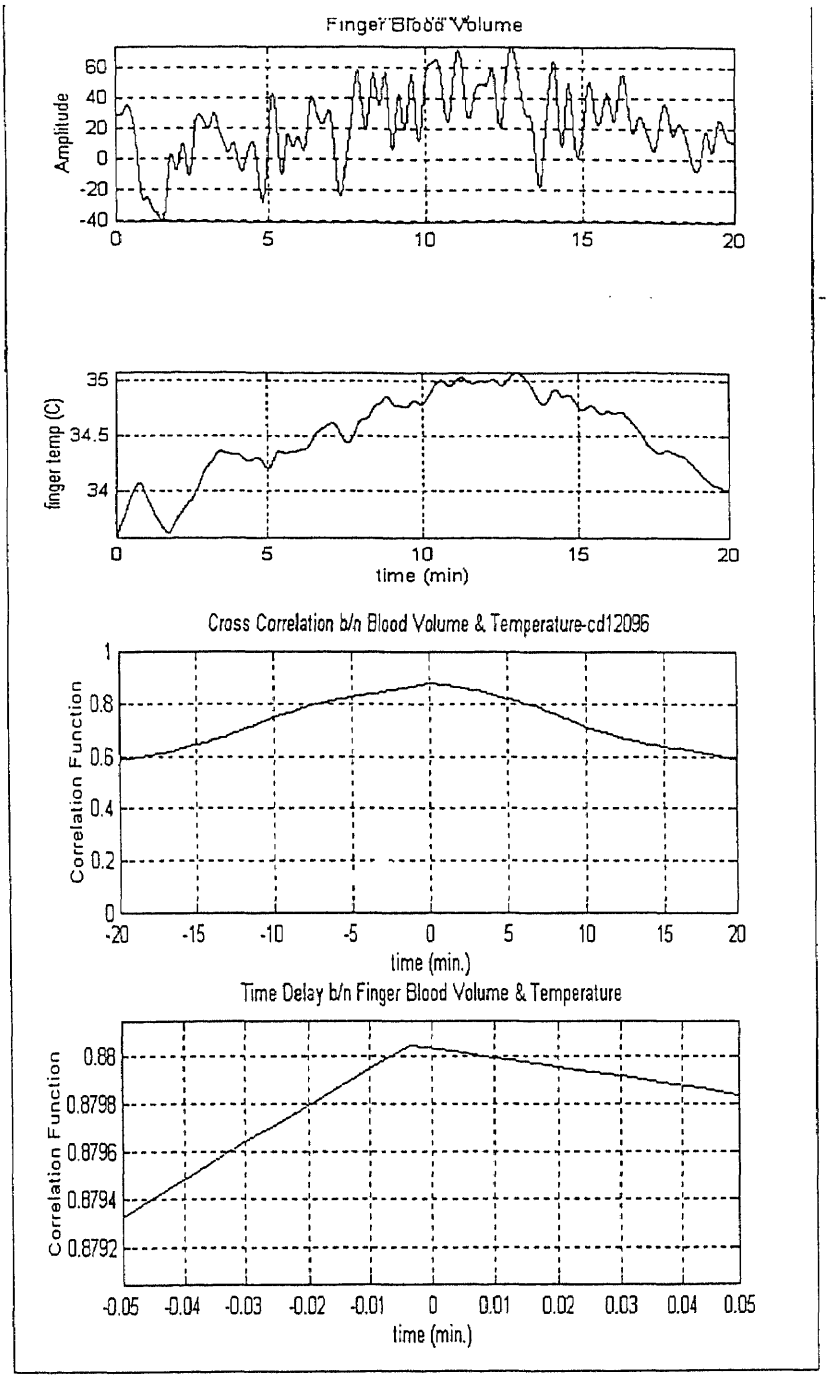


Figure 2.5 Typical Spectral Analysis from Heart Rate Variability (frequency is shown along the bottom axis) [1]

2.2.3 Skin Temp v. Blood Volume

A study which was performed concurrently to this one included an experiment which compared skin temperature to blood volume in the fingertip. In that study, it was observed that the change in temperature closely follows the change in skin blood volume, but at a slower rate. A very close correlation was observed both during increasing and decreasing changes. [3]

These results indicated that there is a delay in the appearance of a change in skin temperature. Although the change in skin temperature appears to initiate at the same time as the "stress change" is initiated, the change was slower than the blood volume. An example of those results is shown in figure 2.6 [3]. A cross correlation between the results shows that there is a time delay between blood volume and finger temperature. This is likely due to the time which is required for heat transfer from the blood vessel to the skin surface to occur. Furthermore, there are effects of heat dissipation which must be fully identified and defined. In order to use skin temperature measurement as a technique for monitoring change, a function for such effects would need to be identified. Based upon these results, direct measurement of skin blood volume is a preferred method.



Blood Flow Experiment (3 mins-EO, 12 mins-Relaxation, 5 mins-Stress):
Cross Correlation and Time Delay b/n Blood Volume & Finger Temperature

Figure 2.6: Comparison of Skin Temperature vs. Blood Volume [3]

2.2.4 Skin Conductivity

It has been shown that skin conductivity changes with imposed stress. Theoretically, sweat rate and volume could serve as measures of physiological strain.[4,6] Dr. Frenkel had also considered this as a possible method for measurement and his results indicate that this method may provide some useful data. [7] However, the use of this method has not been significantly developed to date. Further consideration of this method is warranted, however it is considered outside the scope of this present work.

CHAPTER 3

METHODS

3.1 The Equipment and Tools

3.1.1 Photoplethysmograph (PPG)

The PPG used for this study is:

Model	PPG13
manufactured by	MEDA SONICS
	Mountain View, CA
S/N	SP1733

A Photoplethysmograph (PPG) is a device which measures blood flow. A small sensor, Photopulse®, contains an LED and a phototransitor. The LED transmits infrared light which is reflected by blood in small superficial vessels; the phototransistor detects the reflection and converts it to an electrical signal. The PPG then modulates, amplifies and processes the signal so that it can be displayed and/or recorded. [9]

A PPG has clinical application for:

- Screening significant obstruction of extracranial internal carotid artery
- Assessment of venous insufficiency
- Differential of superficial and deep vein insufficiency
- Assessment of the healing potentials of skin ulcers
- Added safety to carotid endarterectomy by monitoring shunt blood flow during surgery [9]

In some cases, the PPG is used in conjunction with other equipment or evaluation techniques because of its sensitivity. This sensitivity must be considered when using the PPG. The sensor should be attached with minimum applied pressure, and strong incident light and patient motion should be avoided.[9]

Two different types of signals can be obtained. The PPG has a switch so that the amplifier can be either AC or DC coupled, depending upon whether there is a need to observe rapidly changing pulses or cumulative changes from a baseline of blood volume. [9] Each terminal has a potentiometer on the signal output to make it legible or fit the scale of the recording instrument. In this study, the PPG has been set simultaneously in both the AC coupling mode to measure pulsatile arterial waveforms, and the DC coupling mode to read the regional changes in venous blood volume.

3.1.2 Lap-top Computer

model:	LTE 5250
manufacturer:	Compaq Computer Corp.
	Houston, TX

3.1.3 Analog/Digital Signal Converter

A DAQCard™-1200, manufactured by National Instruments, was used to convert the analog signal obtained from the PPG into a digital signal legible to the computer.

3.1.4 LabVIEW Software

software used:	LabView 4.0
preliminary (for study):	LabVIEW Student Edition 3.1
manufacturer:	National Instruments
location:	TX
host software:	Windows 95
manufacturer:	Microsoft Corporation
	Bothell, WA

LabVIEW software is a Virtual Instruments type software; it applies a graphical programming language to combine data acquisition, analysis, presentation and storage in one package. Block diagrams are employed to create a virtual instrument (VI), which imitates real instruments, replacing the need for a circuit board to process signals and data. The block diagram represents the VI's source code; a front panel functions as an interactive user interface by simulating controls and indicators. [10]

This project was initiated with LabVIEW's *Student Edition* for training and then continued with the *Professional Version.* In both versions sample software programs are included. They can be used exactly or can be modified to perform the required acquisition, processing and display task. Of course, circuits can also be created "from scratch". For this project, existing sample programs and unique/individual programs have been used.

3.1.4.1 "Continuous Acquisition to Spreadsheet File": This program, which exists in the LabView package in the location C:\LabVIEW\Examples\Daq\strmdisk, required no modification. It was used directly to read data, convert it to a spreadsheet string, write and store it to the file until the stop button was pressed. It operates by continuously writing voltage data to a text file which can be read by spreadsheet programs.

It acquires data into a circular buffer, continuously, while the data is being read and processed. Once the program creates the file, it begins the data acquisition.[11] A copy of the front panel and the block diagram for this VI is included in Appendix 1-1 and 1-2.

3.1.4.2 "Plot": The "Plot" VI front panel and block diagram are illustrated in Appendix 1-3. This program was configured specifically for use in this study. It is designed to read data which is stored in a file as a spreadsheet string, and display it on a panel. The data acquired from each subject are shown graphically in section 4, *Results* using this VI. The graphical display of data segments used for analysis are also displayed using this VI in chapter 5, *Discussion*.

3.1.4.3 "Peak Detection Example": This VI was used in part to analyze the data.. The front panel and block diagram are shown in Appendix 1-4 and 1-5. The program was provided with the LabVIEW package and can be found in location C:\LabVIEW\Examples\Analysis\peakxmpl. This program contains example signals, and it exists in a loop to run continuously until the stop button is activated. It was modified to read data from a spreadsheet file, process it through the program, and stop at the end of the file.

The program includes adjustable thresholds, above and below which peaks and valleys may be identified. It displays the number of peaks and valleys found and, for each peak and valley, it identifies location, amplitude, and 2^{nd} derivative. The signals obtained in each file contained multiple valleys which corresponded with each singular peak. This program is not capable of correlating that group of valleys with its associated peak.

3.2 Experiment No. 1

3.2.1 The Protocol

Tests were performed in the author's home. A separate room was set-up specifically for the purpose of this study. The room was quiet, isolated with reasonable but low lighting. Surroundings were designed to a establish feeling of comfort and relaxation for the subjects.

The lap-top and PPG were neatly arranged on a desk. All settings and controls were adjusted and turned on prior to subject's arrival to minimize the potential for the subject to develop anxiety over being part of an experiment. A small desk lamp was also on the desk and a portable radio was discretely placed on the floor.

The experimenter sat at the desk with all controls easily within reach in order to minimize any distractions which could potentially be caused by movements. The computer screen was set facing the conductor and away from the subject's chair for easy monitoring and to avoid the potential for biofeedback. A large leather swivel and reclining chair with footrest were placed on the opposite side of the desk. Then the subject was then asked to step into the test room:

1. The subject was invited to sit in the easy chair and get comfortable.

2. While in the chair and facing the conductor, the subject was asked questions pertaining to the his personal medical history. The same questions were asked in each case. The answers were recorded on a prepared data sheet. 9See Appendix 1-6). The subject was told that he would be monitored during different levels of relaxation and that the whole test would last approximately 20 minutes. This discussion lasted about five minutes. The purpose was two-fold: first, to obtain potentially pertinent data and secondly, to allow the subject to reach a reasonable level of comfort/ rest.
3. The subject was then asked and assisted to swivel his chair around so that the back of his chair was facing the conductor. He was assured that the purpose for this was simply to prevent any of the conductor's movements from distracting him from his relaxation.
4. The Photopulse® sensor was then placed on the tip of the subject's left middle finger and secured with clear tape. Care was observed to prevent securing the sensor too tightly in order to avoid constriction of blood flow in the surface of the finger. The basic function of the sensor was described to the subject; the subject was assured that he would receive no shocks or other stimulus from the sensor. The purpose of this procedure was to eliminate any anxiety the subject may have about "being connected" to electrical equipment.

5. The subject was instructed to select a comfortable position and minimize his movement. He was told that the sensor was very sensitive to motion and he should try to keep his finger very still. He was further instructed that the conductor would advise when the test begins and when it ends, and that once the test begins, he should remain quiet and should not talk to me or move until he was advised that the test was over. The subject was then asked to confirm that he was comfortable and asked if he had any questions.
6. The subject was then given "formal" instructions. He was told to sit quietly with his eyes open until the light was turned off. He was told to immediately close his eyes when the light went off and try to relax as much as possible. He was further advised to, at that time, practice any relaxation techniques with which he might be familiar. He was advised that he should ignore any of the conductor's activity. He was then asked if he was ready to begin.
7. After subject's acknowledgment, the beginning of the test was announced.
8. The "zero set" button on the PPG was pressed.
9. Then the run button on the screen was pressed, and monitoring of the subject began.
10. At exactly 4 minutes into the test, the light was turned off.
11. At exactly 8 minutes into the test, the radio was turned on. The radio was not completely tuned into a station frequency so as to create an annoying noise. The volume was maintained at a sufficiently loud (but not exceptionally loud) level.

12. At exactly 12 minutes into the test, the radio was turned off.

13. At exactly 15 minutes into the test, completion of the test was announced.

3.2.2 Data Acquisition

The program entitled, "Continuous Acquire to Spreadsheet File" was used to acquire and store data. For Experiment No. 1, the following criteria were selected:

device: *1*

channels: *0:0*

scan rate: *120.00 scans/sec*

waveform chart: *x and y scales are cont. adjusted to fit current data*

all other values were in accordance with the default values of the program.

3.2.3 The Set-up

The equipment was set-up in accordance with figure 3.1.

3.3 Experiment No. 2

Upon completion of Experiment No.1, it was evident that the PPG was not operating in accordance with its manufacturer's specifications. It was disassembled and repaired. The PPG is capable of retrieving two signals, "arterial" and "venous". In Experiment No. 1, only one signal was obtained. Due to prior use and modification to the PPG, it was not clear which signal was obtained. Experiment No. 2 was designed to obtain both signals simultaneously.

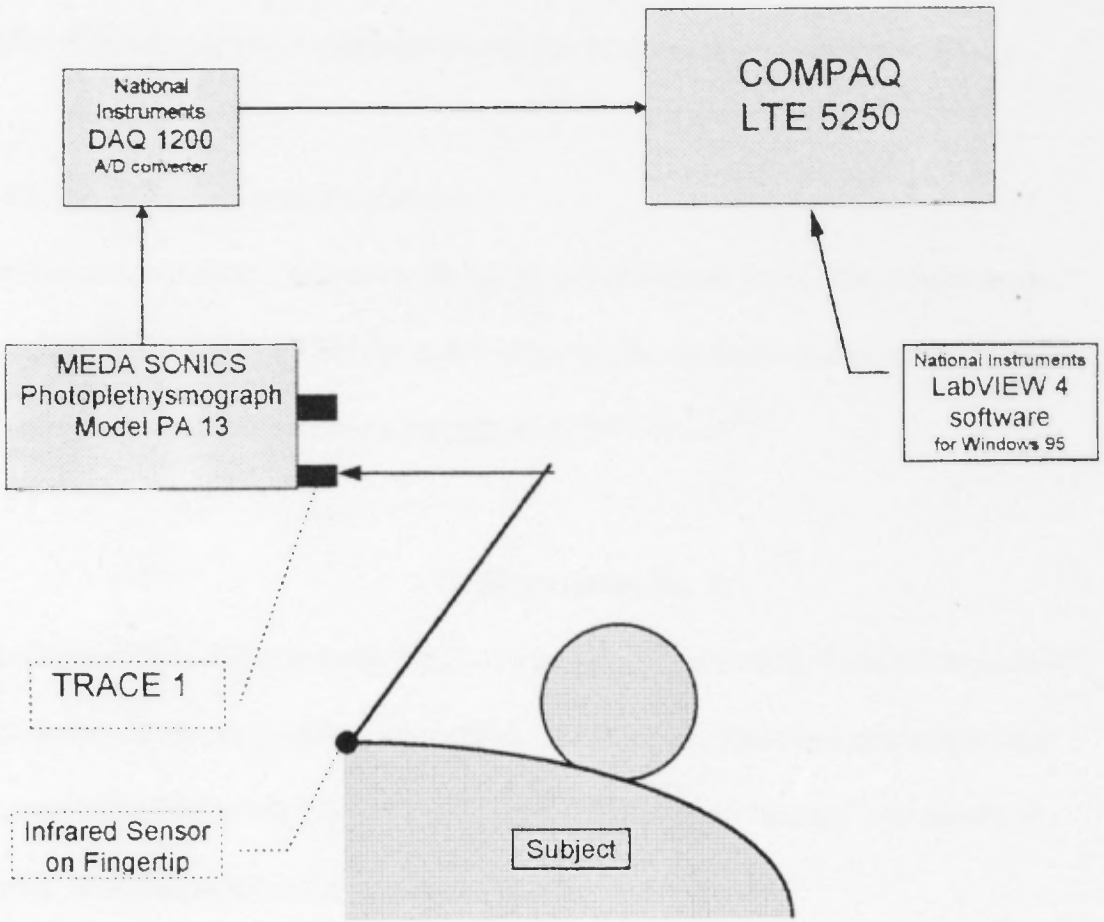


Figure 3.1 Equipment Layout No. 1

3.3.1 The Set-up

Wiring for the equipment was modified to obtain two signals, simultaneously, from the same sensor. A "Y" splice piece was manufactured to accept one signal from the infrared sensor, and split it to feed two separate inputs on the PPG. To prevent damage to the PPG and sensor wire, the "Y" splice was manufactured with plugs to mate with jacks provided on the equipment by the manufacturer. See figure 3.2.

3.3.2 Protocol and Data Acquisition

The Protocol remained identical to that used in Experiment No. 1. The procedure for data acquisition also remained the same, however, due to the acquisition of two signals, the setting *channels* was changed from '0:0' to '1:0'.

3.4 Experiment No. 3

Upon completion of Experiment No.2, two issues were identified. The first issue dealt with a concern about an initialization effect. The Protocol was adjusted to determine whether this effect existed. Step 8, 'pressing of the "zero set" button' was moved to Step 5, an earlier point in the sequence.

The second was one of practicality; each file extended slightly beyond the capacity of a standard 1.44 MB floppy disk. The length of each segment, "Rest", "Relax", "Stress", and "Recovery" was reduced to 3 minutes each. All other aspects of this experiment remained the same as Experiment No. 2.

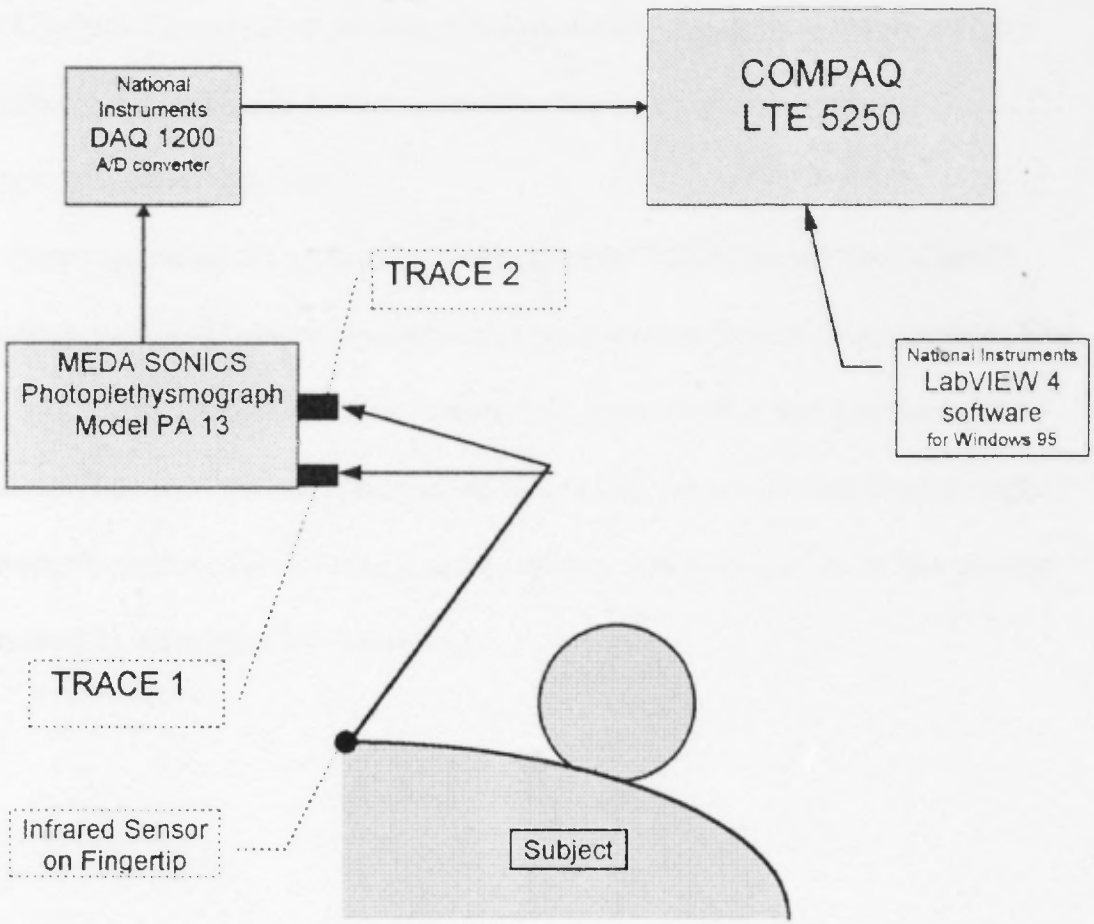


Figure 3.2 Equipment Layout No. 2

CHAPTER 4

RESULTS

As outlined in Chapter 3, three experiments were conducted in this work. Eight subjects were evaluated in Experiment No. 1, two were evaluated in Experiment No.2, and four subjects were evaluated in Experiment No.3. A summary of the personal data for each group of subjects from each experiment is first presented. A sample of the results from each subject tested in that group is included after the summary, the remainder of the results are included in Appendix 2.

Note that the summary includes a column called "Self Assessed Stress Level". Each subject was asked to provide a subjective interpretation base upon the question, "On a scale from 1 to 5, compared to your 'typical day', how stressful was your day, today?" Each subject then provided his opinion of the type of day he had. He interpreted a slightly more hectic than normal day as level 2, a very bad day was level 1, a better than average day was level 4, and a great day was level 5.

Table 4.1 Subject Personal Data Summary, Experiment No. 1

SUBJECT PERSONAL DATA SUMMARY

EXPERIMENT NO.1

Date of Test	Subject ID	Sex	D. O. B.	Age	Self Assessed Stress Level	Health Condition	Comments
					(1 thru 5)	(Y/N)	
1-Sep-97	1	F	11-Nov-61	35	2	N	Subject was not feeling well due to having experienced seasickness earlier in the day.
3-Sep-97	2	F	29-Jun-53	44	4	N	Experiences migranes.
6-Sep-97	3	M	11-Mar-32	65	3	N	
6-Sep-97	4	F	28-Dec-36	60	3	Y	Recent serious concussion. Experiences migranes.
7-Sep-97	5	F	18-Sep-18	79	3	Y	Crones. Sensor may have been fixed too tightly.
7-Sep-97	6	M	6-Sep-14	83	3	N	Subject did not close eyes during relaxation as instructed.
7-Sep-97	7	M	18-Sep-52	44	2	N	
7-Sep-97	8	F	24-Feb-63	34	3	N	Experiences hives in cold/ damp weather; reason unknown.

Stress Level Code	
1	Extremely High
2	Higher than Normal
3	Normal
4	Lower than Normal
5	Extremely Low

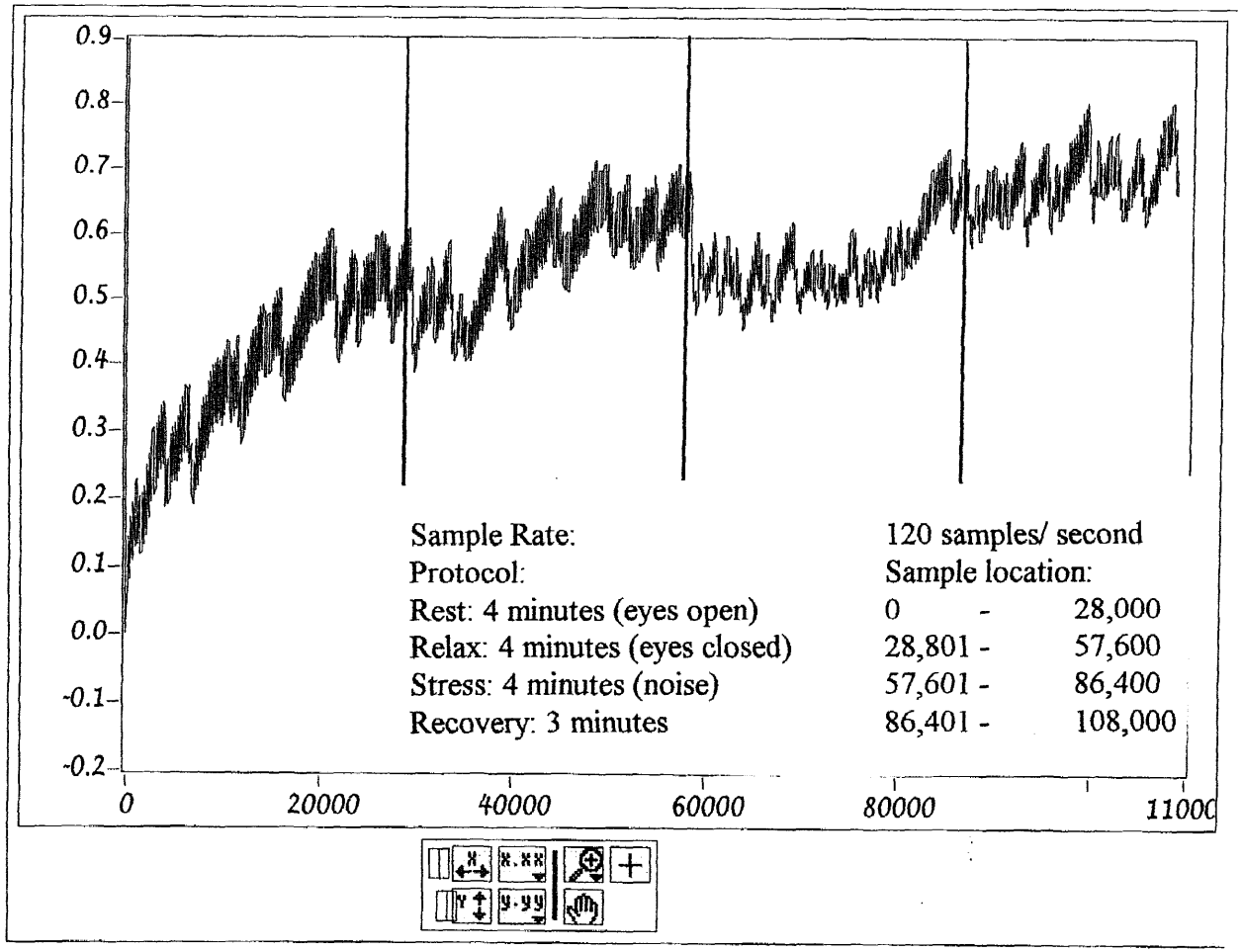


Figure 4.1: Results, Subject No. 1

Table 4.2 Subject Personal Data Summary, Experiment No. 2

SUBJECT PERSONAL DATA SUMMARY

EXPERIMENT NO. 2

Date of Test	Subject ID	Sex	D. O. B.	Age	Self Assessed Stress Level	Health Condition	Comments
					(1 thru 5)	(Y/N)	
15-Dec-97	21	M	19-Aug-50	47	3	N	
17-Jan-98	22	F	28-Aug-68	29	3	N	Experiences migranes. Test was abbreviated to 3 minute intervals (instead of 4) due to time constraints.
					Stress Level Code		
					1	Extremely High	
					2	Higher than Normal	
					3	Normal	
					4	Lower than Normal	
					5	Extremely Low	

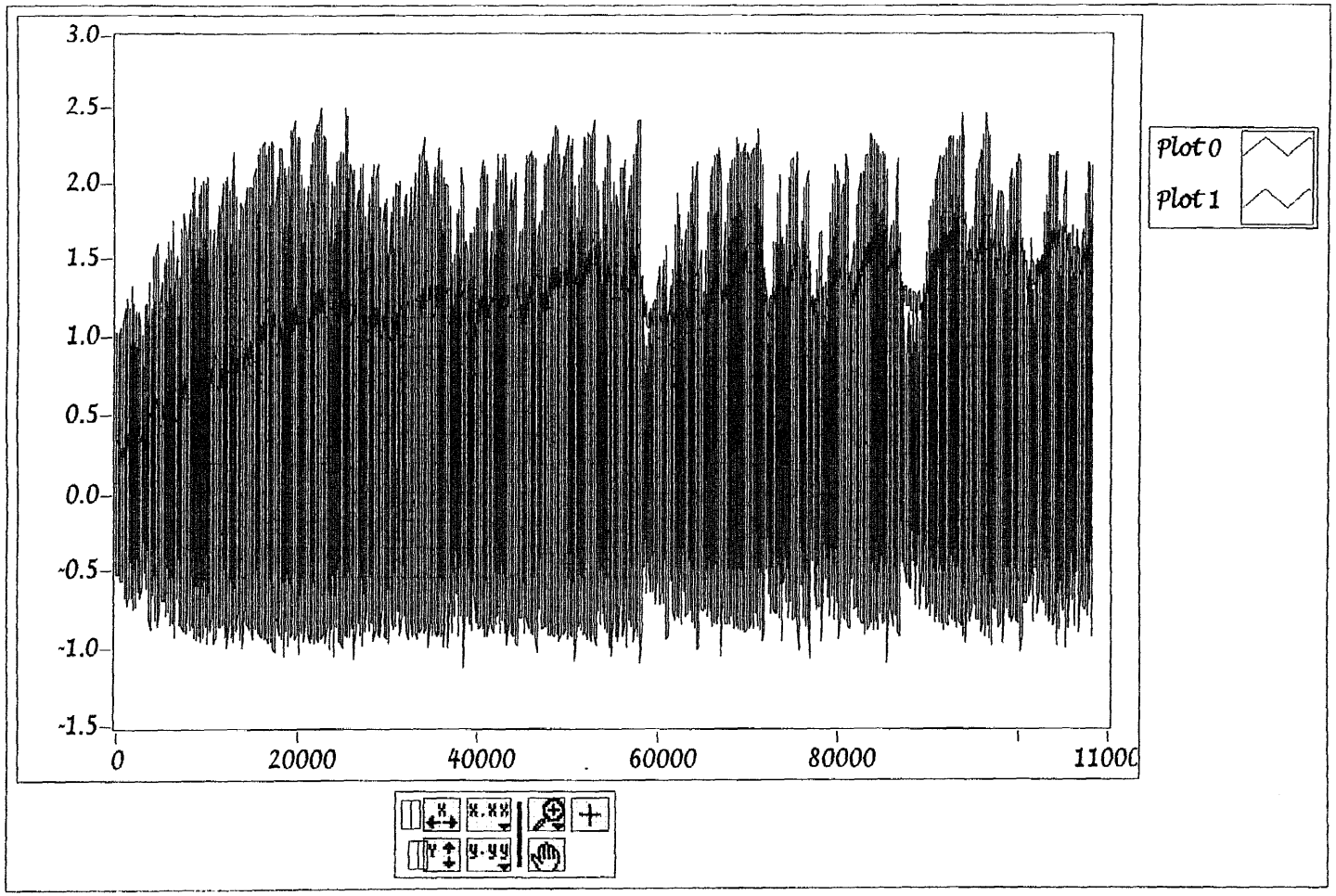


Figure 4.2: Results, Subject No. 21

Table 4.3 Subject Personal Data Summary, Experiment No. 3

SUBJECT PERSONAL DATA SUMMARY

EXPERIMENT NO. 3

Date of Test	Subject ID	Sex	D. O. B.	Age	Self Assessed Stress Level	Health Condition	Comments
					(1 thru 5)	(Y/N)	
11-Feb-98	31	M	14-Nov-27	70	3	N	Subject is in remission from lymphoma. Movement detected @ `2:00 and `11:10 min.
12-Mar-98	32	F	29-Jun-53	44	3	N	
12-Mar-98	33	M	19-Aug-50	47	3	N	
19-Mar-98	34	F	14-Mar-58	40	2	N	Subject explained after test that she likes loud noises--didn't "feel" like stress.
					Stress Level Code		
					1	Extremely High	
					2	Higher than Normal	
					3	Normal	
					4	Lower than Normal	
					5	Extremely Low	

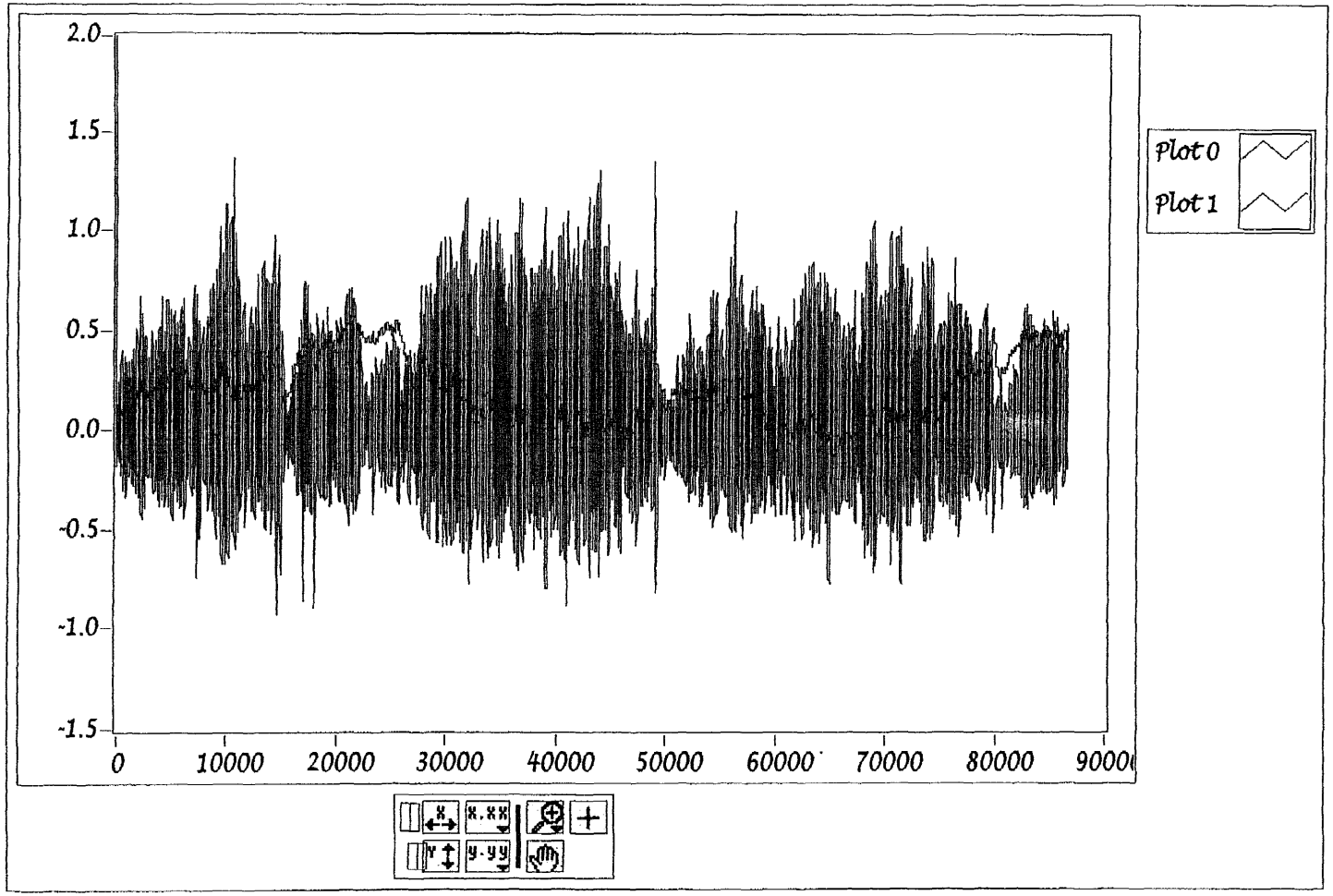


Figure 4.3: Results, Subject No. 31

CHAPTER 5

DISCUSSION

5.1 Neurological Control of the Circulatory System

5.1.1 A Simple Model

The relationship between the neural and cardiovascular systems provides an opportunity to evaluate the functionality of one via the performance of another. By measuring the change in blood volume, it can be shown that a description of the change in blood vessel radius can be presented. That information can be used to correlate to the relative level of sympathetic activity.

A model can be developed which reduces arteriole-capillary blood flow to a form which can be managed reasonably with mathematics. Though the model simplifies the shape and performance of the vessels, it is nonetheless a useful characterization for correlating measured blood volume to the level of sympathetic neurological activity, as illustrated in figure 5.1.

As mentioned earlier, the skin arterioles are controlled only by sympathetic activity. Arterioles contain smooth muscle, which can either relax causing the radius to increase, or contract and cause a decrease in radius. [4] Dilation or constriction of the skin arterioles is therefore directly related to sympathetic activity. Equally significant is that no parasympathetic activity is involved in this mechanism (i.e. dual innervation does not exist in this case), enabling this study to focus on the effects of purely sympathetic activity without the complication of other neurological activity.

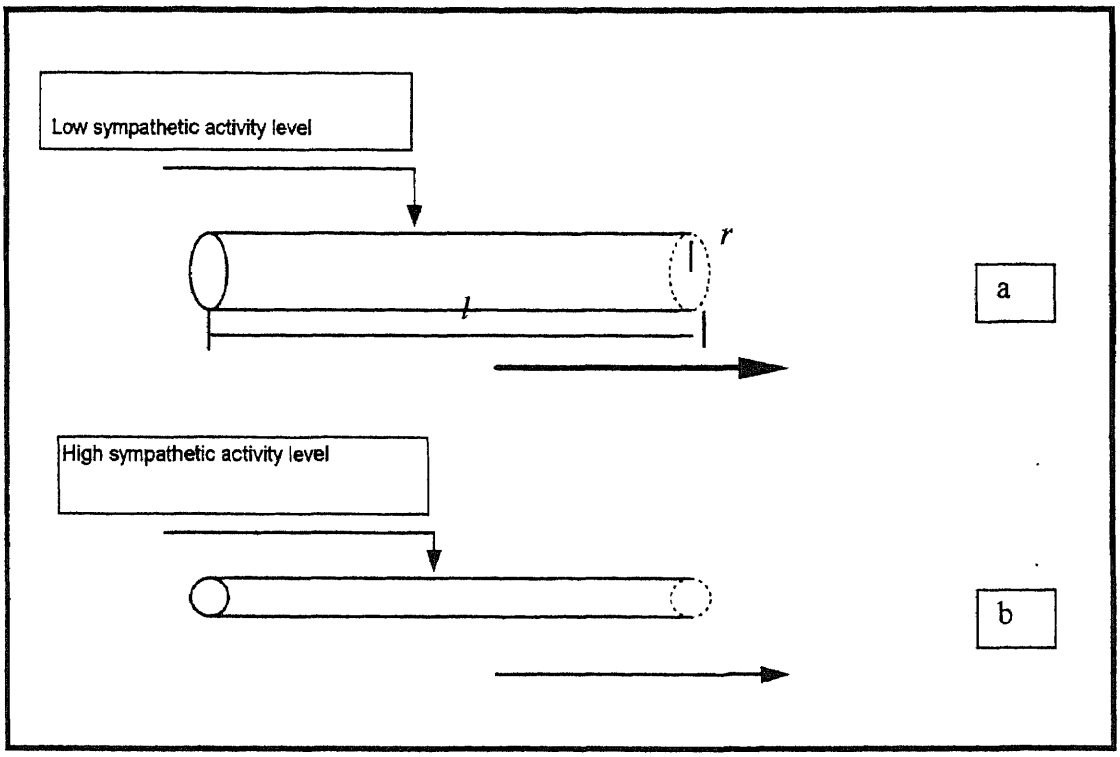


Figure 5.1 Neurological Control of the Circulatory System (a) illustrates a high blood flow rate as a result of vasodilation which occurs in the absence of sympathetic activity; (b) illustrates lower blood flow rate and vasoconstriction which occurs as a result of higher sympathetic activity.

Based upon this known physiology, it is appropriate to postulate that by measuring arteriole blood volume in the skin on the fingertip, one may be able to measure the degree of sympathetic activity in an individual. By establishing a simplified model of blood volume in an arteriole, i.e. a horizontal, cylindrical tube of elastic radius r, the blood volume, V, can be expressed as a function of that elastic radius.

Given a fixed segment of blood vessel length, l, the blood volume in that segment will vary in proportion to the square of that same vessel radius, in accordance with equation 5.1.

$$\Delta V = \Pi \Delta r^2 l \tag{5.1}$$

Since the vessel radius is controlled primarily by sympathetic activity, then a correlation between the change in blood volume and the level of sympathetic activity can be established. Furthermore, since increase in sympathetic activity is generally associated with increased stress levels, a correlation can be proposed directly from measured data—blood volume in the skin at the fingertip—and the relative level of stress of that individual.

$$\Delta V \sim \Delta r^2 \sim \Delta \text{ sympathetic activity} \sim \Delta \text{ level of stress} \tag{5.2}$$

5.1.2 Consideration of Blood Flow Behavior

This correlation can be considered valid when the flow properties of the blood into and out from the designated volume remain consistent. If there were varying flow behavior, it would need to be considered as to whether the change in flow or flow rate would affect the volume of blood at that given point in time. In this study, it is assumed that no change in flow behavior occurs. Blood flow is considered only to be a function of the pressure and resistance in the vessel, as shown in equation 5.3.

$$F = \frac{\Delta P}{R} \tag{5.3}$$

where:

F represents blood flow

ΔP is the pressure difference as measured between two points along the length

R represents the resistance to flow

and R can be expressed as a function of the radius:

$$R = \frac{8\eta l}{r^4 \Pi} \tag{5.4}$$

where:

η represents the fluid (blood) viscosity

l is the tube length

r is the inside radius of the tube

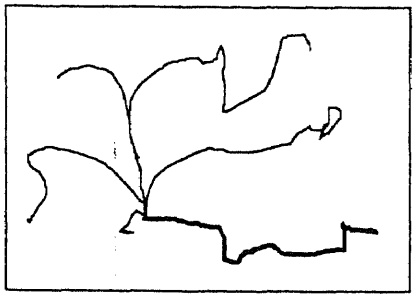
$8/\Pi$ is a constant

This application of the Hagen- Poiseuille law is valid because the following conditions have been met[12]:

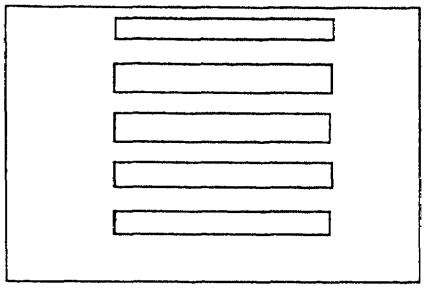
1. The flow is laminar. This is the case for most normal blood flow except possibly near valves or where an occlusion or obstruction may be present.[13].
2. The density of the blood is constant. This is valid within the context of these experiments.[12]

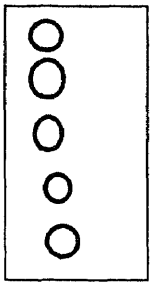
3. The flow is at steady state. This can be assumed for a first approximation. However, this is not exactly the case, because changes in blood flow in fact do occur, especially at the point of change in stress level. Further refinement of a model may need to account for the fact that flow at the transition points is changing. [12]
4. Blood behaves as a Newtonian fluid. Although blood is not a Newtonian fluid, it behaves closely to a Newtonian fluid within the normal physiological range: red blood cell count within the range of 40% - 50%. [13]
5. End effects are not considered. It is assumed that the length of the vessel is long enough to permit full development of the parabolic velocity profile used to describe flow behavior in this model. [12]
6. The fluid behaves as a continuum, and there is no slip at the wall. For this type of fluid, this assumption is valid for a first approximation. Future, more refined models may require that the actual effects of flow through arterioles and capillaries be reviewed for conformance to these criteria.[12]

For any evaluation conducted where these conditions are not met, e.g. for subject with extreme changes in stress level during testing, this model may not be valid.

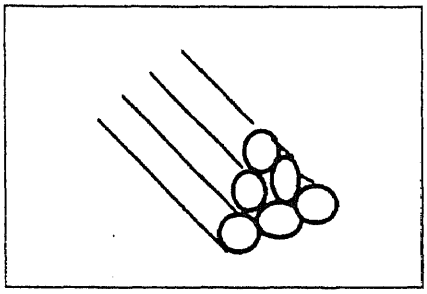


(a) conceptual description of blood vessels branching in the skin:
- multi-directional, 3dimensions
- non-linear
- varying sizes
- non-rigid walls, variable diameter

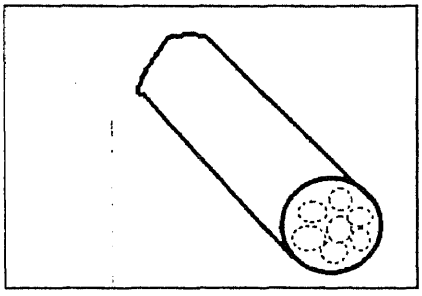




(b) assumptions for first approximation:
- same direction
- linear
- close to same size
- rigid tube, same diameter



(c) closely packed, sharing "inside" walls.



(d) no walls between individual vessels.

Figure 5.2: Model for Understanding the Relationship Between Blood Volume and Vessel Diameter

5.1.3 Deriving the Model

Figure 5.2 shows the assumptions used in the progressive derivation of this vessel flow model from the actual physiological arrangement of blood vessels. Figure 5.2(a) depicts the actual arrangement of vessels in the fingertip; it shows an arteriole feeding into many capillaries which branch in multiples and in many directions. None of these vessels flow in a straight line, their sizes vary, and the vessel walls are not rigid, so their diameter may vary along their lengths. The first step to simplify this arrangement is shown in figure 5.2(b). Each vessel is considered to be flowing in the same direction, nearly the same size, and a rigid tube with the same diameter along its entire length.

Further simplification is still needed. Figure 5.2(c) shows that each vessel is considered to be very close to the next, and therefore considered to share a common wall with its neighboring vessel. Going one step further, figure 5.2(d) shows that each vessel shares a wall which is so thin, that it is negligible, and so the bundle of closely packed vessels can be treated as one. These steps enable one to consider the bulk flow of blood in the finger tip as that which travels through one linear tubular vessel with an adjustable radius, the size of which is controlled by the level of sympathetic activity, see figure 5.1. Note that the model requires that although the radius is changeable, it remains constant along the tube length for each condition.

5.2 Effect of Other Physiological Controls

It can be seen from figure 2.3 that many factors affect the arteriolar radius. In order to establish good control in these experiments, it is critical to understand which of these factors, besides the sympathetic nerves, may be contributing to the measured changes in blood flow. It is preferred to design the protocol and technique so that any other controls would not apply, that is, the effect of any of these factors may be eliminated from each experiment so that a pure measurement of sympathetic activity may be established.

For each subject, it is necessary to know whether these factors contributed to the experimental results. Given the conditions and duration of the experiments, certain assumptions can be made. For example, since the experiments are conducted while the subject remains motionless, the effects of active hyperemia—which is a result of increased metabolic activity—shall be considered as negligible.

For this first step of the evaluation, it can be assumed that the mean arterial pressure remains relatively constant during the experiments, and any effects due to local controls are negligible. The room remained at a constant, comfortable temperature, so the effects of temperature can be discounted. Furthermore, since all subjects tested have normal health patterns, remained comfortable and motionless, and were not taking any medications, the effects from hormones can also be assumed as negligible.

All these assumptions would ultimately need to be verified. In addition, it must be noted that for abnormal subjects, or for a not so well controlled environment, or, for even just a stronger degree of stress change, these assumptions might not be valid. Extreme caution must be exercised so as not to oversimplify or overlook one of these factors which may be contributing to the results in such cases.

5.3 Experiment No.1

Upon review of results from Experiment No. 1, it was suspected that the signal which was acquired through the PPG was likely the "venous" signal. If this is indeed true, the signal includes a time delay and therefore represents some average value for blood flow, but no instantaneous value.(See section 3.1.1). Based upon the belief that the instantaneous values, i.e. the "arterial signal" contain data which may ultimately prove to be most useful, and, secondly, since it was not possible to confirm which signal was actually measured, it was decided that both the arterial and venous signals need to be acquired and compared.

5.3.1 Equipment Sensitivity: Bracing Recommended

The first observation which must be considered is the sensitivity of the equipment. It is extremely sensitive to motion by the subject. Very slight motion, such as a deep breath and even involuntary finger twitching causes extreme changes in the value recorded. Data acquired from subjects nos. 2 and 5 must be discarded due to excessive motion. It is recommended that future studies apply a comfortable but secure rest or brace for the finger from which data is being taken. Care must be used to prevent occlusion of flow or cause for anxiety with the brace. A padded armrest with adjustable ties and which can be secured to the chair armrest is envisioned.

5.3.2 Trends Agree with Expectations

Figure 5.3 (a) & (b) show the location in the data where changes were created during testing of two typical subjects from Experiment No. 1. There are certain consistencies amongst the results, most remarkably at the points of change. At each point where a change was produced, a significant change in the value representing the relative blood volume is noticed. This corresponds with the expectation that blood volume changes occur when the neurological state of the subject changes.

Furthermore, the direction of change agrees with that expected based upon known physiological responses. Note that the amplitude of the signal, for most cases, increases from the transition from rest to relaxation and again from stress to recovery, while it decreases at the transition from relaxation to stress. This indicates increased blood volume when stress is relieved and decreased blood volume when stress is increased.

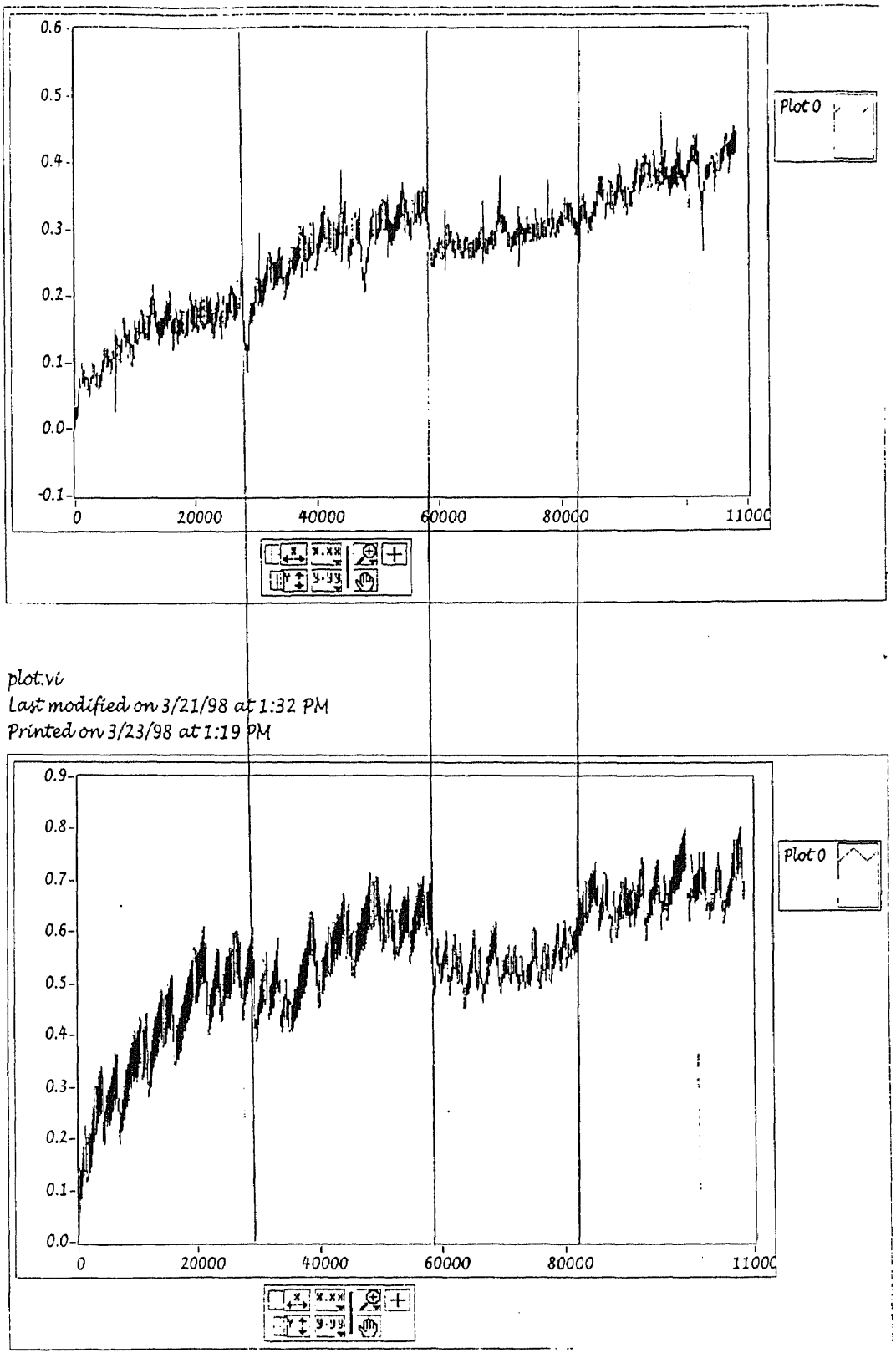


Figure 5.3: Effects of Imposed Changes in Stress Level on Blood Volume for two subjects: Subject No. 1 (top) and subject No. 8 (bottom)

The preliminary indication from this data is that this method is useful for detecting changes in blood flow. It provides detectable and measurable differences in blood flow when a change is induced, and that difference is in agreement with expectations based upon known physiological behavior.

5.3.3 Signal Magnitude is Arbitrary

The strength of the measured signal can be controlled by a potentiometer on the PPG. Significant effort was applied to conduct all tests with the dial in the same position. However, the potentiometer turns freely and has no calibration, so there may be slight variations between tests (no variations were made during each test). In addition, the starting position of the signal on the y-axis is set to zero at the beginning of each test. Therefore, the specific amplitude and position of the recorded signal are arbitrary. The relative size, however, i.e. change in position from "peak to peak" or from "peak to valley" is significant.

5.4 Experiment No. 2

5.4.1 Elimination of Uncertainty, Obtaining Two Signals from the Same Source

The objective of this experiment's design was to obtain both an "arterial" (instantaneous) and "venous" (time constant delay/averaged) signal, simultaneously and from the same source. In an earlier study[3], a student had attempted to achieve this using the PPG and two signal detectors, each placed on two different fingers.

In an effort to develop a well controlled experiment, a different approach from that earlier work was prepared. First, the PPG was repaired to operate as it was designed. As such, the PPG is capable of reading a signal and processing it simultaneously into a "venous" result or an "arterial" result. Secondly, there is concern that data acquired from two different fingers, although potentially very similar, may not be exactly the same.

Therefore, to eliminate that variable in the design of the experiment, the "set-up" was re-wired. The wires were laid-out so that there was only one source (one finger) which generated the signal, and that signal was split and processed simultaneously to produce both a "venous" and an "arterial" result (See Equipment Layout No. 2: connections for each are identified as 'Trace 1' (arterial) and 'Trace 2' (venous) on the PPG).

This change in wiring essentially added the ability to acquire an arterial signal without affecting any other differences to Experiment No. 1. A second group of subjects were evaluated. The protocol for this round of experiments remained identical to the protocol for Experiment No.1. From this information, an accurate comparison between the two signals may be obtained.

5.4.2 Comparison of the Arterial and Venous Results

The results collected from Experiment No.2 enable confirmation that the signal from the data collected in Experiment No.1 was the venous signal. The venous signal is a processed signal and includes a delay and averaging function. The arterial signal is an unprocessed or 'raw' signal. Figure 5.4 (a) & (b) show a close-up of both signals obtained from a typical subject during Experiment No.2. The segments selected are transition points where the trend of each signal can be most notably compared. The venous signal is the smaller, smoother signal. It can be seen, in each case, that due to the effects of processing on the venous signal, that the change is less dramatic and is delayed compared to the arterial signal.

The venous signal may, in fact, be more useful for clinical applications where data needs to be monitored for feedback or where trends need to be observed. It is, however, not as accurate a picture as the arterial signal. For the purposes of this evaluation, the raw arterial signal, or some other processed form of that signal may be more desirable because it gives a more accurate picture of what is happening instantaneously.

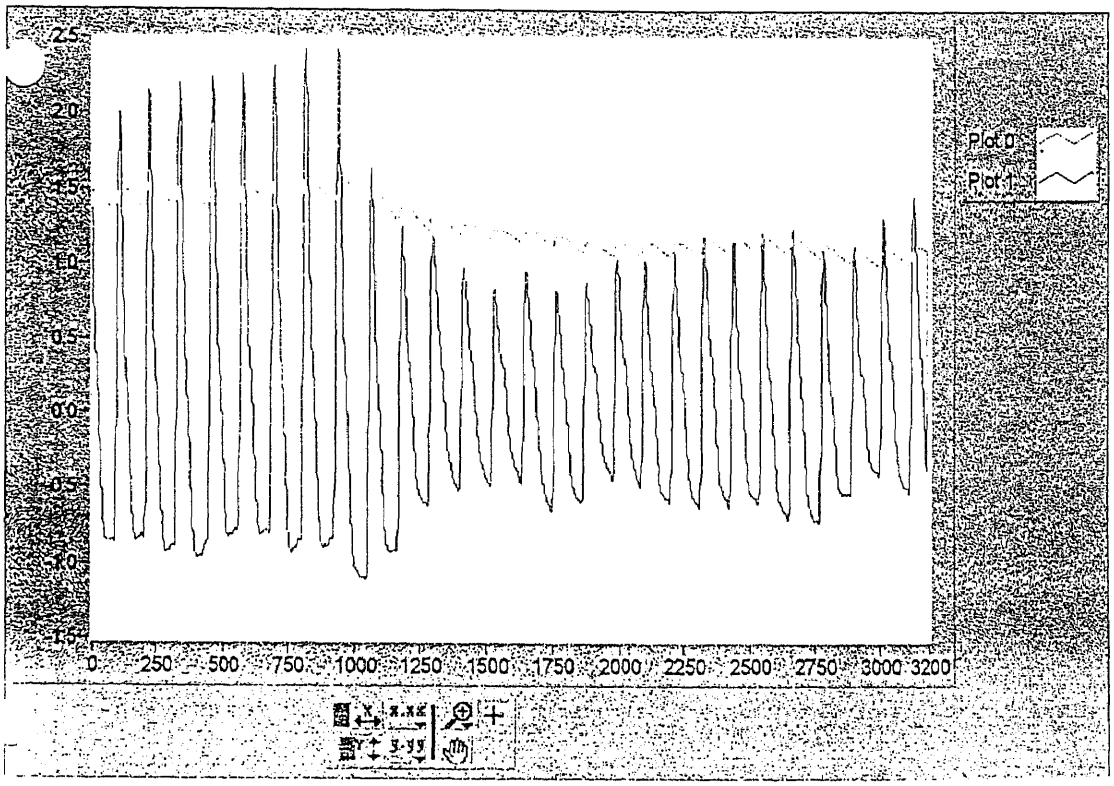


Figure 5.4: Comparison of the trends from the Venous and Arterial Signal, plot 0: venous, plot 1: arterial.

5.5 Developing a Correlation Between the Signal and the Events

5.5.1 Selection of the Appropriate Signal

As just mentioned, it is reasonable to proceed with this evaluation using the arterial signal on the basis that the arterial signal provides more accurate and immediate data describing the actual events. The question is, therefore, "how can the signal be used for such purpose?" More detailed analysis is needed. That information must be processed into a useful correlation between the change in blood volume and the varying degrees of stress.

In this evaluation, it must be remembered that the amplitude of the signal is somewhat arbitrary. (See section 5.3.3) Therefore, direct correlation of the amplitude to the degree of change should be avoided. Rather, the relative difference between each position on the y-axis of the signal be compared.

To do this, the signal must be processed. Some reasonable and potentially useful ways to process the signal include evaluation of:

- Peak to Peak Variation
- Peak to Valley Variation
- Percent Difference in Position Between Peak and Valley
- Percent Difference in Position Between Peaks
- Percent Difference in Position of Peak from Average of Previous Peaks

5.5.2 Correlation of Peaks and Valleys

This type of evaluation requires that the peaks and valleys of the signal be identified along with its coordinates. This is fairly straightforward, however, a challenge is presented by the need to correlate a peak with its respective valley. Figure 5.5 shows a "close-up" of the arterial signal which reveals that, for each peak, there are multiple corresponding valleys. It was attempted by to extract the peaks and corresponding valleys by two methods.

5.5.2.1: Use of "Peak Detection Example": It was desired to obtain the location and magnitude of each peak and corresponding valley for both the arterial and the venous signal. Attempts were made to use "Peak Detection Diagram" for this purpose. However, due to its inability to provide a correspondence between a group of valleys and their associated peak, this was not an efficient approach. Significant modification to the program would be required.

Nonetheless, this method should not be abandoned for future work. It may be very possible to modify this program, or develop one with similar features, to achieve the desired results. The problems with the use of this method were twofold. The first is relatively simple to address. The data file collected for each subject was very long and may be causing some errors. It is recommended that each file be reduced to smaller segments prior to processing.

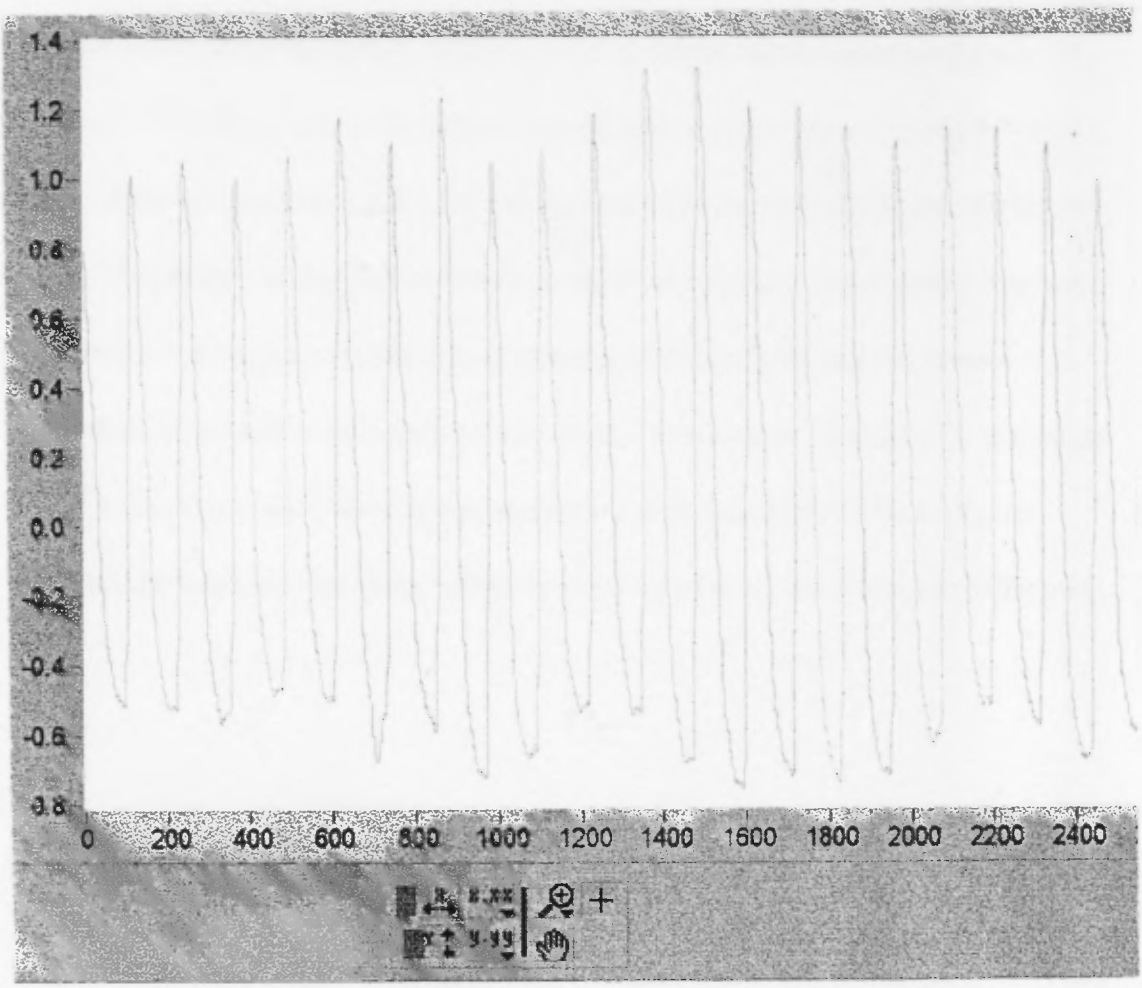


Figure 5.5: Close-up of an Arterial Signal

The second issue is more complex and caused the need to find alternative methods. This issue has to do with the fact that multiple valleys correspond with one peak. This program, "Peak Detection Example", as written, is not able to correlate the multiple valleys with one peak. In order to use this program, it would need to be modified. A subroutine, or loop, would need to be included after the identification of each group of valleys to either average that value or select the largest of those values, and use that location as a single valley to correspond to the accompanying peak. To accurately identify a 'group of valleys', their relatively close proximity along the x-axis in comparison to the next group would need to be considered in that subroutine.

This effort was attempted but it should be noted that it is not trivial. Not only does such work require very high programming proficiency, it requires serious consideration as to how the group of valleys can be accurately identified by one value. There is significant work for a future researcher to both address the best way to represent the value for the valley and to develop a program which operates effectively.

5.5.2.2 "Manual Extraction": In order to obtain timely information, in this case, the peaks an their corresponding valleys were extracted manually. First, a representative file, "SUBJECT 21", was selected. From viewing the "Plot" of the entire file for this subject, three segments of interest were identified, and their positions noted, as shown in figure 5.6. These segments were selected because a significant change in blood volume was observed at these locations. In addition, the observed changes in blood volume correspond to the change in state of the individual between relaxation and stress. For example, 'segment a' is selected in the time when there is a change from relaxation to stress. Another change is observed between stress and recovery; this is shown in 'segment b'. "Segment c' shows large fluctuations after the initial change to stress.

'Segment a' was established as that which lies between 56,000 and 64,000 (each value representing the actual number of the sample taken); 'segment b' was established as that which lay between 84,000 and 94,000; 'segment c' was that falling between 63,000 and 69,000. A final file for each segment containing only peaks and valleys was established. The plots for each segment, 'a', 'b', and 'c' are illustrated in Appendices 3-1, 2, and 3, respectively.

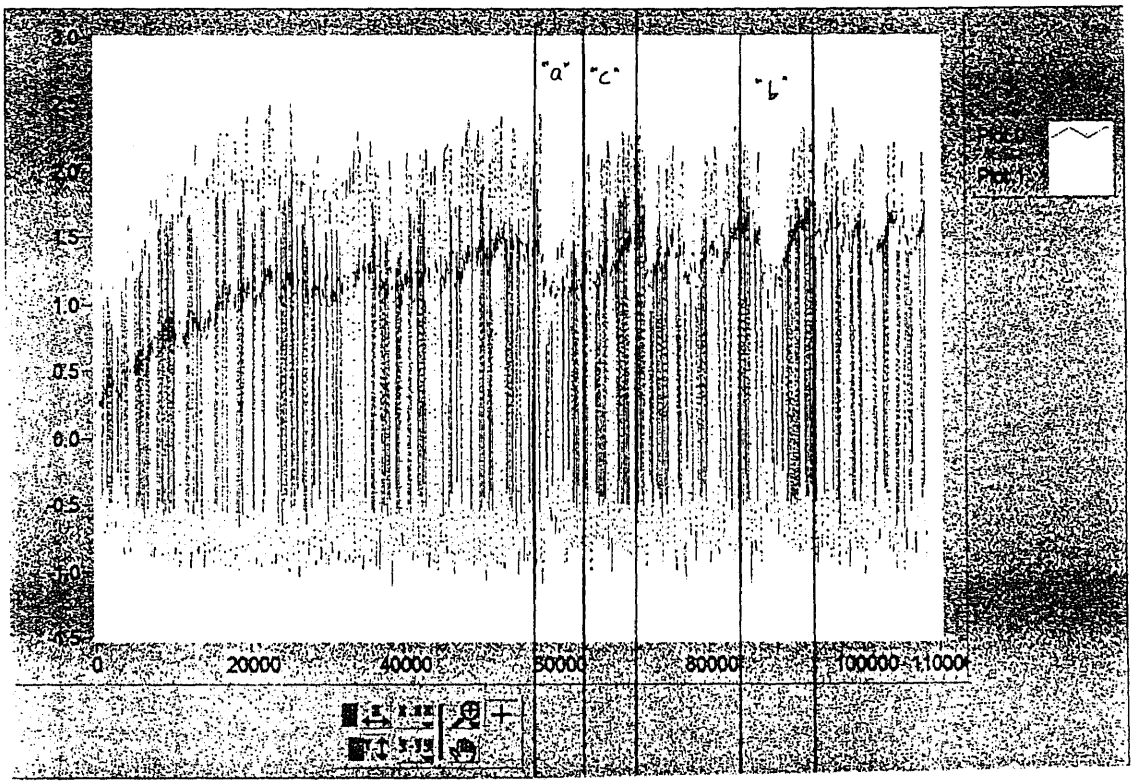


Figure 5.6: Three segments of interest from Results of Subject 21.

5.5.2.3 Data Correlation After Manual Extraction of Peaks and Valleys: As further described in Section 5.5.2.2, the peaks and corresponding valleys for parts of one file were extracted manually. This was extremely time consuming and is not the recommended method to be used in further development. Rather, it was used only to help gain an understanding of the available data so that it can be further evaluated on a preliminary basis. As it has been determined from the preliminary evaluation that the data obtained is useful, it is recommended that the effort be invested in developing a computerized processing method as outlined in Section 5.5.2.1.

As noted earlier, the results of the manual extraction of peaks and valleys for certain segments of one subject's file are plotted in Appendices 3-1, 2, and 3. From one of these segments, (segment "a" of Subject 21, shown in Appendix 3-1), the difference between the peak and valley were calculated and plotted. The results of this exercise are shown in figure 5.7.

This was achieved using an EXCEL spreadsheet, WORD files, and LabVIEW plot software. Again, it is important to note that this was cumbersome. The plot diagram in LabVIEW is not compatible with EXCEL, and translation via WORD was required. It is desired that such an operation be performed directly from the raw signal, and future researchers should explore other methods or software.

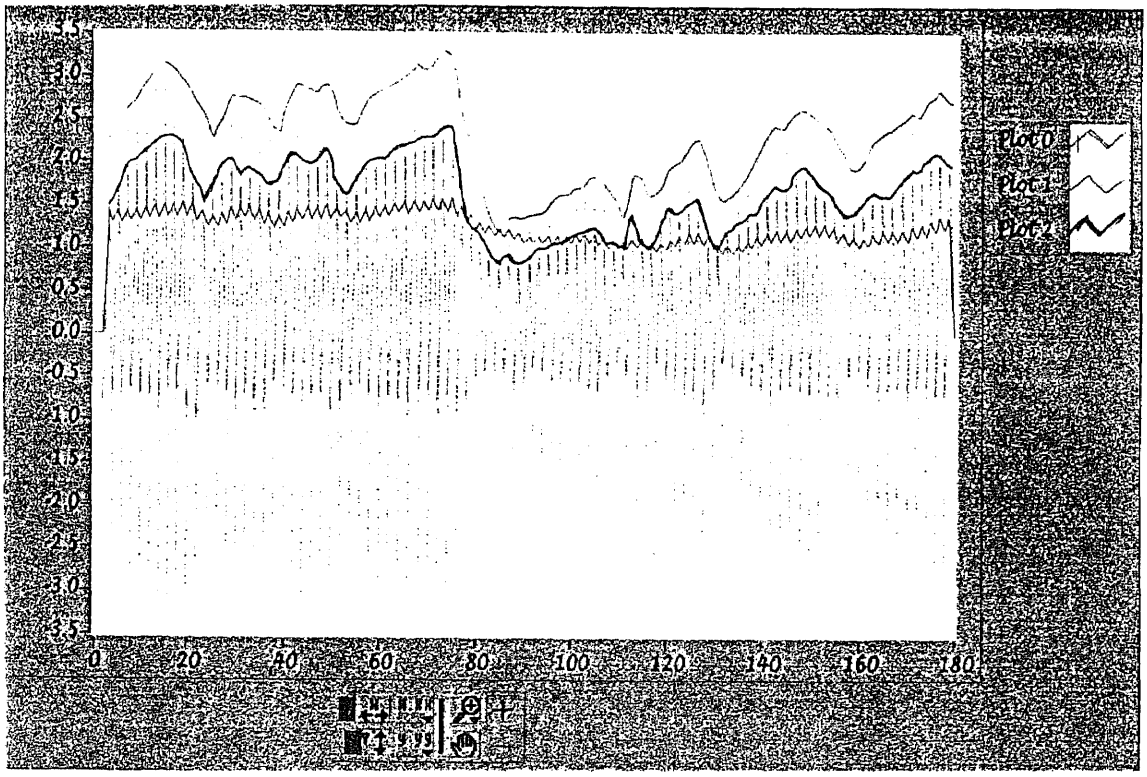


Figure 5.7: Comparison of Three Signals; where the venous signal (Plot 0), arterial signal (Plot 2), and the difference between peak and valley (Plot 1), are displayed.

A line has been drawn, by hand, from peak to peak of each the raw arterial signal, and the processed "difference" signal. Visual inspection identifies a very close correlation between each line.

Again, this is only a preliminary evaluation. This correlation should be verified using proven techniques as established by signal processing engineers. Such techniques involve the direct comparison of first, a signal against itself as the benchmark 100%, and then of the two different signals in the most synchronous position along the y-axis. A high percentage value using such a method confirms the high degree of correlation.

It is important to remember that the data was extracted and processed manually, so some human error may exist. Furthermore, this result is only from a small segment from one file. Multiple files should be evaluated prior to verification of a true correlation. However if a correlation indeed exists, it may be suggested that the arterial signal can be processed directly. This would eliminate a significant degree of complexity in processing the signal.

Recall, however, that one of the purposes of finding a "difference value", rather than a direct value, was to eliminate the arbitrary nature of the signal amplitude. From the applied correlation method, it should be explored as to whether a scalar value or equation can be identified to adjust the raw signal amplitude to the "difference value".

5.5.2.4 Processing Methods: Figure 5.8 (a) shows, again, the venous and arterial signals—peaks and valleys only—for segment 'a' from subject 21. Figure 5.8 (b), directly below it, on the same scale for the y-axis, (but different scale on the x-axis) are Plot 0, the "raw arterial signal", which is repeated for clarity in this scale, and a calculated value representing the percent change from one peak to the next peak, and likewise, from one valley to the next. The value was calculated by:

$$[\text{Peak\#2} - \text{Peak\#1}] / \text{Peak\#2} * 100 = \%\ \text{change} \qquad (6.1)$$

The difference between valleys was calculated similarly.

There are two aspects of the % change graph which should be considered. First, the height of the spike is indicative of a strong change, but secondly, the width of the spike corresponds to the duration of change. It is desired to establish a correspondence to the trend indicated by the position of each peak, and still eliminate the arbitrary magnitude factor.

By looking at the calculated signal, it would appear as though there are many changes in this segment. Though careful study may be applied to discern the "major changes' from the "minor fluctuations", it is difficult to interpret from this signal. Therefore, alternate calculations may be considered.

To eliminate some of the distraction from this signal, but still retain data which provides an accurate correspondence to the trend in peak values, alternate methods of calculation were considered. Figure 5.8 (c) shows the same signal as 5.8 (b), however, the values for the % difference between valleys were eliminated, and replaced by the % difference between its corresponding peak. Figure 5.8 (d) shows the same signal, but with only the peak values. The values for the valleys have been eliminated from both the raw arterial signal and the calculated % difference from the previous spike.

Finally, figure 5.8 (e) shows the peak values only for the raw arterial signal, and the % difference of a peak compared to the average value of the previous 5 peaks. This signal lends itself to legible correspondence to the trend of the individual peaks. The averaging calculation helps to eliminate spikes due to abrupt, short lived changes. Note, however, that unlike the venous signal—which includes an averaging function—this signal exhibits no time delay, and may provide a better description of the magnitude and duration of the change.

Though this averaging calculation successfully eliminates "noise" so that an effective correlation can be established, the value is independent of the arbitrary settings of the equipment and relative only to the previous level of activity within the same individual. Though the calculations used in this method may require further optimization, it is an appropriate method by which the change in sympathetic neural activity may be identified.

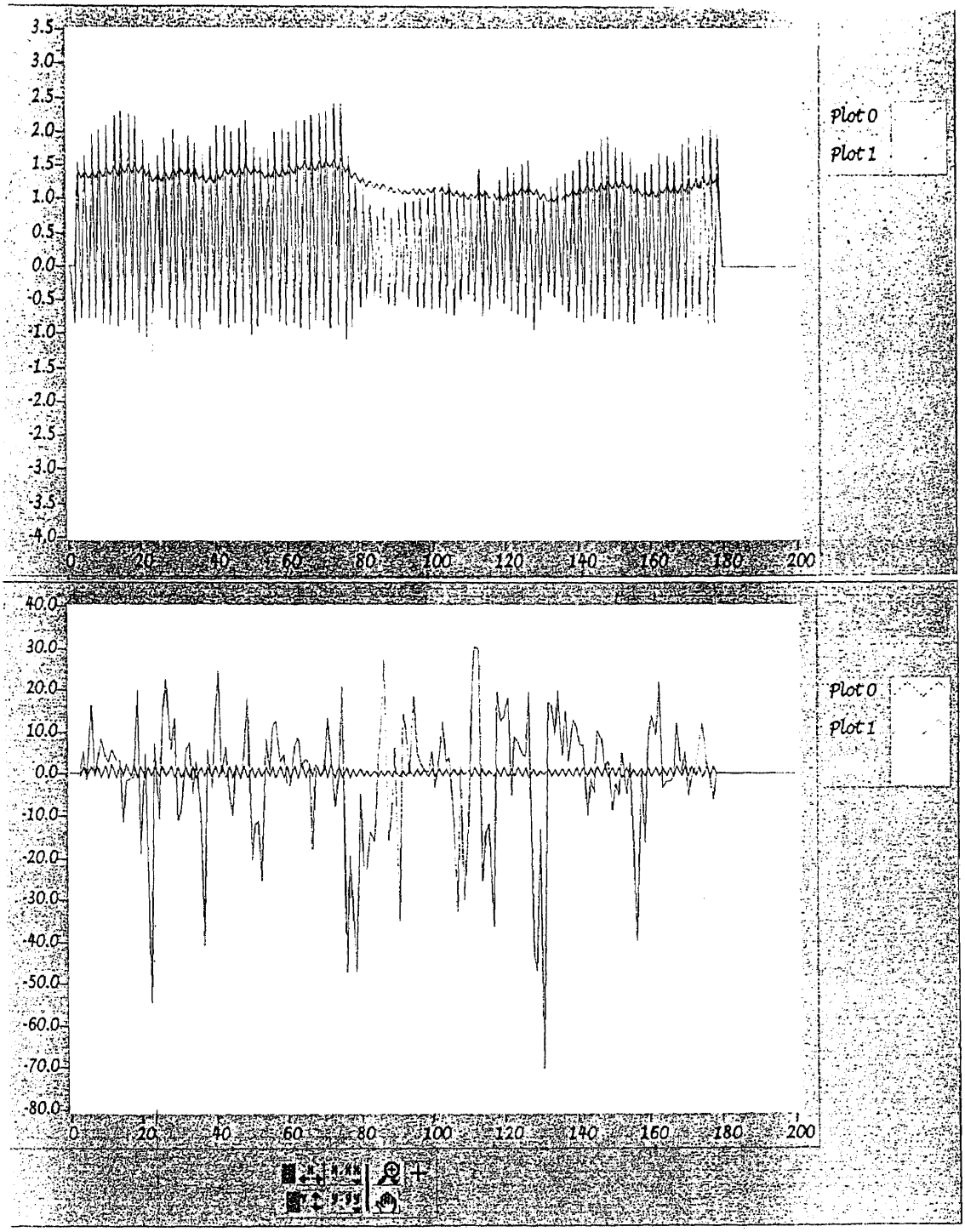


Figure 5.8 Processing Methods (a) subject 21 'segment a' arterial peaks and valleys only (b) plot 0: raw arterial signal peaks and valleys; plot 1: % difference between peak and previous peak and likewise between valleys

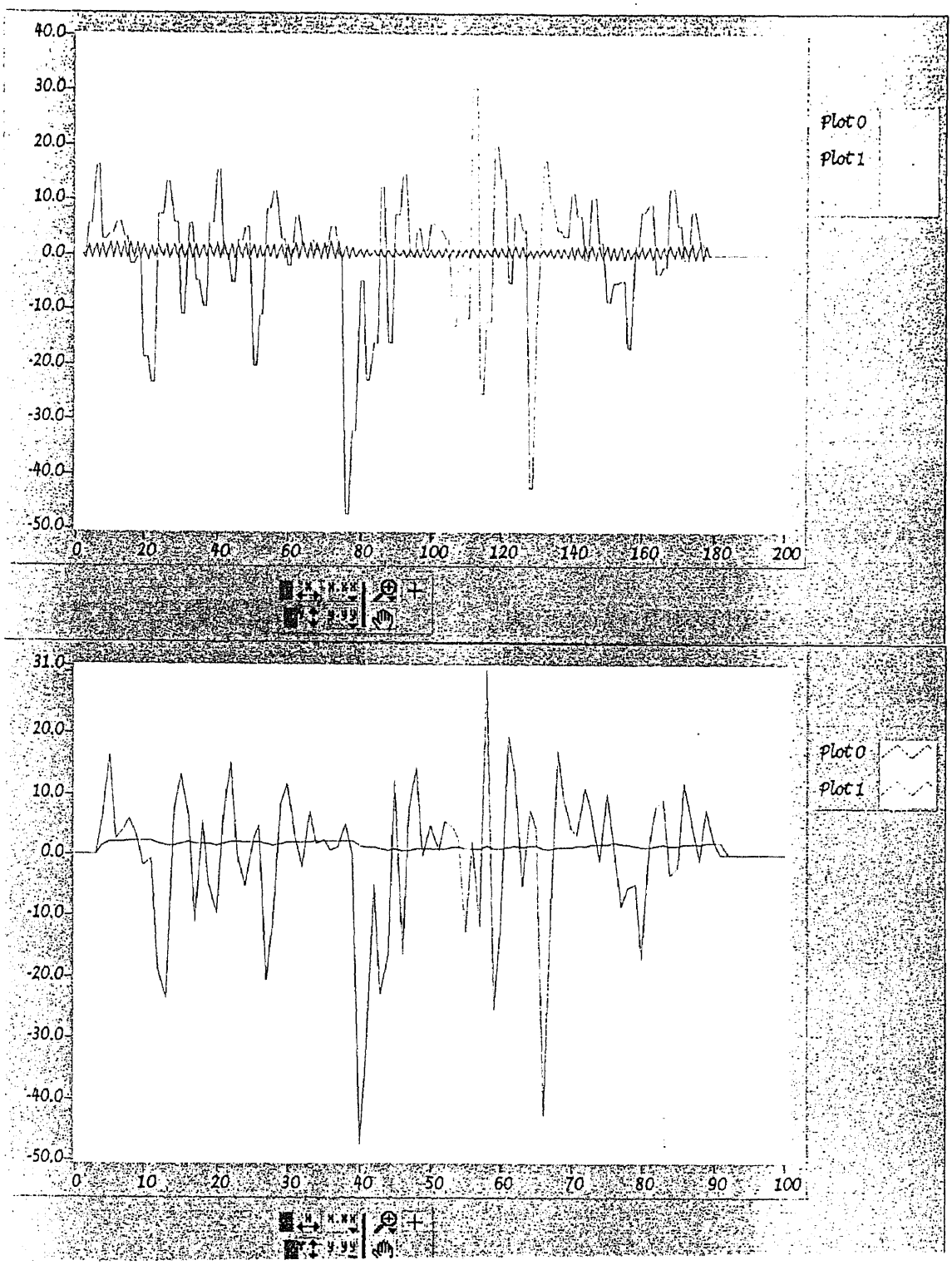


Figure 5.8 Processing Methods (c) plot 0: raw arterial signal peaks and valleys; plot 1: % difference between peak and previous peak only. (d) plot 0: raw arterial signal peaks only; plot 1: % difference between peak and previous peak.

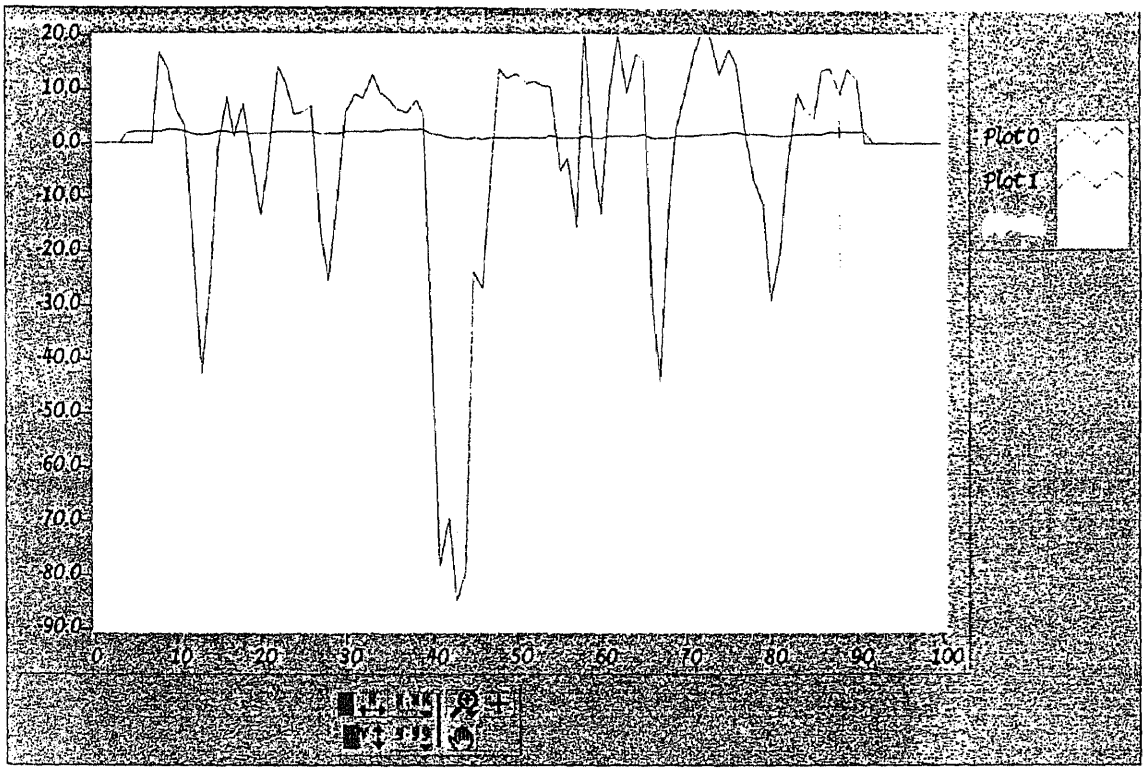


Figure 5.8 Processing Methods. (e) plot 0: raw arterial signal peaks only; plot 1: % difference between peak and average of previous 5 peaks.

5.5.3 Incorporating Heart Rate Variability

This technique of fingertip blood volume measurement provides an interesting opportunity. Although this study concentrated strictly upon identifying a method to accurately acquire data which can describe sympathetic activity, it may possibly be used to describe a complete picture of the autonomic neural activity. As described in Section 2.2.2, Heart Rate Variability employs a method by which an EKG measurement is used to determine the changes in heart rate between beats.

Similar information is also provided by the data acquired in this study. This could be determined by the difference between peaks along the x-axis. This should be verified in an experiment which measures both fingertip blood flow and EKG and the results compared.

In addition, information about the respiration rate is required for Heart Rate Variability evaluations. To date, no consideration for acquiring this data has been given to the experiments in this study. If it is proven that HRV data can be obtained with this method, future experiments should be developed to include a method for acquiring, storing, and processing respiration rate along with blood flow data.

5.6 Experiment No. 3

5.6.1 Protocol Adjustment: Elimination of the 'Zero Set' Artifact

It was observed that a steep rise, or change in the vertical position of the signal, occurred immediately as each experiment began. A concern for this rise was identified on the basis that the expectation would be, since the subject has been at rest for several minutes, and has not been asked to relax further, there should be no change and the signal should be level during this period.

Since the remainder of the signal moved in accordance with expectations, this particular segment was suspect. It was hypothesized that the steep climb was due to an artifact which occurred from when the equipment was "set to zero" immediately prior to commencing the acquisition of data. It was believed that the equipment was still adjusting itself electrically, causing interference with relative size of the signal, thus falsely identifying the location of the data along the Y-axis.

The protocol adjustment used in this experiment was designed to eliminate that artifact. From the results, it can be seen that there was indeed a "climbing effect" artifact from the 'zero set' step in the protocol used in earlier experiments. Furthermore these results show that the revised protocol used in this experiment effectively corrected this issue. This adjusted sequence in the protocol is recommended for future evaluations.

5.6.2 The Test Length: Reduced Slightly for Manageability

The second change which was made in the protocol established for earlier experiments was to reduce the length of the test. This change was made not so much for convenience as it was for the practical use and manipulation of the acquired data. The revised test length was determined by two concerns.

The first concern was to ensure that enough time was spent during each segment of the test so that the data accurately represents the state of the subject. The second concern was to reduce the length of the file so that it could be more readily manipulated and use less memory space.

Through observation of earlier experiments, it was decided that each segment, rest, relaxation, and stress, could be reduced to 3 minutes and still produce representative results. The data obtained in this experiment verifies that 3 minute segments are sufficiently representative. This revised test length of 12 minutes with equal 3 minute intervals of rest, relax, stress, and recovery is recommended for future work..

CHAPTER 6

CONCLUSION

6.1 Meeting the Objectives

The experiments conducted demonstrate that the technique which has been proposed and developed in this work is indeed very practical and promises to be useful. Further work is required to fully develop the proposed technique and to verify its effectiveness. Since the preliminary results obtained from this work exhibit such high potential, it is highly recommended that future work be performed using the results of this work as a basis and guide.

Throughout Chapter 5, specific issues have been identified. As each issue was discussed, specific comments or recommendations regarding the success and/or the potential improvement of that issue are noted. Some general comments and summary are provided herewith.

6.2 Experimental Design

The experimental system, as designed for these experiments, proved to be very effective. By conducting the tests in the author's home, the environment was comfortable for the subject. It provided a realistic condition to enable the generation of realistic and accurate data. It also enabled the solicitation of more and various types of subjects.

6.4 Validity of Assumptions

This evaluation has proceeded on the basis that the changes in blood volume at the fingertip are a result only of independent sympathetic activity, with no influence from other physiological effects. Such assumptions are reasonable for the given conditions as discussed in Section 5.2. Two issues should be considered, however, in future work.

First, if possible to design an experiment which verifies the assumptions, this should be done. Secondly, the basis for the assumptions must be observed. Any change to the protocol or type of subject should be evaluated for its fit into the assumptions prior to the application of such.

6.5 Future Development

6.5.1 Verification of Results

Two types of studies can be employed to further validate the results. First, the experiment can be applied to subjects with a known disease and while experiencing that disease both during the application of known, effective therapy and also in the absence of that therapy. The actual data acquired from those experiments should be compared to the predicted values. This would serve to both verify the technique and to help fine tune the correlation of results to performance.

Secondly, controlled population studies should be performed. Since only test subjects have be evaluated, subsequent population studies are required to determine this technique's validity in a sample of "normal" individuals. Further controlled population studies would then be needed to compare the effectiveness of this procedure between population segments with different behavioral and health characteristics, and between those with "normal" and "abnormal" conditions. The results of all these future studies could then be used to help calibrate the measured results.

6.5.2 Adding Heart Rate Variability

As described in Section 5.5.3, the technique developed in this work may ultimately be used to monitor both sympathetic and parasympathetic activity. In addition to the information about sympathetic activity which has been discussed, the signal which was acquired using this method provides sufficient information about the heart rate to identify "inter-beat intervals". It is possible that a heart rate variability evaluation may be performed to describe the parasympathetic activity.

The technique would require augmentation in two ways, however, in order to execute such an evaluation. First, the respiration rate would need to be acquired. It is important to remember that the protocol ensure that the respiration rate is in the high frequency range. Secondly, the data processing features of this software should be explored to determine whether it can be used to perform the necessary power spectral analysis of the recorded inter-beat intervals.

6.6 Effectiveness of New Evaluation and Therapy Techniques

Successful clinical implementation of this technique would help to significantly advance the evaluation, treatment, and prevention of stress related disorders. The sciences which are applied for these purposes today are often inexact. Today, it is not possible to quantitatively define the condition of an afflicted subject. This does not mean that effective evaluation and treatment procedures are not available. There are many cases where a professional can use his judgment and experience efficiently and effectively. [14]

However, such practices have been developed as a result of the accumulation of many observations and experiences. For those conditions where such experience has not been accumulated, the evaluation and therapeutic application is less direct and more complex. There are, indeed, many autonomic neurological conditions where it is difficult to identify the nature of an affliction, the effectiveness of a treatment, or modes in which the development of a condition may be prevented.

Drugs, Medical Therapy, Exercise, Herbs, Biofeedback, Meditation, Light Therapy, are all methods by which neurological disorders have been treated.[4, 8, 14, 16] Some are more widely accepted than others. Conventional methods, i.e. Drug treatment and therapy prevail as the preferred treatment in the Western world. [14] This is because most successful experiences come from such methods.

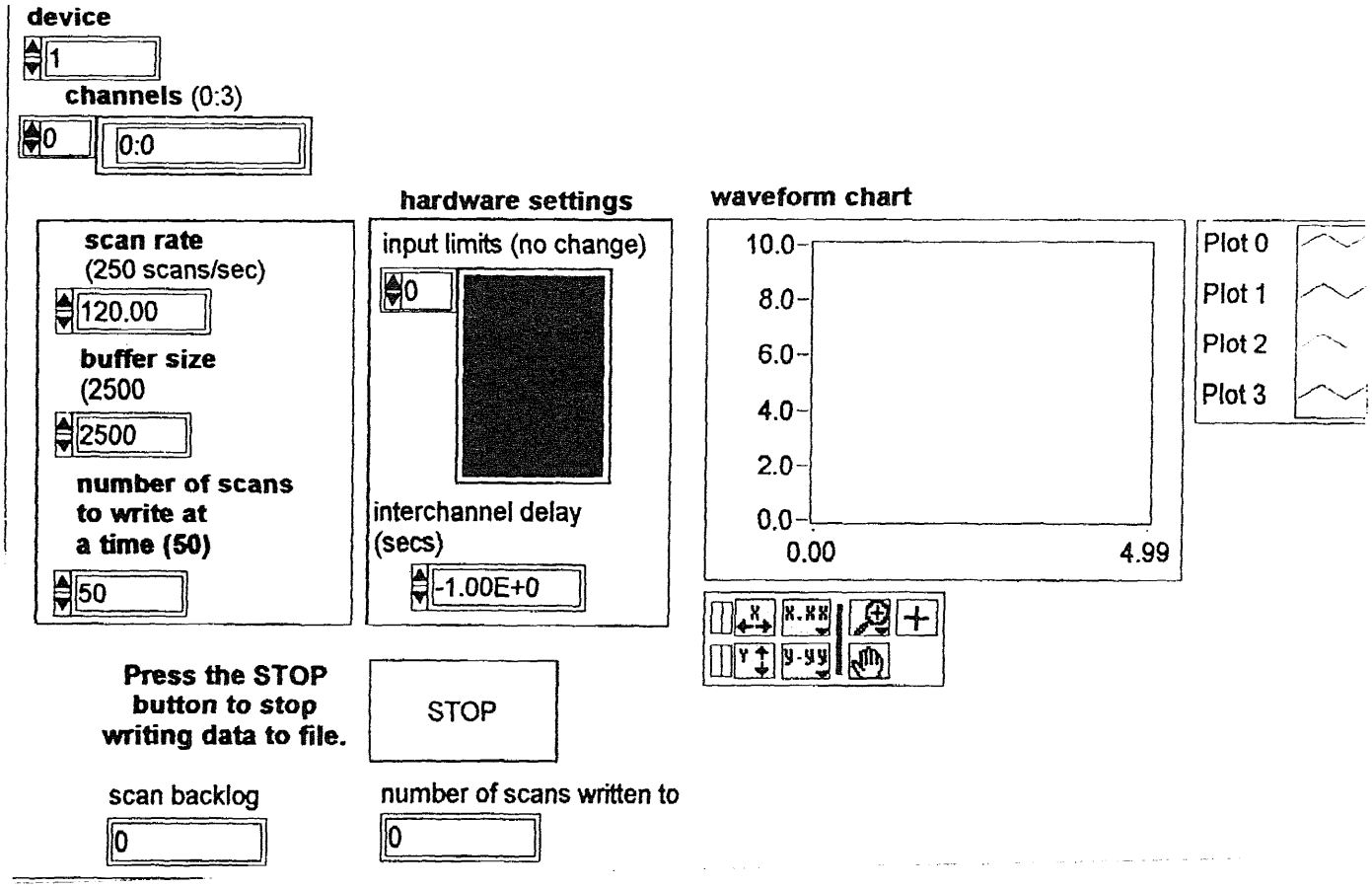
This should not be interpreted, however, as though alternate methods are not effective. Rather, it is that such methods are not well understood or have been thoroughly investigated. It is quite possible that alternate methods are not as readily accepted, simply due to minimal experience or scientific medical evidence that they are effective. Further advancement of the technique presented in this study may help to better prove or understand such alternative methods.

There are many potential benefits to such alternative methods. It is possible that such methods could be more effective, reduce or eliminate side effects, or provide quicker results. In addition, they could provide solutions more simply, with less cost and more ready availability. Furthermore, they could help to identify and get closer to treating the cause of the illness—rather than treating results or symptoms of the illness.

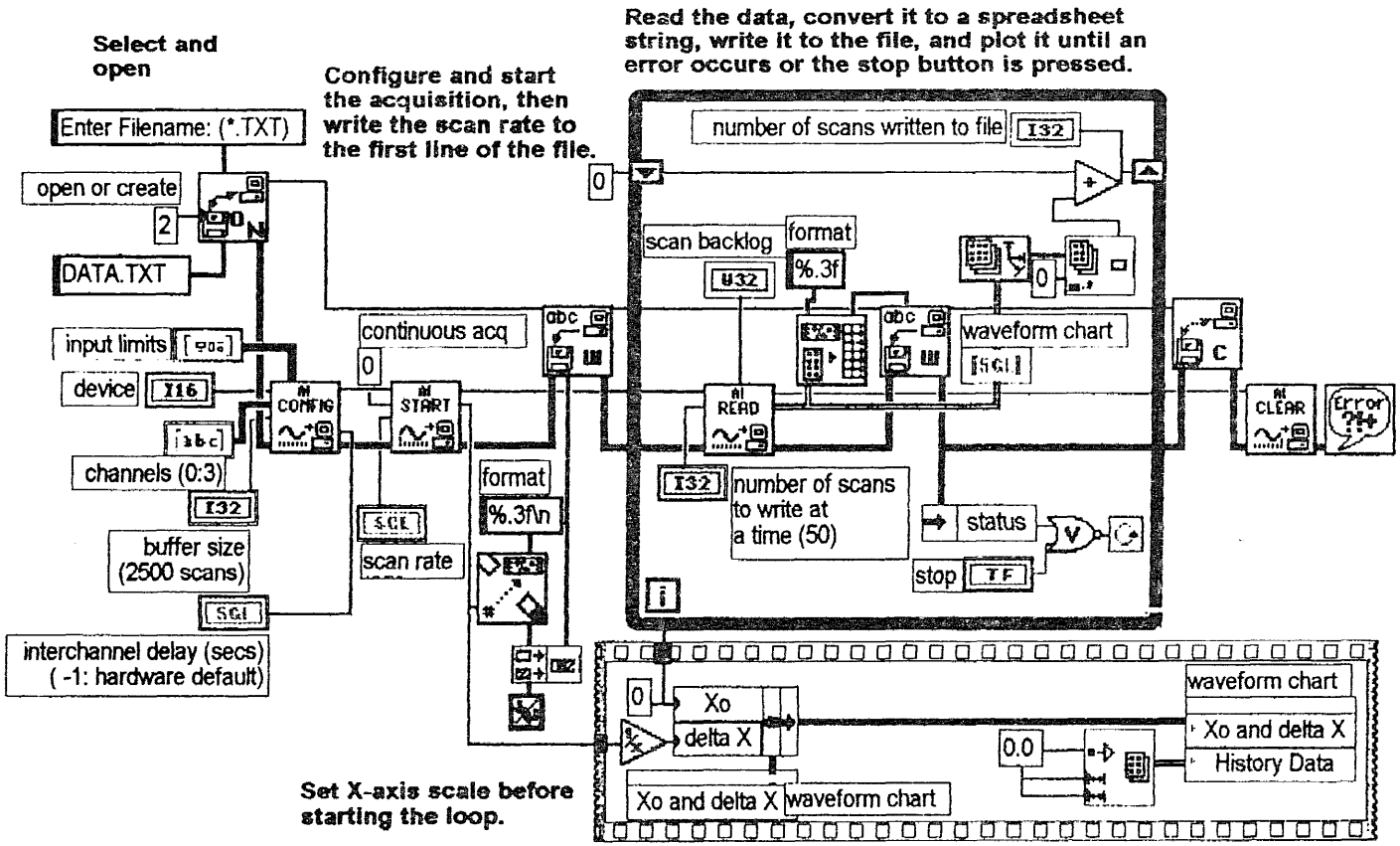
The benefits to advancements in the ability to define, evaluate and treat autonomic conditions are far reaching. Certainly, a better general understanding of autonomic disorders is needed. The effectiveness of conventionally accepted practices may be validated or improved, and alternative—possibly better—methods may be identified. The results of this study indicate that it may very well be possible to quantify and understand the sympathetic autonomic activity. The methods devised in this study, with more development, should lead to the understanding needed to advance the treatment and evaluation of autonomic conditions.

For this reason it is critical that this work be completed and piloted as outlined.

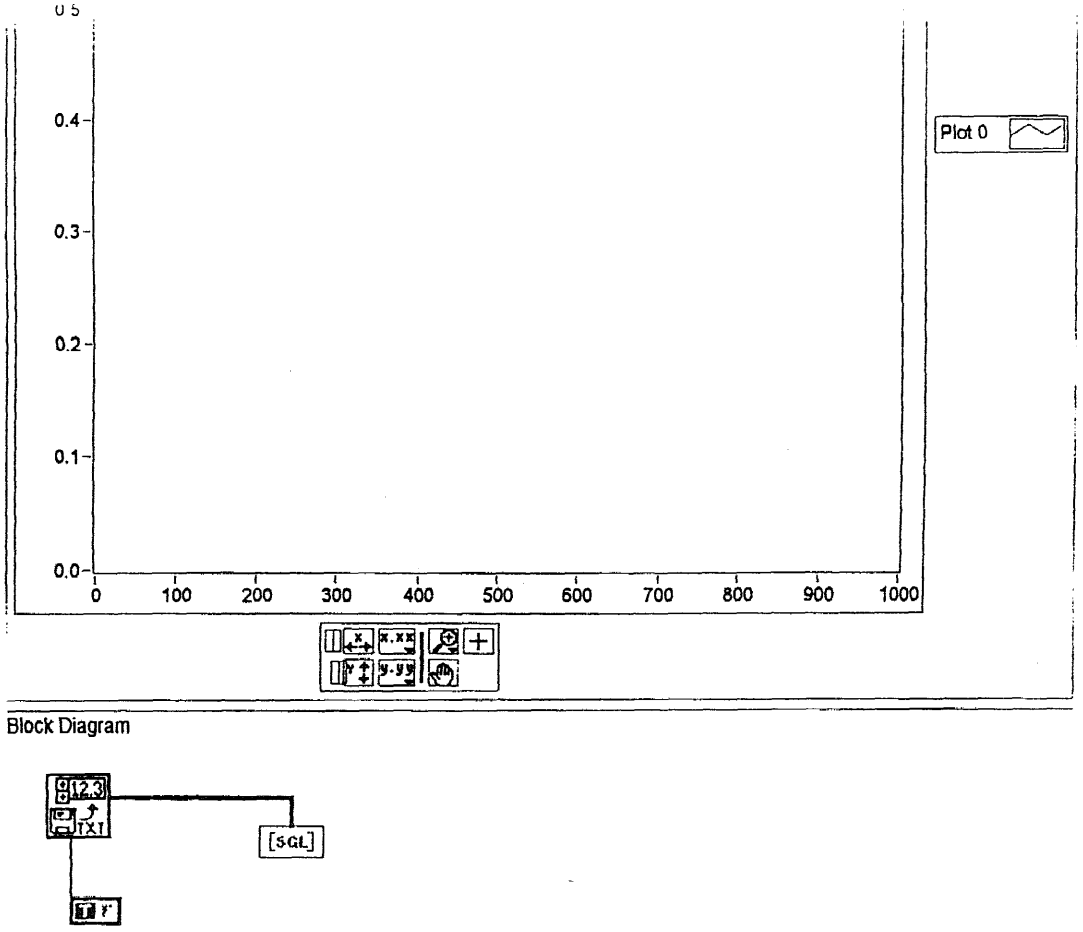
APPENDIX 1



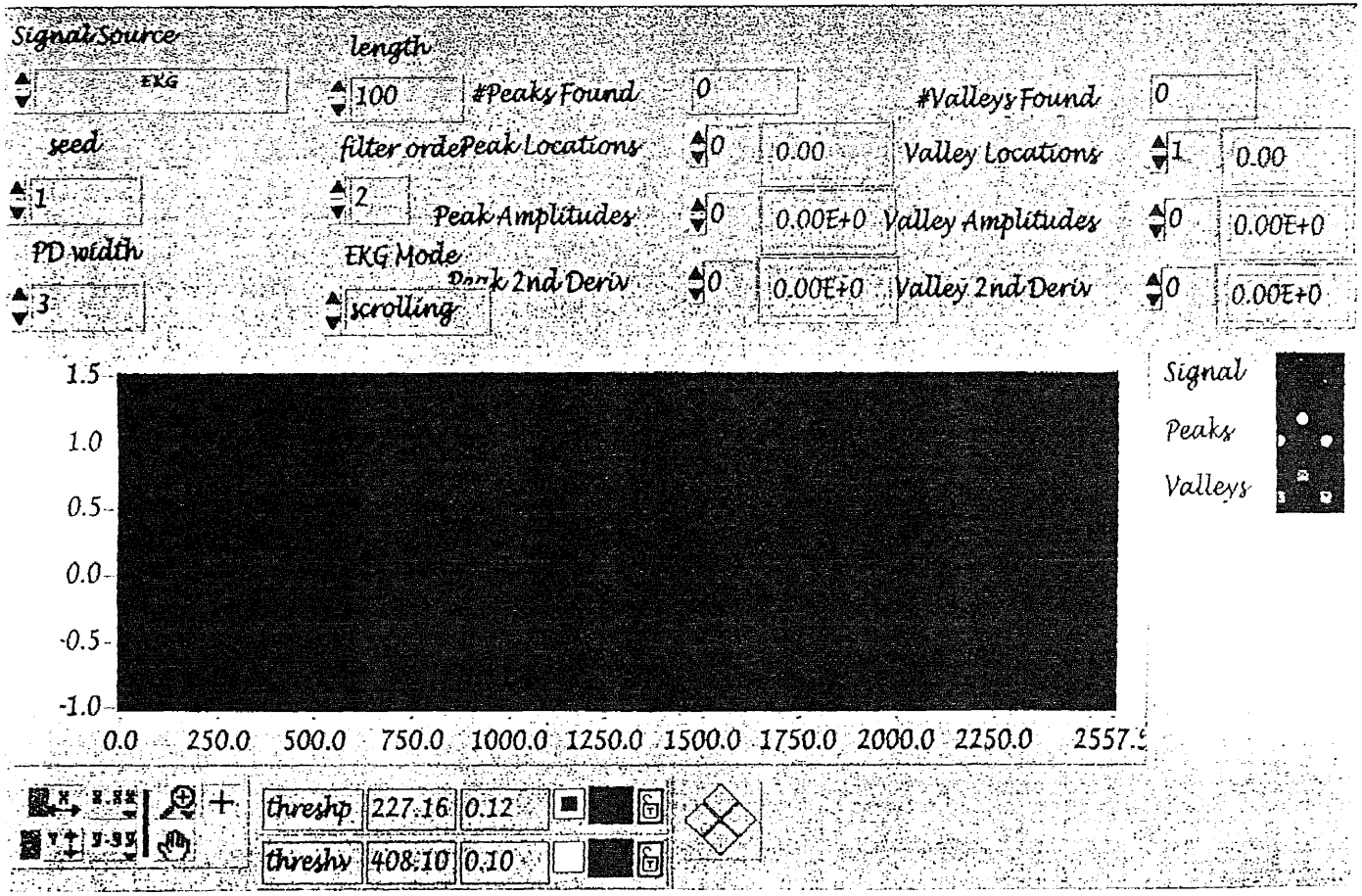
Appendix 1-1: Front Panel, "Continuous Acquisition to Spreadsheet File"



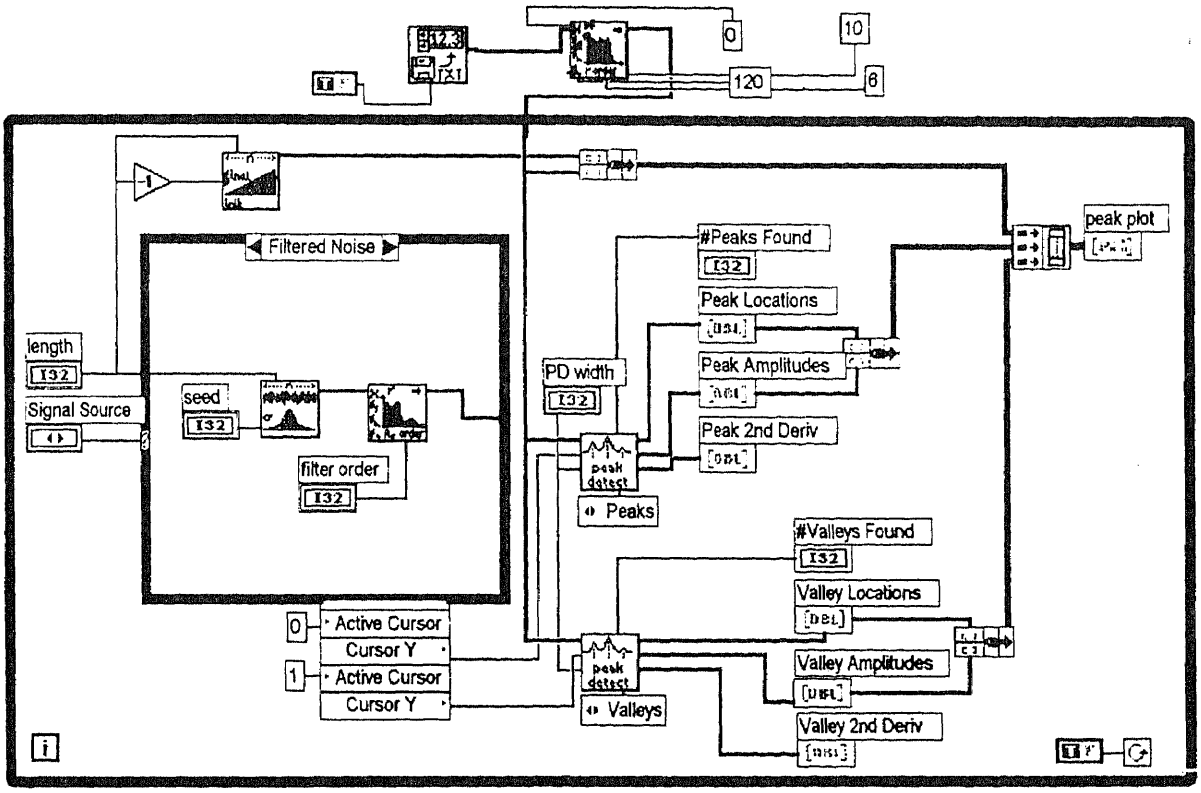
Appendix 1-2: Block Diagram, "Continuous Acquisition to Spreadsheet File"

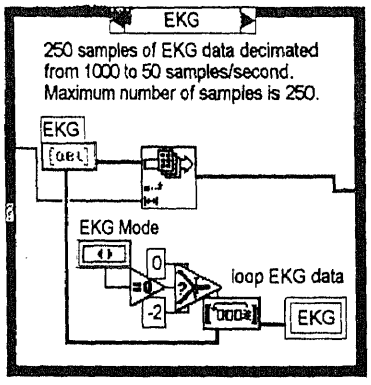


Appendix 1-3: Front Panel and Block Diagram, "Plot"



Appendix 1-4: Front Panel, "Peak Detection Example"





Appendix 1-5: Block Diagram, "Peak Detection Example"

SUBJECT PERSONAL DATA SUMMARY

Date of Test ☐

Subject ID No. ☐ ☐ M ☐ F

Date of Birth ☐ Age ☐

Health History:

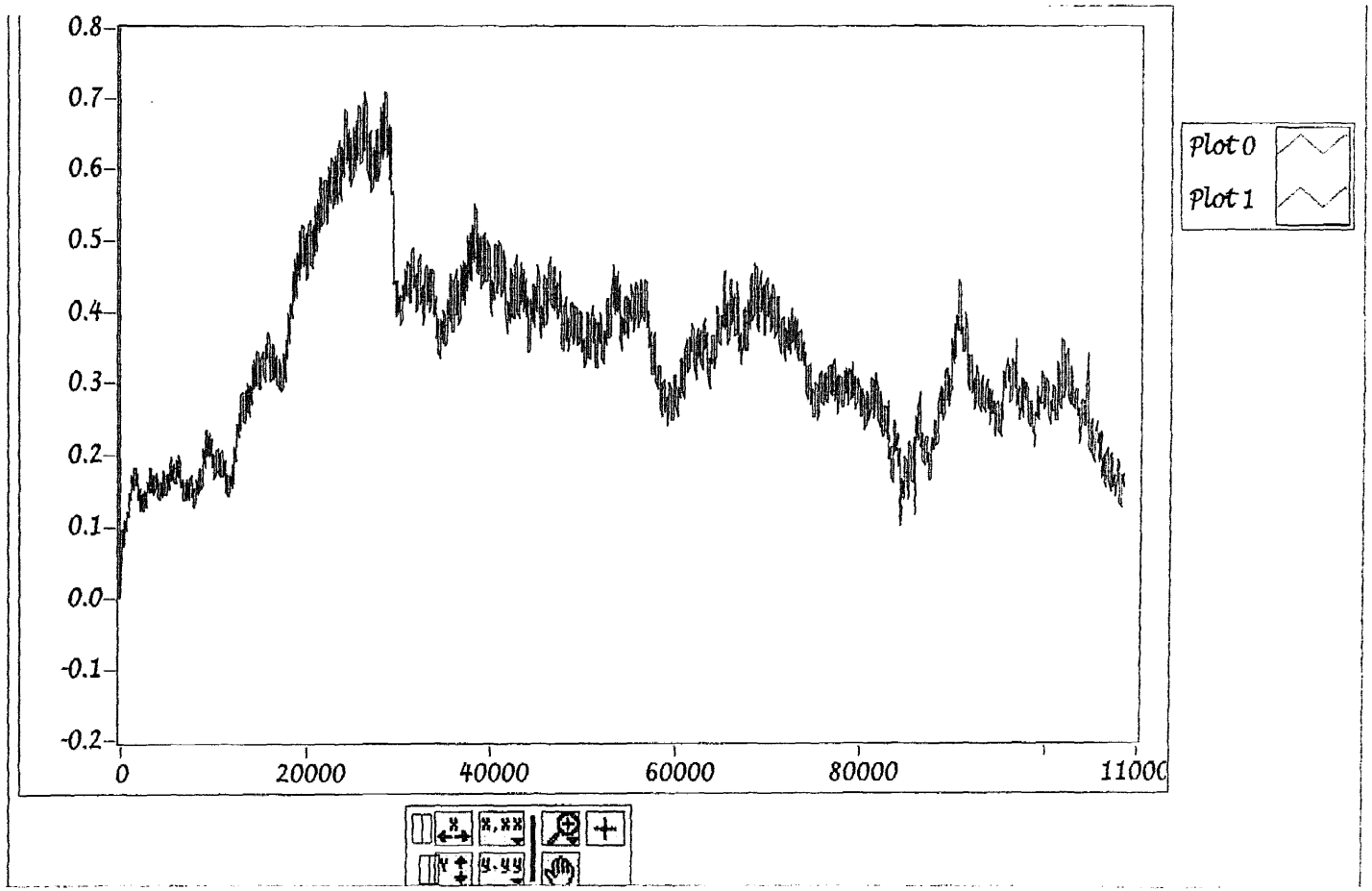
	YES	NO	Explain
Circulatory or Heart Condition?	☐	☐	
Respiratory Condition?	☐	☐	
Neurological Condition?	☐	☐	
Other Serious Condition?	☐	☐	

Subject's Description of Current Stress Level:

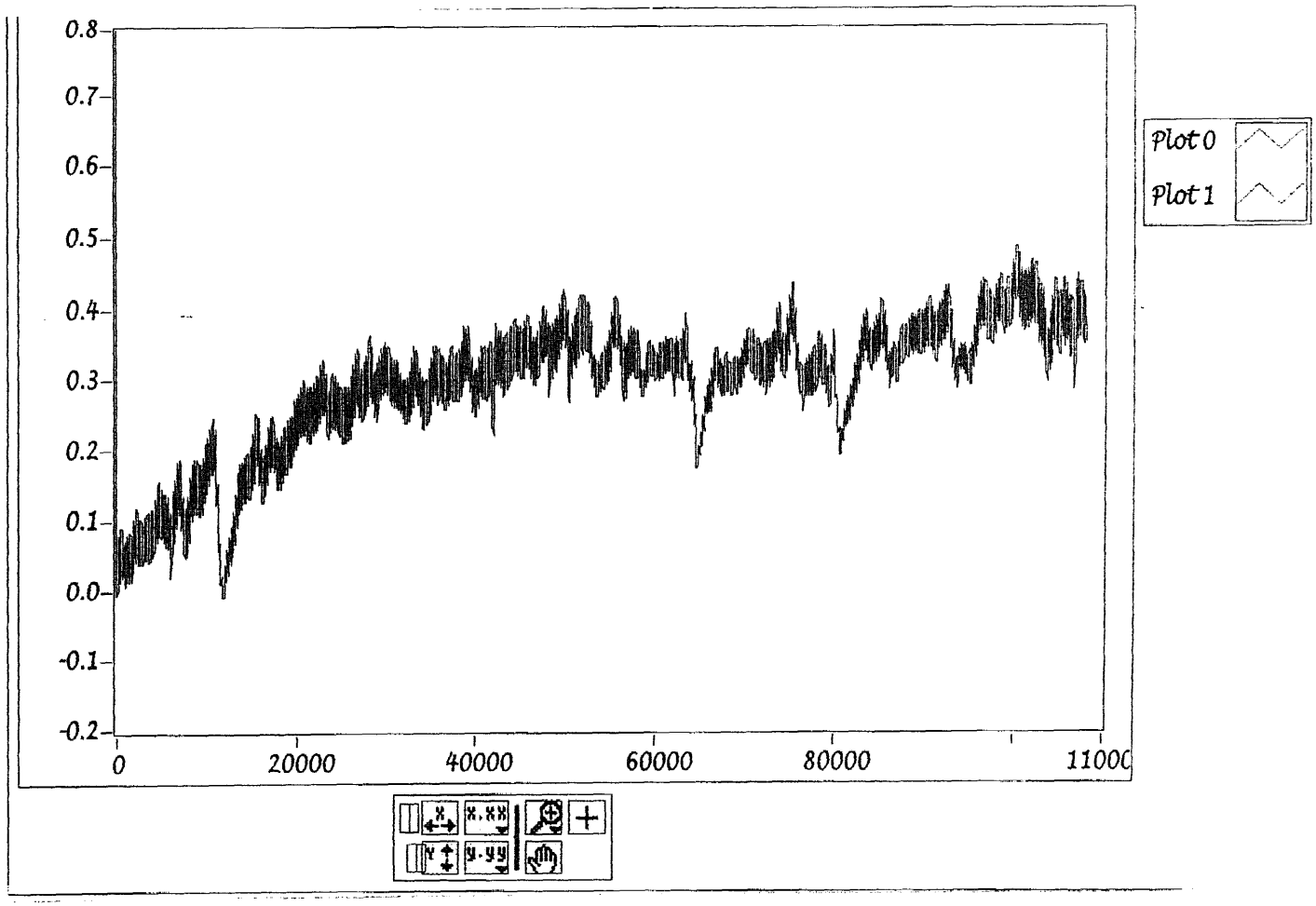
1	☐	Extremely High
2	☐	Higher than Normal
3	☐	Normal
4	☐	Lower than Normal
5	☐	Extremely Low

Appendix 1-6: Personal Data Summary Questionnaire Form

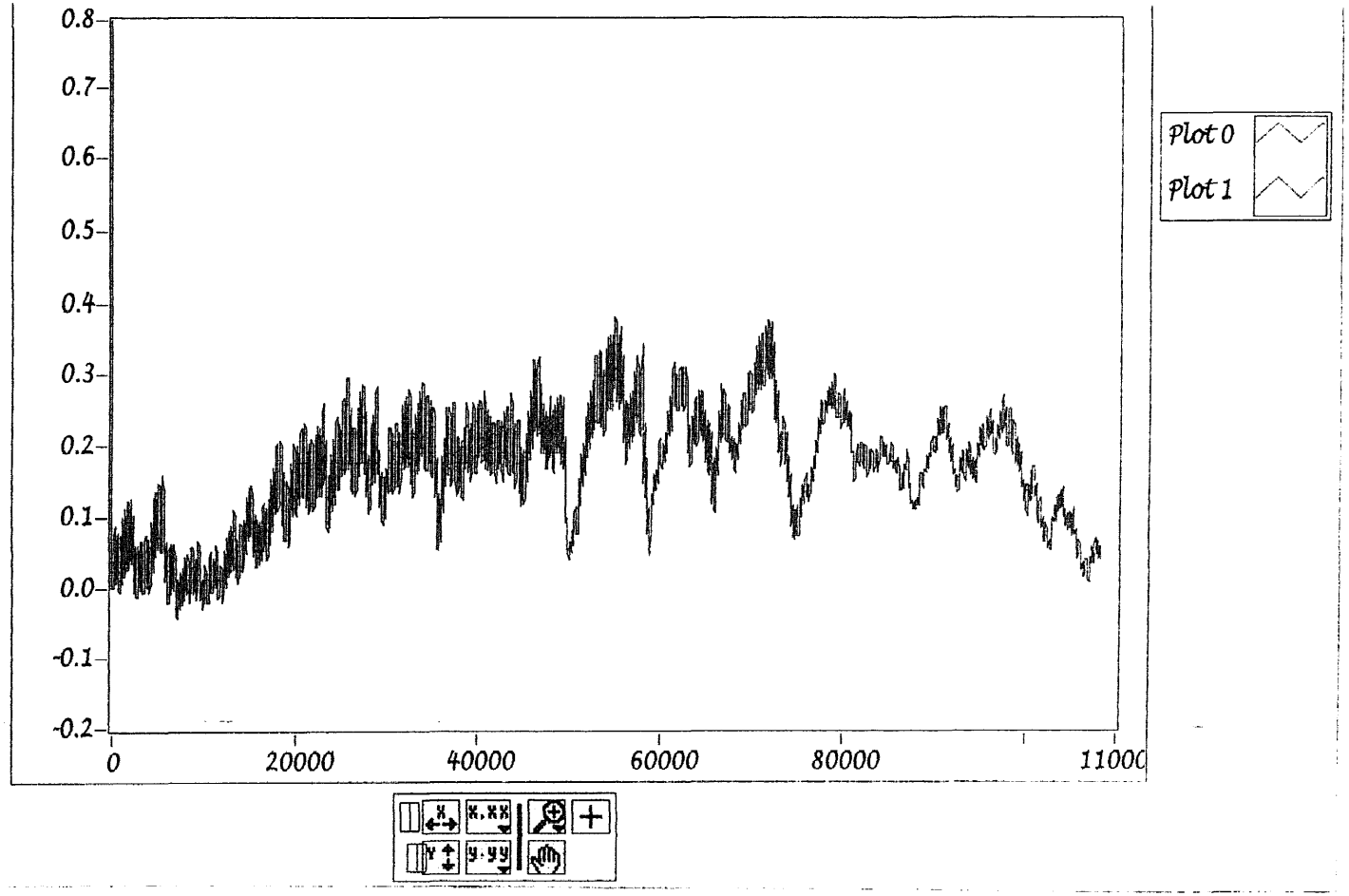
APPENDIX 2



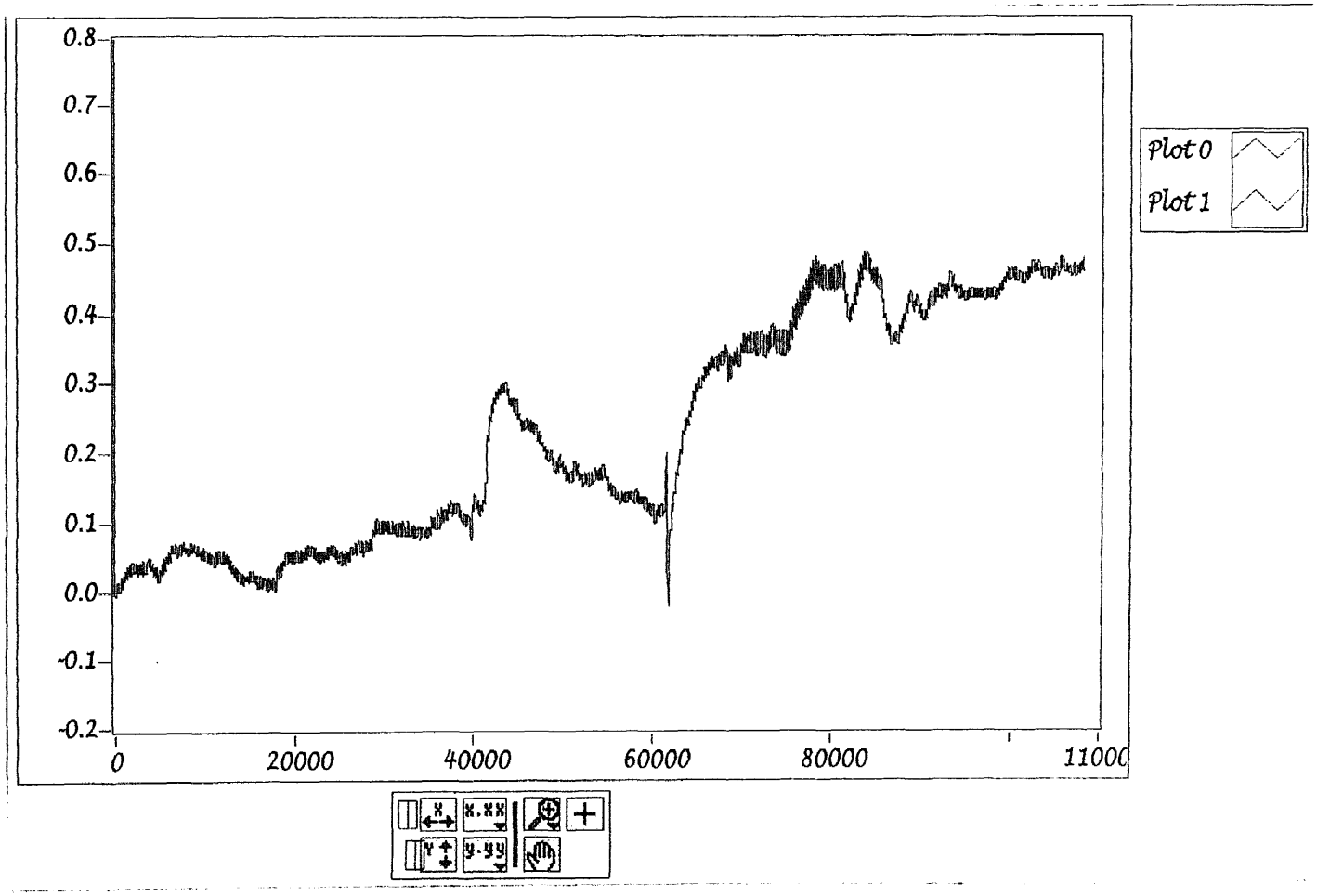
Appendix 2-1: Results, Subject No. 2



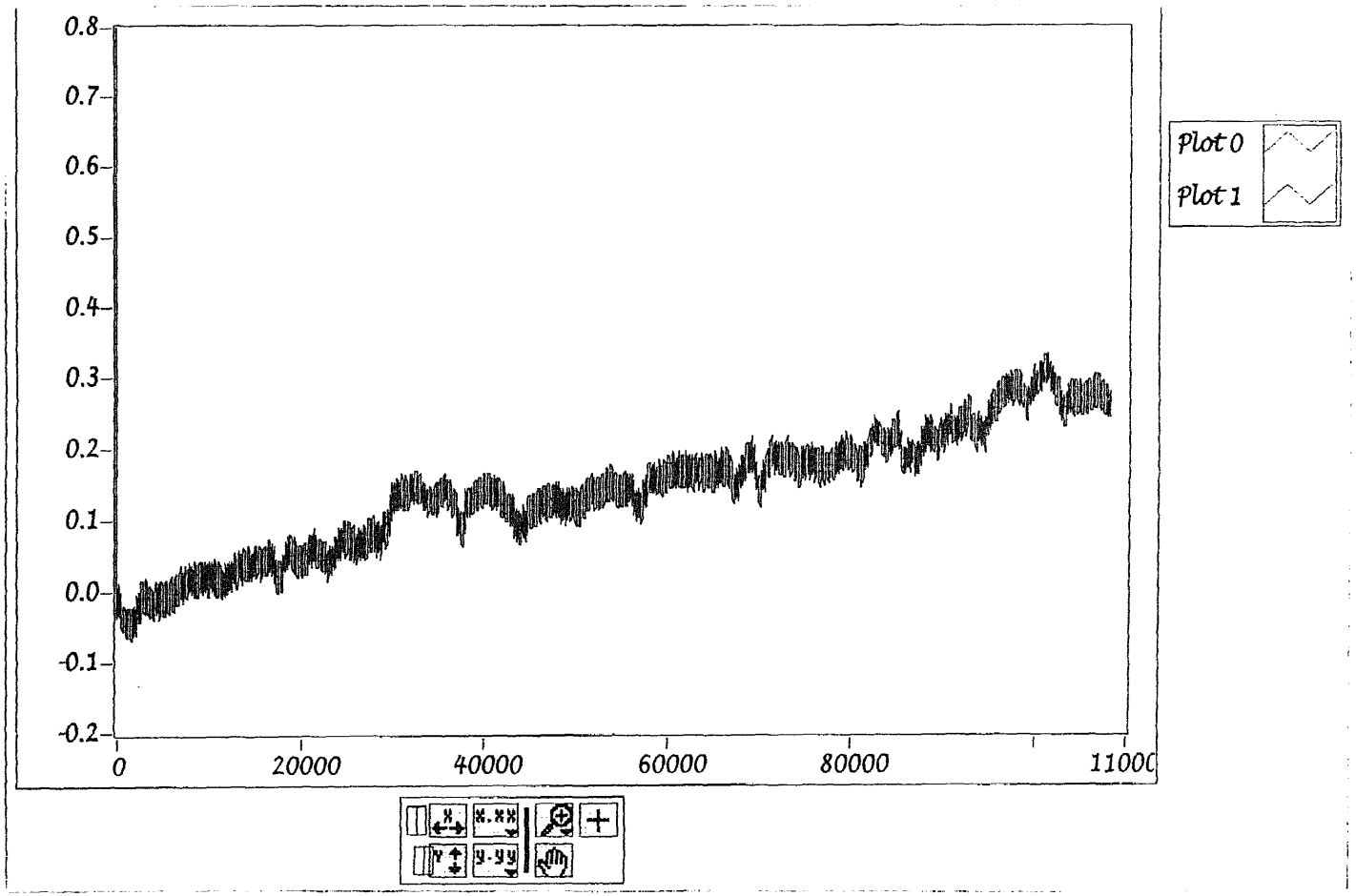
Appendix 2-2: Results, Subject No. 3



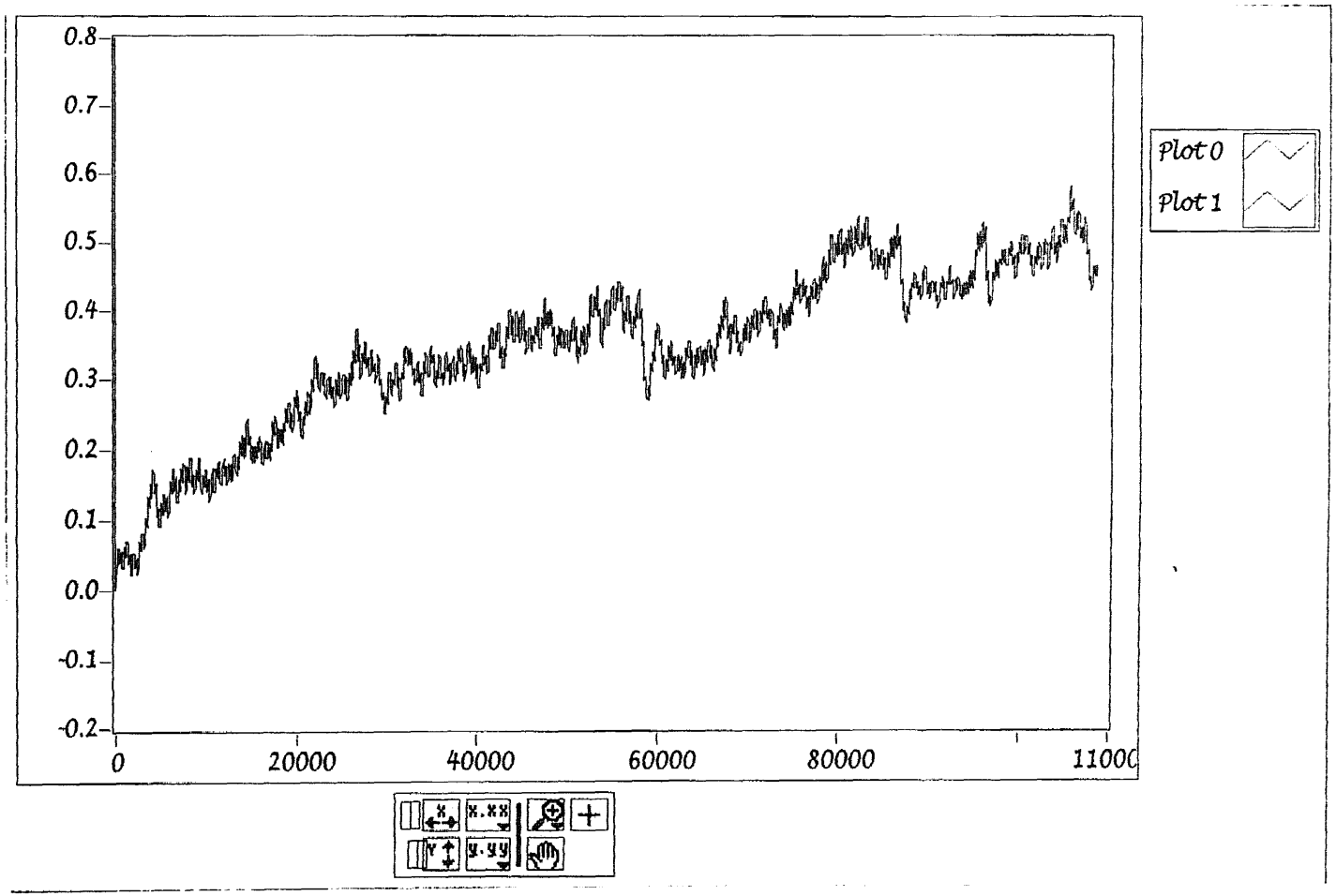
Appendix 2-3: Results, Subject No. 4



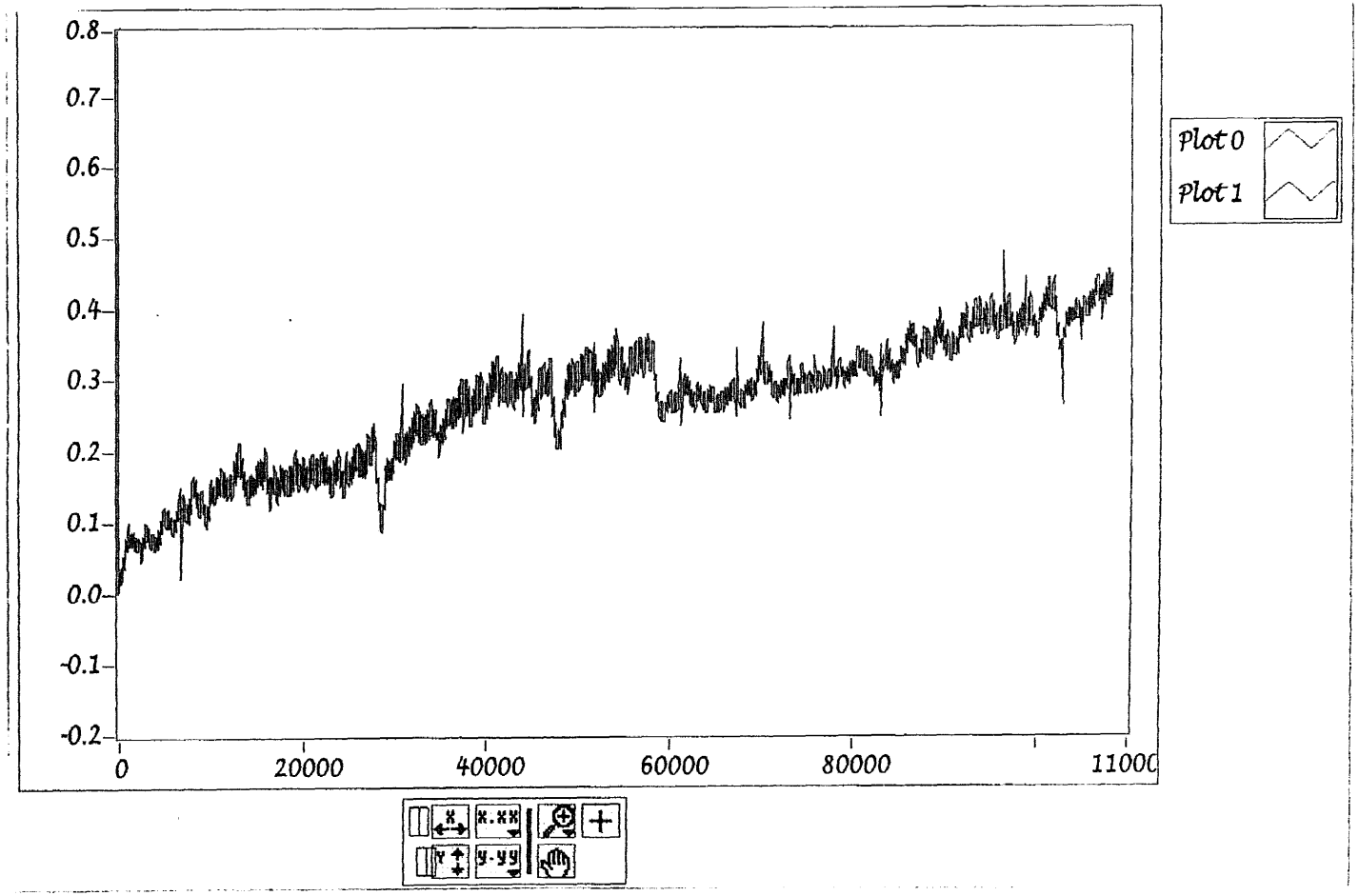
Appendix 2-4: Results, Subject No. 5



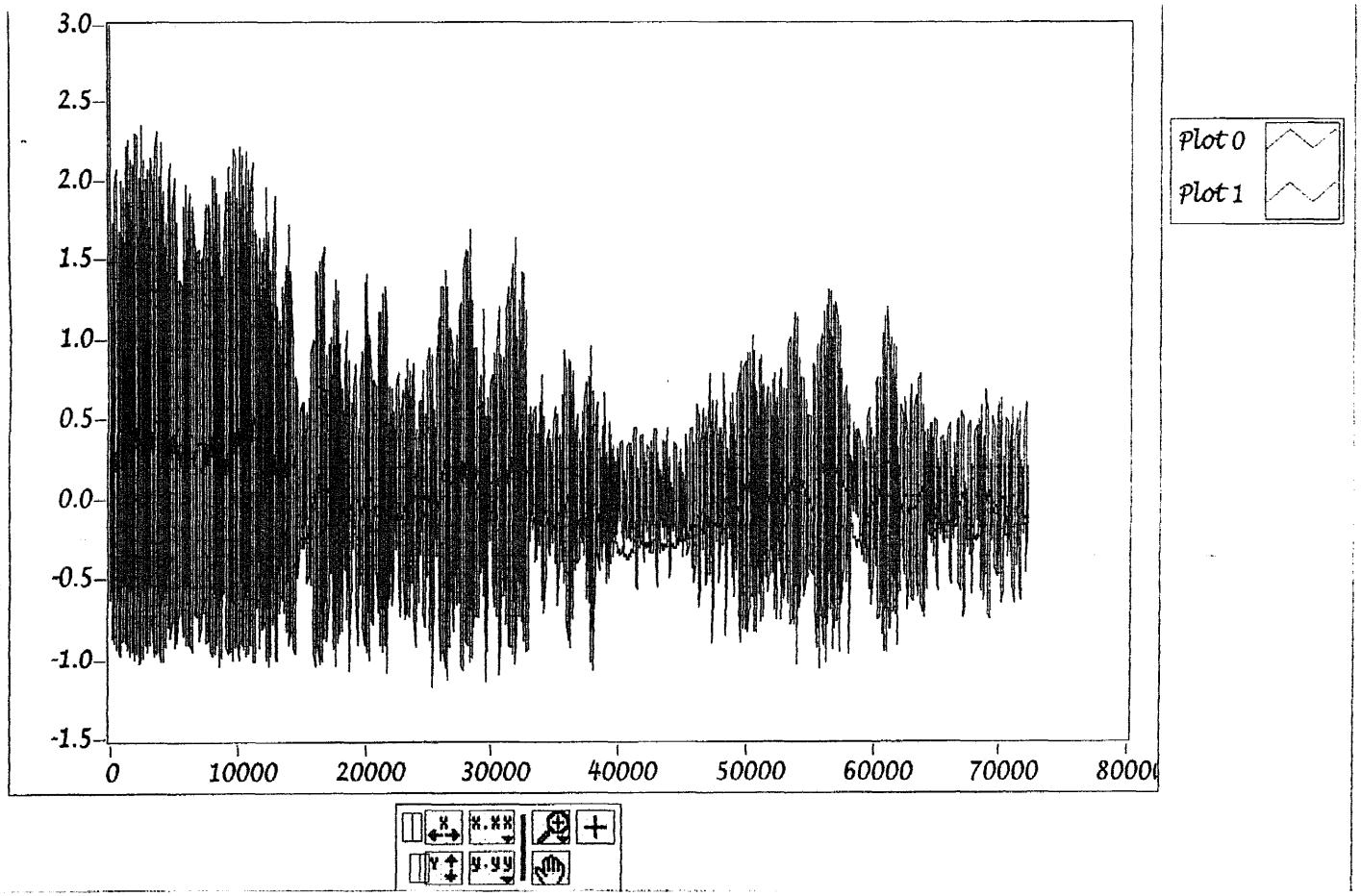
Appendix 2-5: Results, Subject No. 6



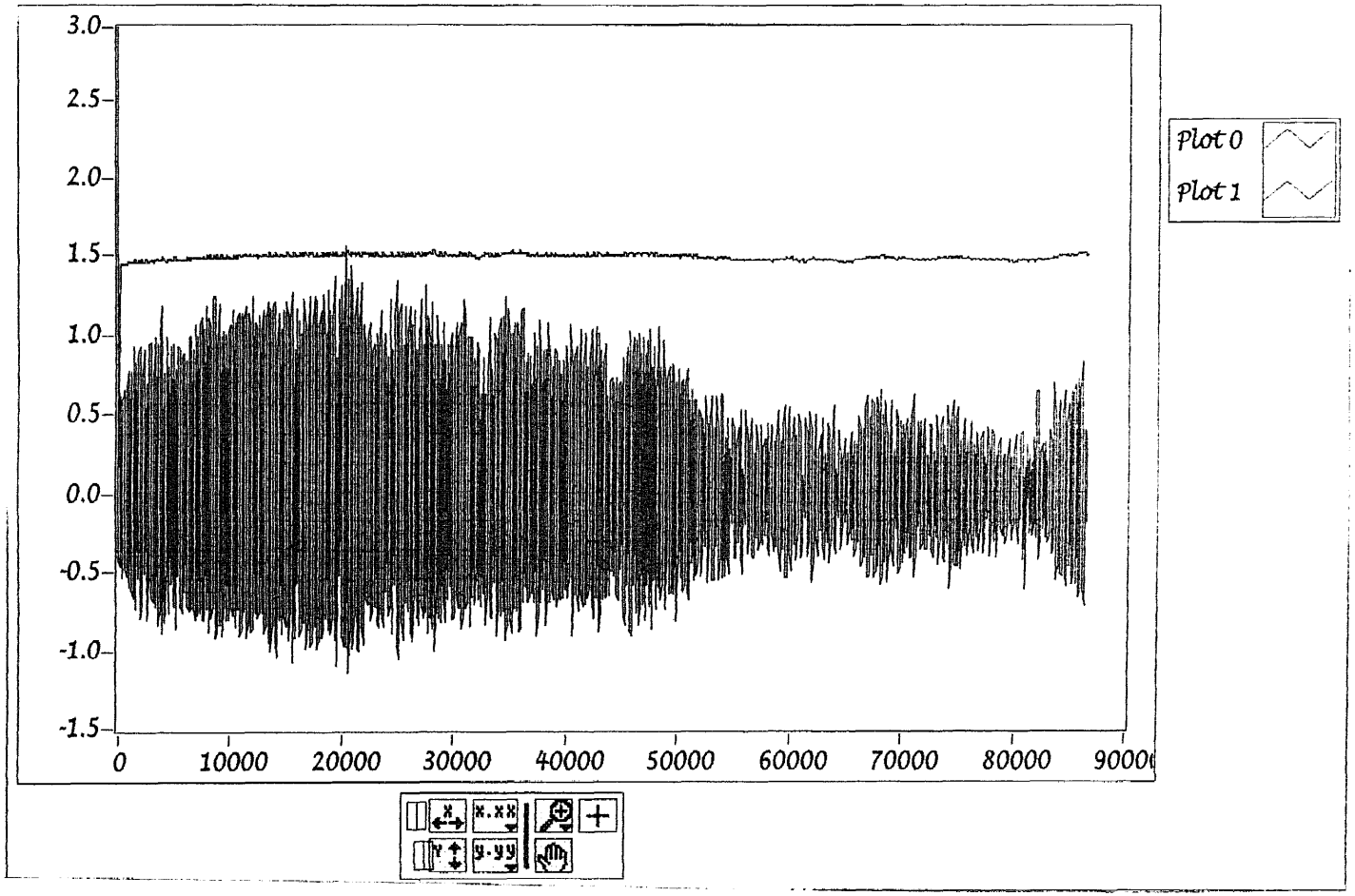
Appendix 2-6: Results, Subject No. 7



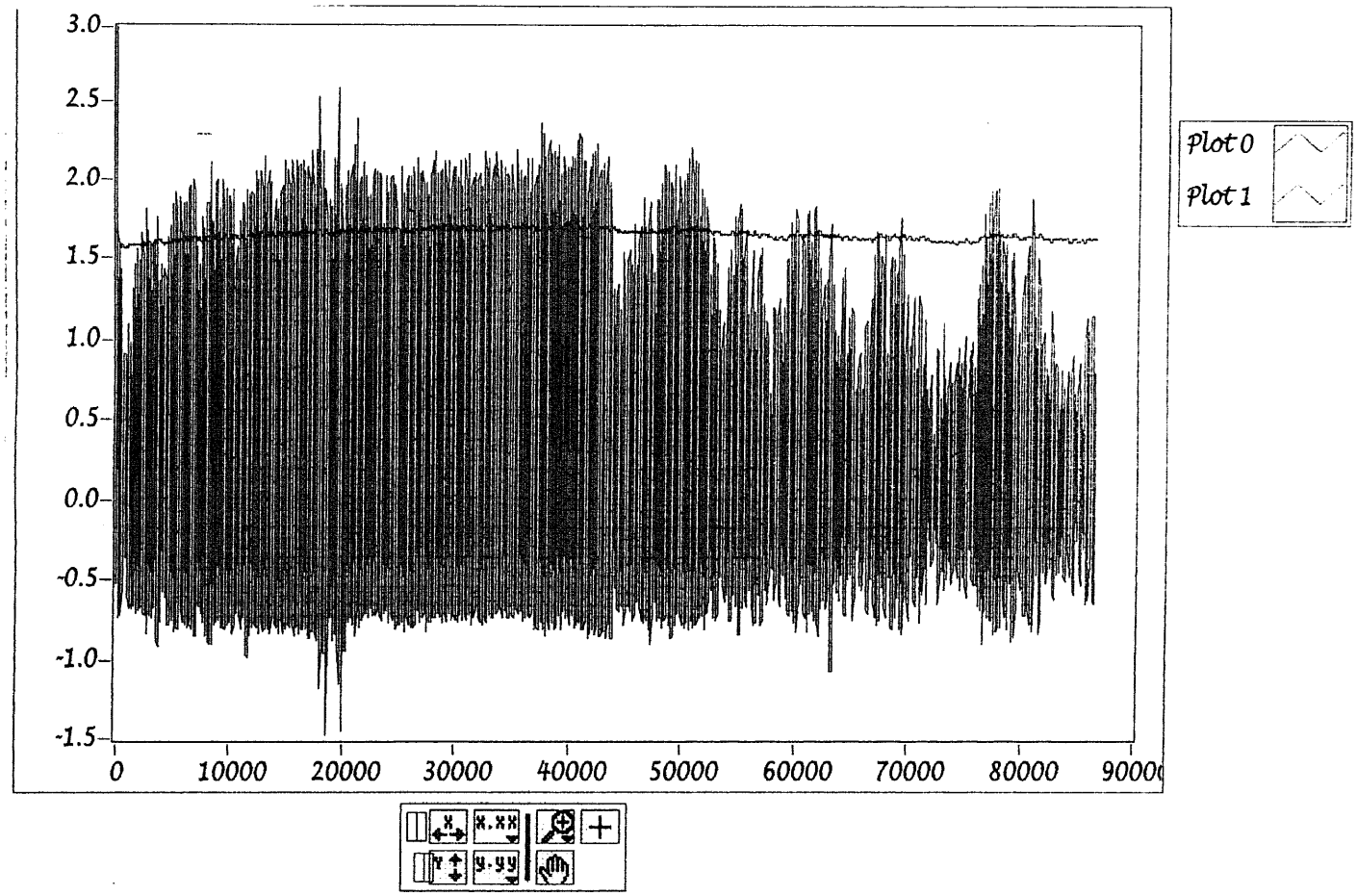
Appendix 2-7: Results, Subject No. 8



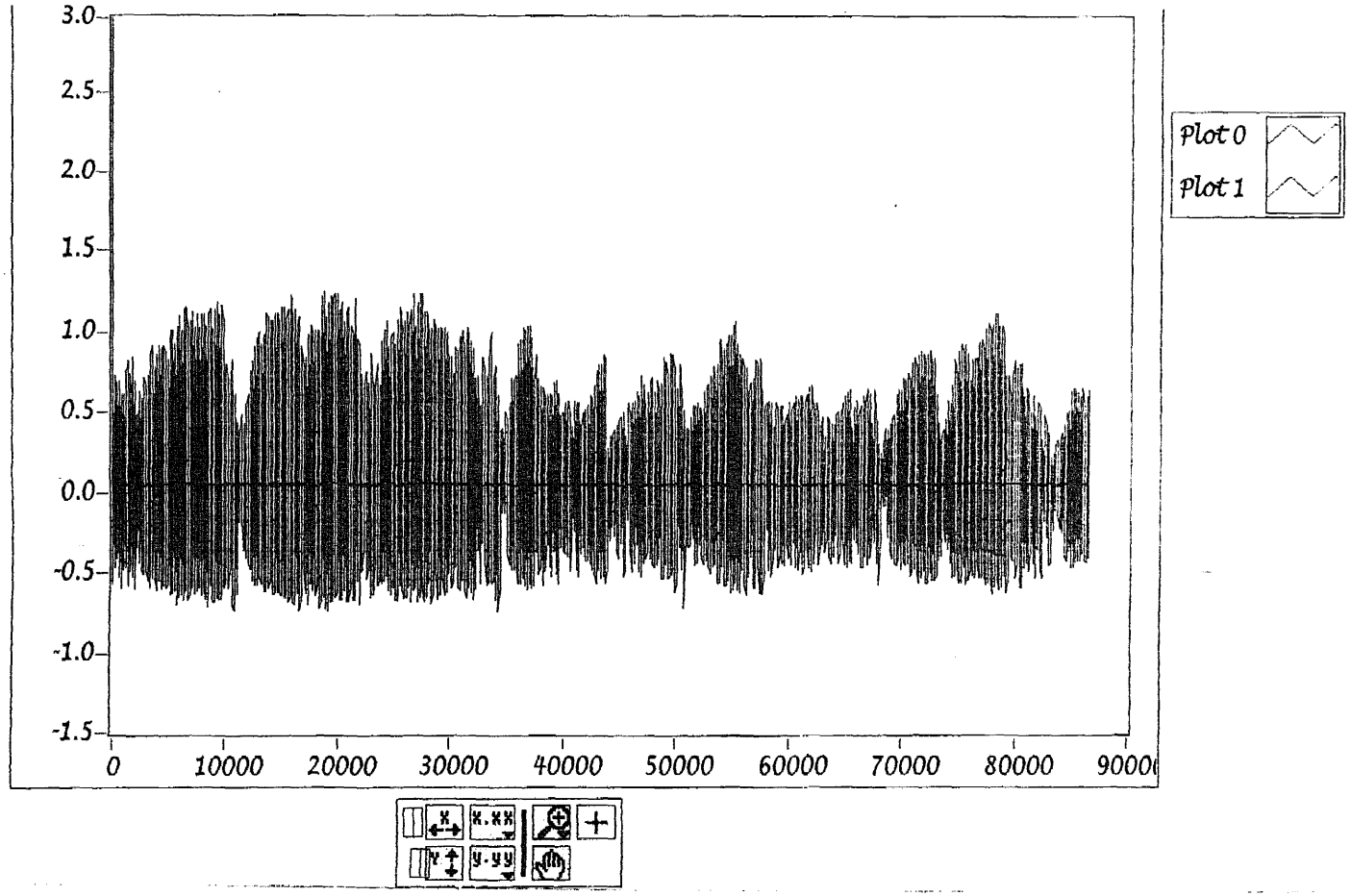
Appendix 2-8: Results, Subject No. 22



Appendix 2-9: Results, Subject No. 32

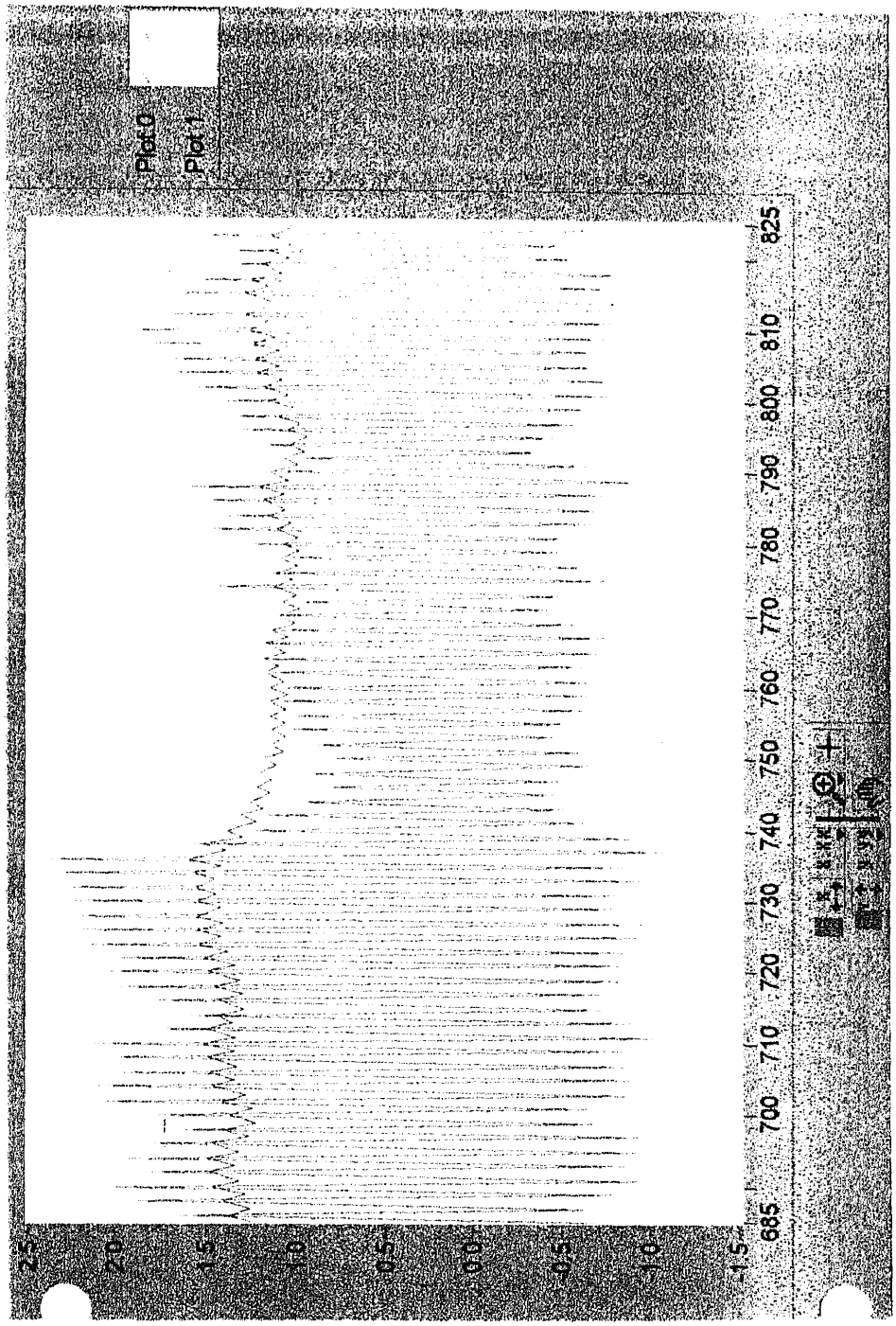


Appendix 2-10: Results, Subject No. 33

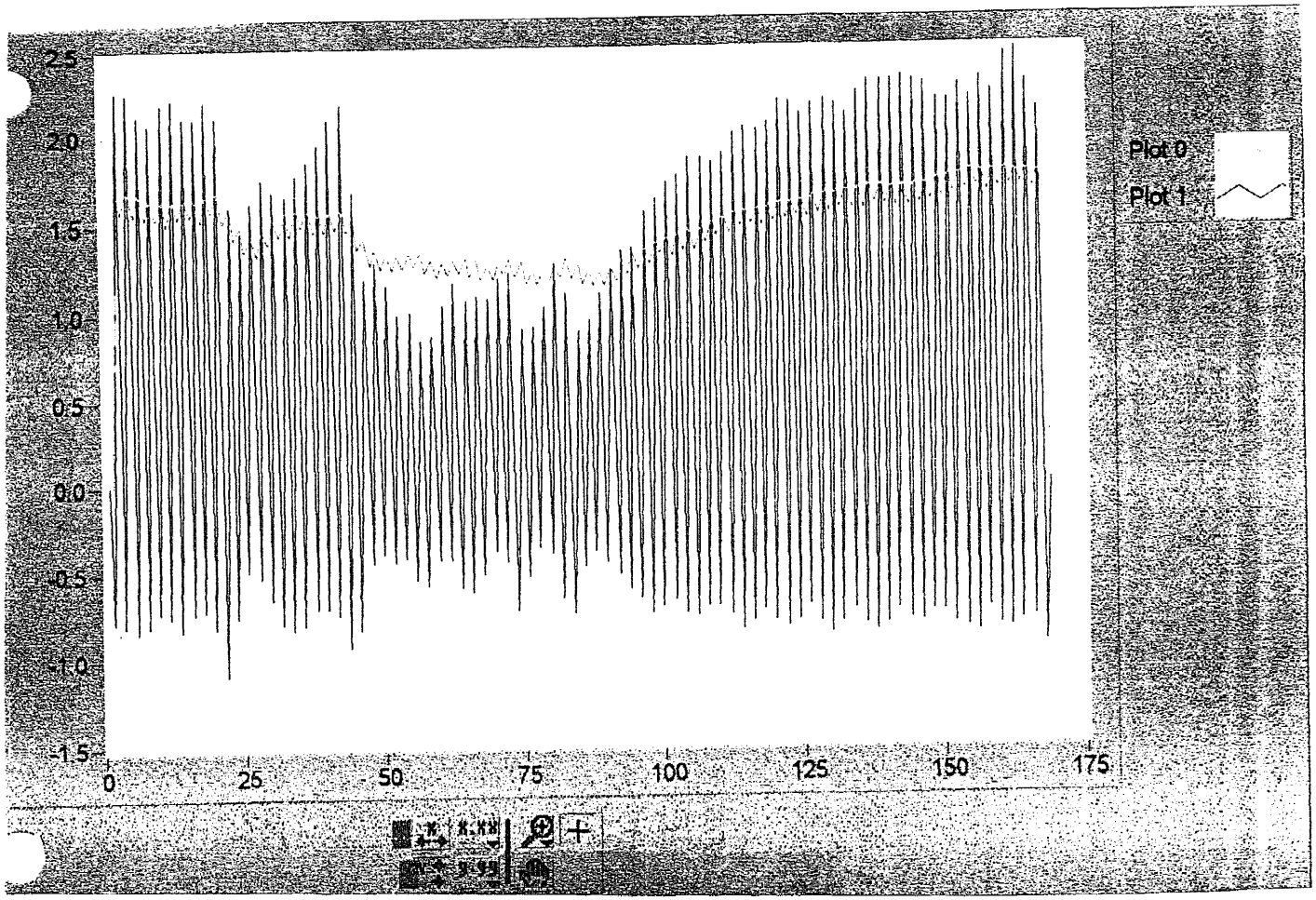


Appendix 2-11: Results, Subject No. 34

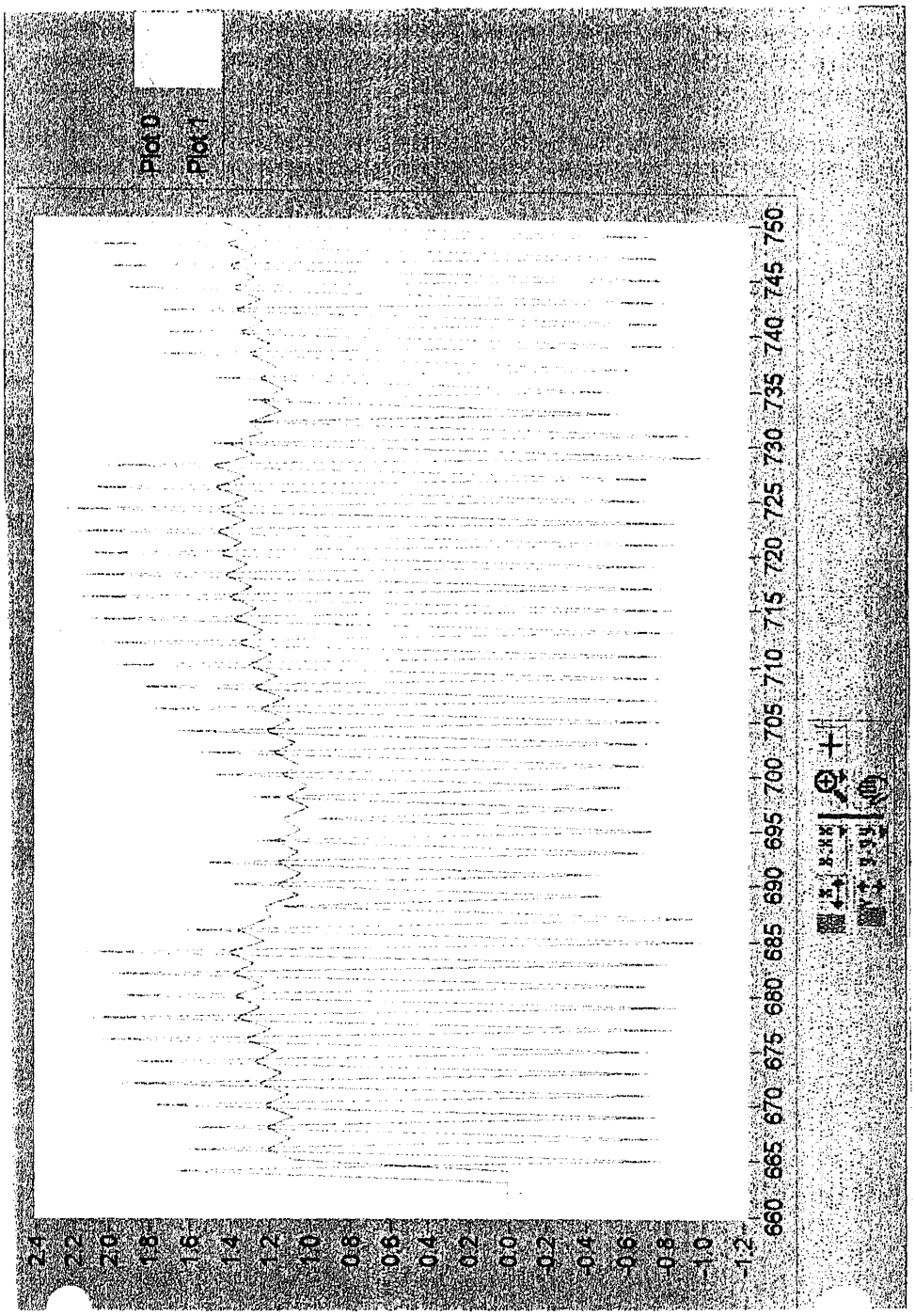
APPENDIX 3



Appendix 3-1: Modified Results; Subject 21, 'segment a', 'Peaks and Valleys Only"



Appendix 3-2: Modified Results; Subject 21, 'segment b', "Peaks and Valleys Only"



Appendix 3-3: Modified Results; Subject 21, 'segment c', "Peaks and Valleys Only"

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