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TIME SERIES ANALYSIS OF RESPIRATION COMPONENT  
IN HEART RATE VARIABILITY

Anuradha R. Iyengar

Thesis submitted to the Faculty of the Graduate School  
of the New Jersey Institute of Technology in partial  
fulfillment of the requirements for the degree of  
Master of Science in Electrical Engineering 1987

APPROVAL SHEET

Title of Thesis: Time Series Analysis of Respiration  
Component in Heart Rate Variability

Name of Candidate: Anuradha R. Iyengar  
Master of Science in Electrical  
Engineering, 1987

Thesis and Abstract  
Approved:

_____	_____
Dr. Stanley Reisman	Date
Professor	
Dept. of Electrical Engineering	
New Jersey Institute of Technology	
Newark, NJ 07102	

_____	_____
	Date

_____	_____
	Date

## VITA

Name: Anuradha Ramaswamy Iyengar

Degree and date  
to be conferred: M.S.E.E., 1987

Secondary education: M.E.S. College of Arts, Commerce &  
Science, Bangalore, INDIA 1978

Collegiate Institutions attended	Dates	Degree	Date of degree
Bangalore University	1978	B.E (Electronics)	1983
New Jersey Institute of Technology	1984	M.S.E.E.	1987

Major: Electrical Engineering

Minor: Computer Science

Positions held: Software Engineer  
Infosys Consultants Pvt. (Ltd)  
Bangalore, INDIA

ABSTRACT

*J Reisman*  
*5/13/87*

Title of Thesis: Time Series Analysis of Respiration  
Component in Heart Rate Variability.

Anuradha R. Iyengar, Master of Science in Electrical  
Engineering, 1987

Thesis directed by: Dr. Stanley Reisman, Professor,  
Dept. of Electrical Engineering

Time series signal processing techniques (Fourier based) were applied to analyze the relationship between heart rate and respiration. This analysis takes advantage of the different timing characteristics of the autonomic nervous system inputs to analyze their influence on the heart rate.

Data from three experiments were analyzed. The first set of data was from helicopter pilots of the US Army. They injected atropine into themselves on certain days. The effect of atropine on the heart rate spectrum and the relationship between heart rate and respiration was studied. It was found that atropine abolishes the respiration peak in the heart rate spectrum indicating that the respiration peak is vagally mediated. Also the respiration spectrum could be used to locate the respiration peak in the heart rate spectrum.

An experiment was then carried out to see how stable the respiration peak was in the heart rate spectrum. Five subjects were used in this study. It was found that the respiration peak is quite stable from day to day.

The effect of paced breathing and stress on the heart rate spectrum was then studied. An experiment was designed for this and data was collected from eight subjects. It was found that there was a strong negative correlation between frequency of respiration and the magnitude of the respiration peak. Further studies need to be done to learn more about this.

Spectral analysis of heart rate variability and respiration is a quantitative measure of autonomic activity. It is hoped that, by understanding the various components in the heart rate spectrum, a non-invasive means of detecting heart defects could be achieved.

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## INTRODUCTION

### 1.1 HEART RATE VARIABILITY

This thesis is a study of heart rate variability due to the activity of the autonomic nervous system in general due to the parasympathetic component in particular.

It has been proved that rhythms can often be markers of normal functional states. In the present context, the general hypothesis is that rhythmical beat to beat oscillations of one cardiovascular controlled variable might provide some criteria to interpret the autonomic activity. It is also known for example, in the heart rate under stable conditions there are rhythmical fluctuations due to respiration (respiratory sinus arrhythmia). Various papers have been written<sup>1-3</sup> in recent times which deal with studying variability of electrocardiographic R-R interval by using computer techniques.

Heart rate is one of the most familiar measures of cardiovascular status. The term 'heart rate' is commonly associated with average heart rate but it is a well known fact that the heart rate varies on a beat to beat basis due to cardiovascular control systems such as the autonomic nervous system. It has been suggested by Axelrod et al<sup>2</sup> that studying heart rate variability could lead to a noninvasive assesment of the 'tonic' autonomic regulation of heart frequency.

The mean heart rate is largely determined by a balance between the mean levels of activity in the cardiac

sympathetic and para-sympathetic nerves. A decrease in vagal activity can be compensated for by a decrease in sympathetic activity as far as average rate is concerned. Since these two pathways are independent we have to conclude in principle that many combinations of level of sympathetic and parasympathetic activity will yield the same result in mean heart rate. However recent work has shown that different cardiac control systems contribute oscillations at characteristic frequencies so that their effects on heart rate can be separated by time series analysis techniques.

The nonrandom components of R-R variability usually are assessed with spectral techniques based on the fast Fourier transform inspite of the fact that the heart rate variability is not strictly periodic. This aspect has been taken care of by certain mathematical techniques. As the interbeat interval (IBI) is not periodic a continuous signal is generated from the IBI data and then sampled at the same rate as the respiration. This is explained in depth in the chapter on computer and mathematical techniques. Spectrum analysis is a sophisticated mathematical technique that breaks a complex waveform, like the heart rate oscillations, into a constituent set of frequencies, with an estimate of the magnitude of each frequency component. The same analysis is applied to the respiration signal to produce a respiration spectrum. The respiration spectrum is used to help interpret the heart rate spectrum.

Three different frequency components, or peaks, have

been identified in the heart rate spectrum: a low frequency peak, a peak in the vicinity of 0.1 Hz, and a peak at the nominal respiration frequency of 0.25 Hz<sup>4</sup>. Figure 1.1 shows an example of a heart rate spectrum in the left panel, with the accompanying respiration spectrum in the right panel. The best understood component of the heart rate spectrum is the peak associated with the dominant respiration frequency. The respiration peak in the heart rate spectrum reflects the respiratory sinus arrhythmia. It is purely parasympathetic in origin, being abolished by muscarinic blockade and by vagotomy<sup>5</sup>. The mid-frequency peak (around 0.1Hz) has been suggested by Hyndman and Kitney<sup>6</sup> to be related to baroreceptor activity. However, this peak is found to be highly variable and further work is required to understand the nature of this component. Power in the low frequency peak appears to come from parasympathetic and sympathetic activity. Note that the respiration peak in the heart rate spectrum of figure 1.1 occurs at the same frequency as the dominant peak in the respiration spectrum.

## 1.2 ELECTROCARDIOGRAM

The heart's electrical conduction system initiates an electrical impulse called an action potential in the SA (sinoatrial) node located in the right atrium. The SA node is the normal cardiac pacemaker. Its rate of discharge determines the rate at which the heart beats. The ECG machine obtains an electrical signal that is related to cardiac activity. Electric currents accompany heart muscle

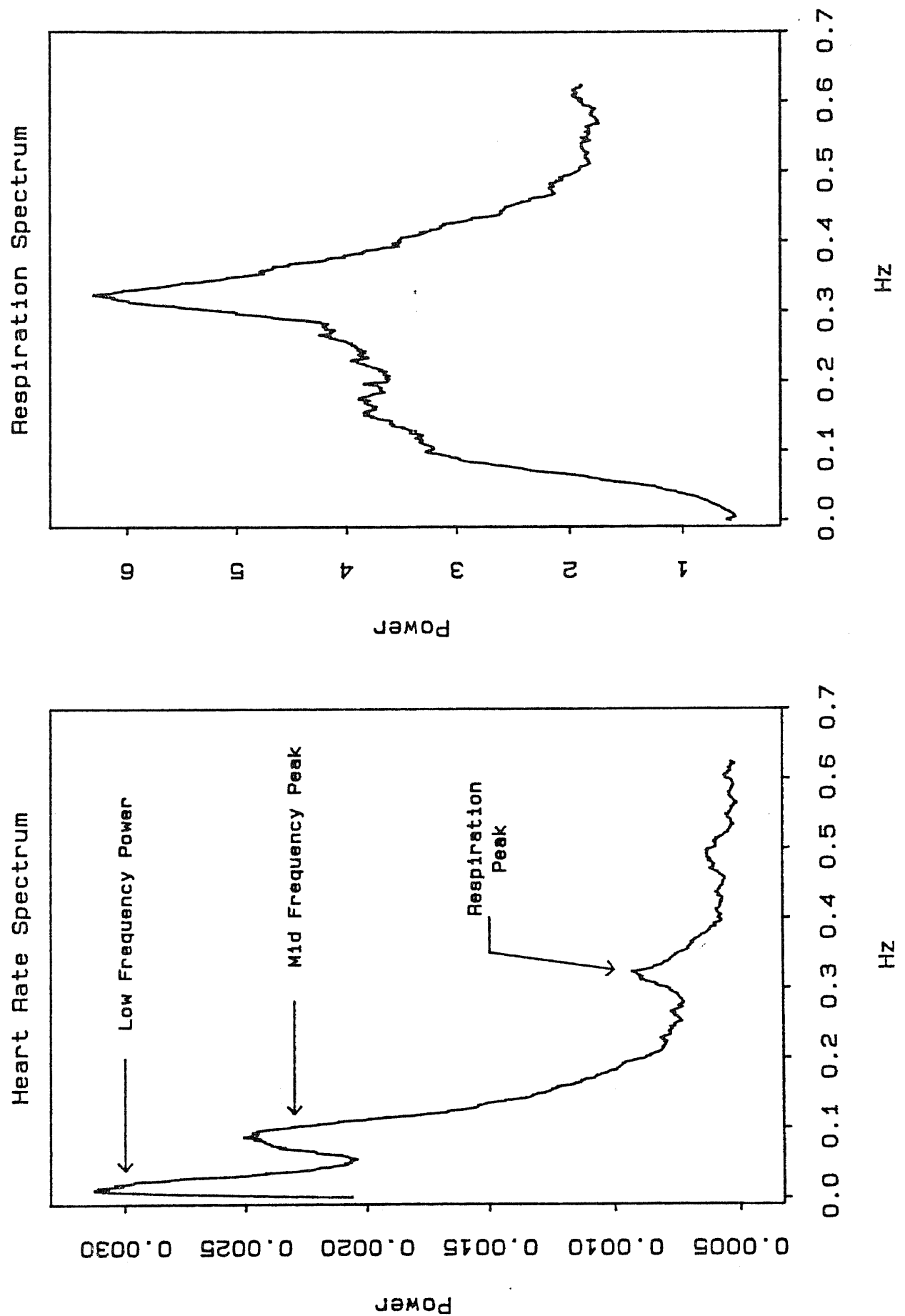
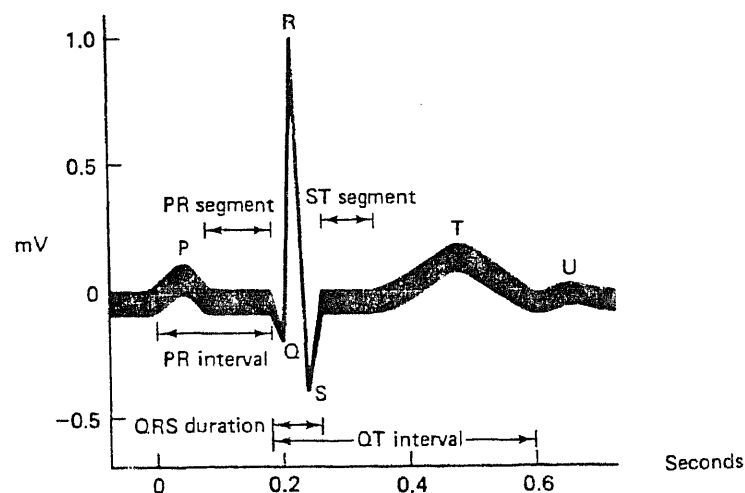


Figure 1.1 Heart Rate Spectrum and Respiration Spectrum

contraction and produce a time varying field. Because the body fluids are good conductors, fluctuations in potential that represent the algebraic sum of the action potentials of myocardial (heart) fibers can be recorded from the surface of the body. Electrodes on the skin surface pick up these potentials for input to the ECG machine. Once an action potential has been initiated and the heart is responding to this by contracting the muscles another action potential cannot activate the heart until a certain amount of time called the refractory time has elapsed.

The ECG can be recorded in a number of ways. The method chosen is the simplest to implement and gives all the required information. The ECG signal could be picked up on any part of the body, but obviously the signal will be stronger and with less noise closer to the heart. The ECG signal has a characteristic shape and is made up of a P wave, QRS complex and T wave. The ECG of a normal individual is as shown in figure 1.2.



A wave of excitation spreads over the atria, producing



the P wave and causing the atria to contract. The excitation is delayed in the AV (atrioventricular) node resulting in the P-R interval. Then the wave of excitation spreads over the ventricles, causing them to contract and produces the QRS complex. Recovery of ventricular depolarization produces the T wave.

In the normal human heart, each beat originates in the SA node. The heart beats about 70 times a minute at rest. The rate is slowed during sleep and accelerated by emotion, exercise, fever and many other stimuli<sup>7</sup>. In healthy young individuals the heart rate varies with the phases of respiration. The effect of respiration may be absent during quiet breathing but is readily seen when the depth of breathing is increased.

### 1.3 AUTONOMIC NERVOUS SYSTEM

The motor portion of the nervous system that controls the visceral functions of the body is called the autonomic nervous system. This system helps to control certain activities almost entirely and others only partially. The autonomic nervous system is activated mainly by centers located in the spinal cord, brain stem and hypothalamus.

The autonomic impulses are transmitted to the body through two major subdivisions called the sympathetic and parasympathetic systems. Varied effects on different visceral functions of the body are caused by stimulating the sympathetic and parasympathetic nerves. Their effect<sup>8</sup> on a few organs is shown in the table 1.1. Certain organs are

excited or show excitatory effects due to sympathetic stimulation and others show inhibitory effects.

Likewise, parasympathetic effect causes excitation in some organs but inhibition in others.

Table 1.1 Comparison of the effects of parasympathetic and sympathetic stimulation

ORGAN	EFFECT OF SYMPATHETIC STIMULATION	EFFECT OF PARASYMPATHETIC STIMULATION
Eye: Pupil	Dilated	Contracted
Ciliary muscle	None	Excited
Sweat glands	Copious sweating	None
Heart: Muscle	Increased rate	Slowed rate
	Increased force of contraction	Decreased force of atrial contraction
Coronaries	Vasodilated	Constricted
Mental activity	Increased	None

Also, when sympathetic stimulation excites a particular organ, parasympathetic stimulation often inhibits it, which shows that the two systems occasionally act reciprocally to each other. However, most organs are dominantly controlled by one or the other of the two systems, so that except in a few systems, the two systems do not actively oppose each other. It cannot be generalized whether the effect of parasympathetic or sympathetic stimulation of a particular organ will cause excitatory or inhibitory effects in that organ.

In general, sympathetic stimulation increases the overall activity of the heart. This is accomplished by increasing both the rate and force of contraction of the

heart beat. Parasympathetic stimulation cause mainly the opposite effects, decreasing the overall activity of the heart.

We could say that sympathetic stimulation increases the effectiveness of the heart. However, sympathetic stimulation unfortunately also greatly increases the metabolism of the heart while parasympathetic stimulation decreases its metabolism and allows the heart a certain degree of rest.

The sympathetic and parasympathetic systems are continually active, and the basal rates of stimulation are known respectively as sympathetic tone or parasympathetic tone. The value of the tone is that it allows activity of a stimulated organ.

Large portions of the sympathetic nervous system often become stimulated simultaneously, a phenomenon called mass discharge. This characteristic of sympathetic action is in keeping with the usually diffuse nature of sympathetic function, such as overall regulation of arterial pressure or of metabolic rate. Of course, in a few instances sympathetic activity does occur in isolated portions of the system.

In contrast to the sympathetic system most reflexes of the parasympathetic system are very specific. Particularly in the interest of this research, parasympathetic cardiovascular reflexes usually act only on the heart to increase or decrease its rate of beating.

#### 1.4 STATEMENT OF PROBLEM

This project studies heart rate variability due to autonomic nervous activity using time series analysis. The work concentrated mainly on the effect of the parasympathetic nervous system on the heart rate.

The study examined five areas as follows

1. The relationship between respiration and heart rate.
2. The stability of the heart rate spectrum.
3. The effects of atropine on the heart rate spectrum.
4. The effect of paced breathing on the heart rate spectrum.
5. The effect of stress on the heart rate spectrum.

The work concentrated on the respiration peak because it is the best understood component of the heart rate spectrum and because it reflects the parasympathetic inputs that are the focus of this study.

Data was available from twelve helicopter pilots of the U.S. Army. Their ECG and respiration was recorded for several hours while they flew a helicopter simulator. At some point in time on certain days they injected themselves with 2mg. or 4mg. of atropine. Atropine has the effect of inhibiting the parasympathetic nervous system.

It was investigated whether the respiration spectrum could be used to detect the respiration peak in the heart rate spectrum even when the peak was small or ambiguous. It was also investigated if there was a relationship between the magnitude of the peak in the respiration spectrum and the magnitude of the peak in the heart rate spectrum. It is

found that there is no simple relation between the magnitude of the peaks at the respiration frequency in the two spectra. Stability of the heart rate from day to day for a given individual was studied. This factor is quite crucial for understanding how the heart rate spectrum can be used. The stability of the spectra was examined on the days the pilots were not given drugs. However, the possibility that the effect of atropine lasted more than a day could not be ruled out. Additional data was then collected from five subjects. ECG and respiration was collected from three men and two women between the ages of 22 and 33 with no known disease. It is found that their spectra is more stable from day to day.

The effect of atropine was then studied. The respiration peak was visible around .25Hz and after the administration of atropine the peak diminished rapidly and was barely detectable. The power in the peak decreased and the peak amplitude decreased to a fourth of its original height. It is quite evident that the respiration peak reflects a parasympathetic input to the heart that can be abolished by muscarinic blockade which is consistent with findings by other researchers.

An experiment was then designed to study the effect of paced breathing and stress on the heart rate. Data was collected from eight subjects in the age group 23 to 44. All of them were non smokers and data was collected at approximately the same time everyday. The effect of paced

breathing was, the predominant high frequency component in the heart rate spectrum. The same subjects showed a predominant low frequency component when breathing spontaneously. The power in the respiration peak is found to decrease with the increase in frequency of paced respiration.

Cardiovascular control systems change in many pathological situations and it seems natural that these changes might be detected by analysis of heart rate variability. Ultimately we hope to provide a non-invasive tool to detect heart defects. It is hence, first necessary to study the effect of known parameters such as the parasympathetic nervous system on the heart rate.

## 2. MATHEMATICAL AND COMPUTER TECHNIQUES

### 2.1 INTRODUCTION

Heart beats are considered as point events. i.e., the individual characteristics (shape, amplitude) of each beat are neglected but its time of occurrence or equivalently the interval between successive beats is taken as a relevant variable.

From the raw signal, the ECG variations of the interval length are not easily discerned. Hence another representation method is needed to display the signal. Existing methods for the statistical analysis of series of events were developed for stochastic series and are not always suited for the analysis of physiological point event signals. Therefore techniques are needed that convert the point event signals to a form that is accessible to standard system analysis techniques (e.g. averaging, spectral analysis). In addition the converted signal should preferably be visually informative.

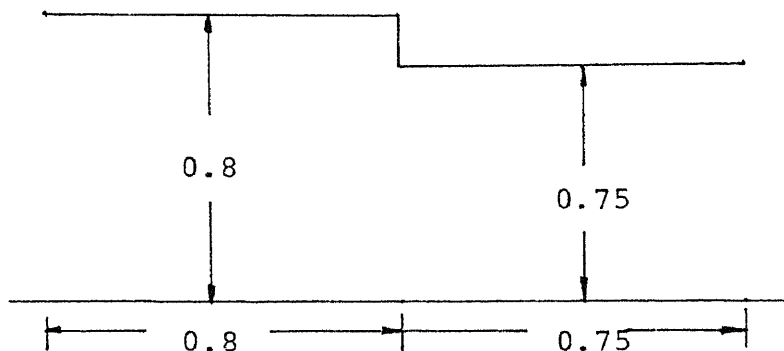
There are several analysis methods available<sup>9</sup>. In this study the R wave in the ECG was taken as the event of interest. The method used the time intervals between R waves or otherwise called the interbeat interval (IBI) to form a continuous analog signal.

### 2.2 INTERPOLATION

The heart rate is not strictly periodic, as the length of IBIs vary. To take the Fourier transform we need data sampled at equidistant intervals. As we are studying the

variability of the heart rate, we need to obtain an analog signal from our IBI signal and then sample it. The sampling is done at the rate at which the respiration signal was sampled, so that we study the relationship between the two spectra more easily. The sequence of interbeat intervals is interpolated to provide a continuous data stream at the sampling rate that is used for respiration. A program was written in Fortran to do this. In this interpolation scheme, the IBI signal is given the value of the IBI for as long as the IBI lasts. Thus, if the sampling rate is 20 Hz an IBI of 0.8 sec produces sixteen 0.05 sec bins with a value of 0.8. If the next IBI was 0.75sec then you would have fifteen bins of value 0.75. The sequence of pulses is transformed into a sequence of steps as shown in figure 2.1.

Figure 2.1 Interpolation



There are various other ways to interpolate the IBI data. This scheme was used because the results were meaningful and this method did not give any extraneous information. It was also found that smoothing out the sharp corners did not make any significant improvement in the results. Figure 2.1 shows the interpolated data.



## 2.3 OUTLIERS

The resulting IBI signal is adjusted for outliers. Having data following a certain pattern over a period of time, it is possible to predict the range of the values. Values which are too far out of this range, i.e. values not considered statistically consistent with the data are called outliers and are clipped. Outliers are defined according to Tukey<sup>10</sup> as points that are

$$\begin{aligned} x &< \text{1st quartile} - 1.5 * \text{interquartile range} \text{ or} \\ x &> \text{3rd quartile} + 1.5 * \text{interquartile range} \end{aligned}$$

Outliers that are defined by this method are more than  $4^{2/3}$  standard deviations ( $p < 0.00003$ ) out in a normal distribution. Therefore only extreme outliers are subject to adjustment. Figure 2.2a shows the interpolated data and figure 2.2b shows the data with the outliers removed. Note the change in scale of figure 2.2b.

## 2.4 DETRENDING

The data is then smoothed. Data smoothing refers to the measures which are introduced into the formulation of a data processing scheme in order to reduce the effects of observational errors (commonly called noise). Since data smoothing generally has also a mutilative effect on the signal component, it presents a need for careful analysis to achieve desirable results. In our study the data was first detrended. The data is detrended using a robust locally weighted regression procedure<sup>11</sup>. The term trend refers to the slow changes across a time series, such as a tendency for the mean heart rate to increase over a collection

Interpolated data

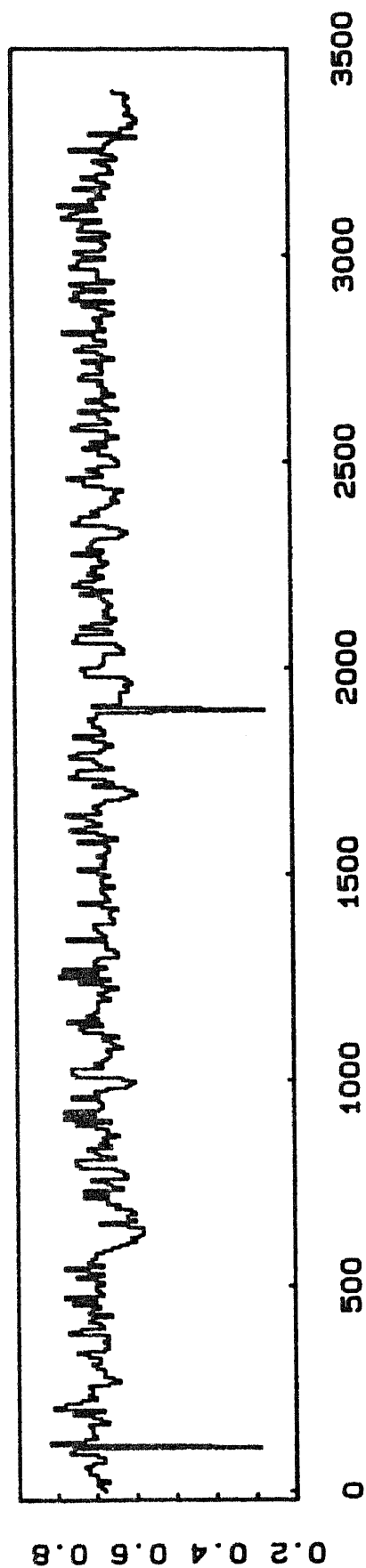


Figure 2.2a Interpolated data

Clipped data

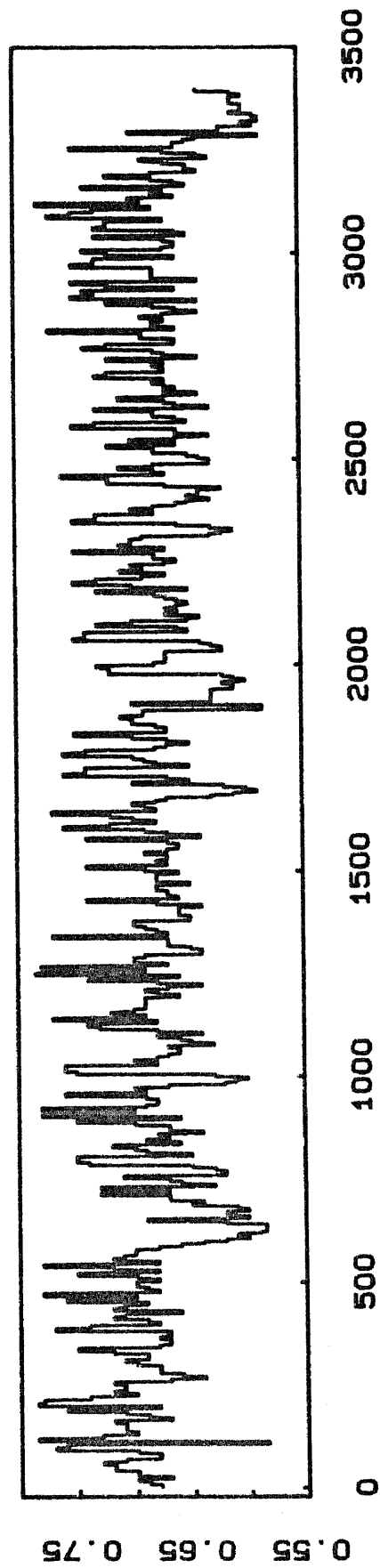


Figure 2.2b Clipped data

period. These trends are close to zero frequency and can be removed by a high pass filter. This is a nonlinear process<sup>12</sup> and the reason for using such a process is that the data is not stationary. A routine called 'LOWESS' is used, which calculates the low pass filtered trend estimates and subtracts the fitted estimates from the raw data. This procedure removes very low frequency trends which can distort the spectrum.

## 2.5 WINDOWING

The process of considering only a finite number of terms, of an infinite series is called windowing. The process of terminating the series after a finite number of terms can be thought of as multiplying the infinite-length series by a finite width window function. The term 'window' is quite descriptive in the sense that it determines how much of the original series we can 'see'. In the case where the series is abruptly terminated without modification of any coefficients, we may consider the window to be rectangular. The rectangular window has been considered as the source of convergence difficulties<sup>13</sup> or leakage. There are better windows to terminate the series with a finite number of terms. We can consider the terminated series as the product of the infinite length series and a window function. Since multiplication in the time domain corresponds to convolution in the frequency domain, the actual frequency response may be considered as the convolution of the desired frequency response and the

frequency response (Fourier transform) of the window function which turns out to be a sine function  $\frac{\sin \pi f \tau}{\pi f \tau}$ . The result is spreading of the spectral components away from the correct frequency causing an unwanted modification of the spectrum. This is mathematically represented by

$$\bar{H}(f) = \frac{T}{2\pi} \int_{-\pi/T}^{\pi/T} H(\bar{f}) \frac{\sin \pi (F-\bar{f})}{\pi (F-\bar{f}) \tau} d\bar{f}$$

Figure 2.3 shows the transform of a signal with infinite samples (a) compared to one with abruptly terminated samples (b). The spreading is mainly due to the fact that our window function does not converge rapidly at the ends.

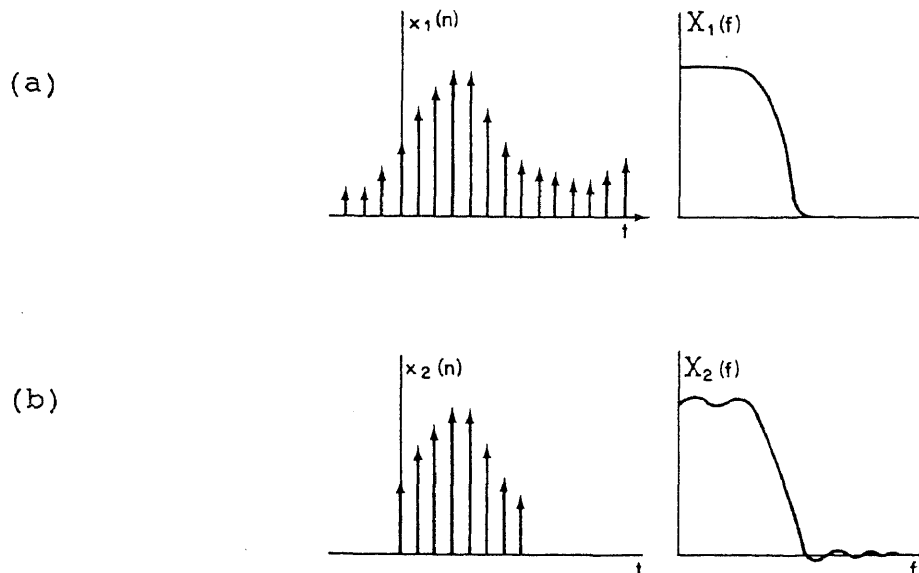


Figure 2.3 Illustration of leakage effect produced by abrupt termination of the signal

Rectangular windows are acceptable in some applications, and would have worked adequately in ours. However, to

obtain the maximum possible accuracy, another suitable window was chosen to alleviate the leakage effect.

In the windows which will be discussed, all functions will be represented in continuous time form for ease of development (function of  $t$ ). To apply them to discrete time systems, replace the variable  $t$  with  $nT$ . The variable  $n$  can then assume all values from 0 to  $M$ , the maximum number of samples. All functions are even and are assumed to have a width  $\tau$ . Only the positive side of the function will be shown. In use, it will be shifted  $N/2$  points to the right so that the window is centered on the time sample interval before multiplying by the window coefficients.

The amplitude vs. frequency response of the window will be presented in terms of decibel function,  $W_{db}(f)$ , that is normalized with respect to the D.C. value  $W(0)$ .  $W_{db}(f)$  is defined by<sup>13</sup>.

$$W_{db}(f) = 20 \log_{10} \frac{|W(f)|}{W(0)}$$

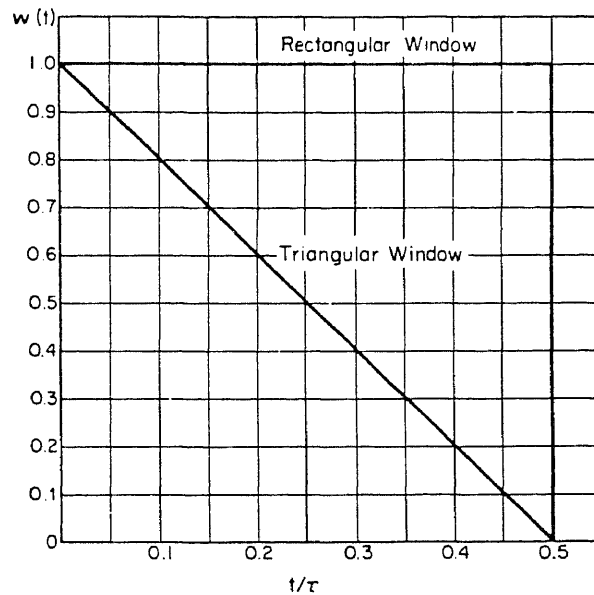
The amplitude response curves are presented as a function of  $f/F$ , where  $F$  is defined as

$$F = 1/\tau, \quad \tau \text{ is the sampling interval.}$$

Rectangular and triangular windows are shown in figure 2.4. The rectangular window is considered as a basis for reference in looking at the other functions. Table 2.1 lists a few common window functions and their transforms. The plots of these functions are shown in figures 2.5, 2.6 and 2.7.

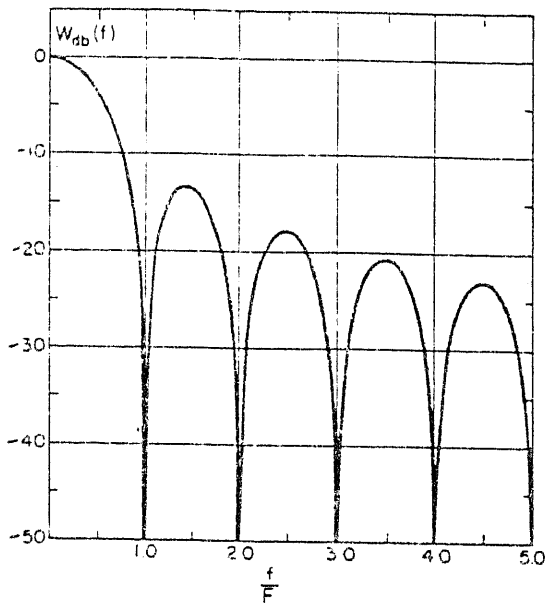
For the window function to have minimal effect on the desired amplitude response of the spectrum when it is convolved, it is necessary that the window spectrum approximate an impulse function in some sense.

Figure 7.1

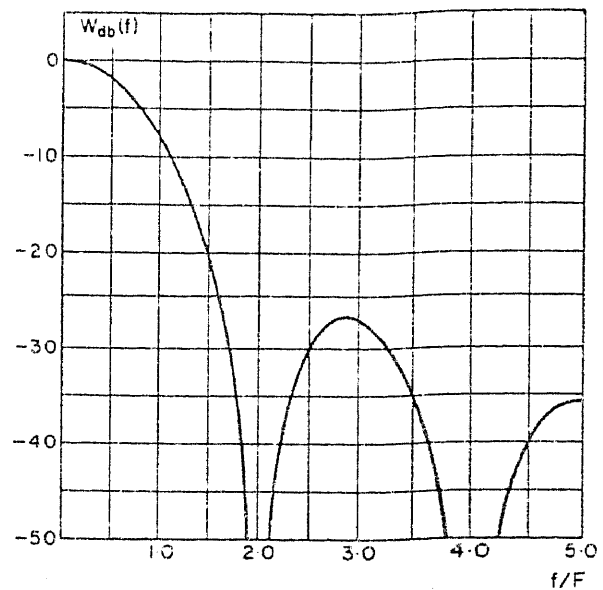


Rectangular and triangular window functions.

That is, we are trying to concentrate maximum energy at the center of the spectrum and ideally, we would need an infinitely long window to accomplish this. In general the spectrum of a window function should have a main lobe which is as narrow as possible and side lobes as small as possible relative to the main lobe. The main lobe gives rise to the transition band (a region between a stop and a pass band) and the side lobe gives rise to the wiggles (the Gibbs phenomenon) which may be regarded as 'contamination' from parts of the function that are adjacent to where we are



Decibel amplitude response of rectangular window function.

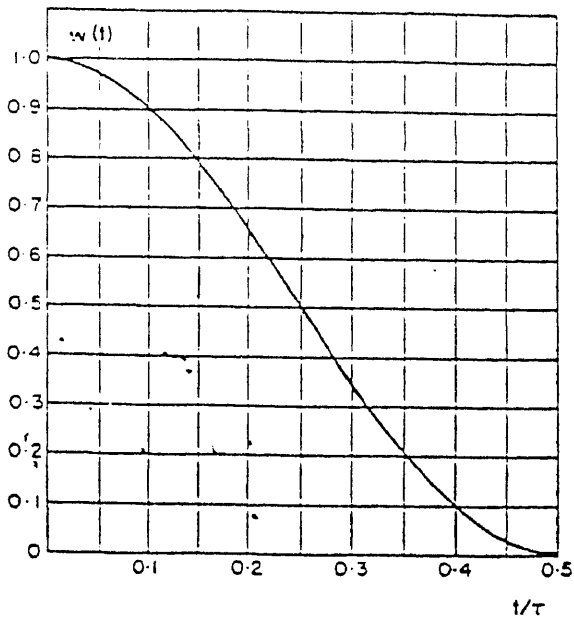


Decibel amplitude response of triangular window function

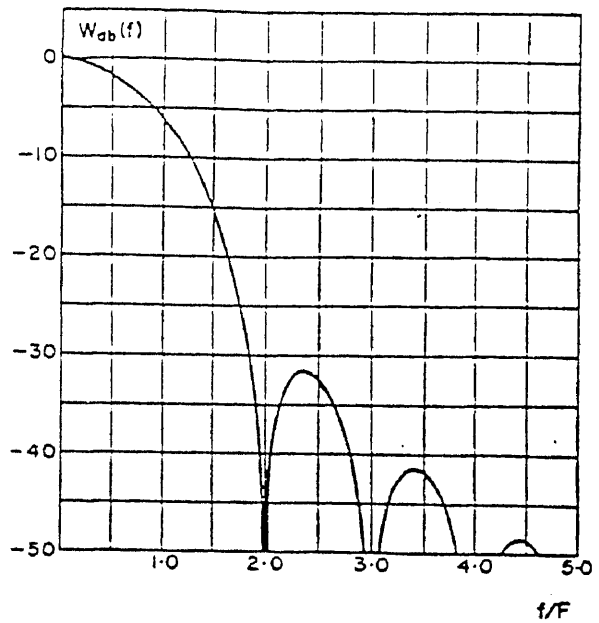
Figure 2.5 Decibel amplitude response of rectangular and triangular window functions

Table 2.1 Window functions

WINDOW	DEFINITION	TRANSFORM
RECTANGULAR	$w(t) = 1$ for $ t  \leq \frac{\tau}{2}$ $= 0$ elsewhere	$W(f) = \frac{\tau \sin(\pi f \tau)}{\pi f \tau}$
TRIANGULAR	$w(t) = 1 - \frac{2 t }{\tau}$ for $ t  \leq \frac{\tau}{2}$ $= 0$ elsewhere	$W(f) = \frac{\tau}{2} \left[ \frac{\sin(\pi f \tau / 2)}{(\pi f \tau / 2)} \right]^2$
HANNING	$w(t) = \cos^2 \frac{\pi t}{\tau}$ for $ t  \leq \frac{\tau}{2}$ $= 0$ elsewhere	$W(f) = \frac{\tau}{2} \frac{\sin \pi f \tau}{\pi f \tau} \frac{1}{1 - (f \tau)^2}$
HAMMING	$w(t) = .54 - .46 \cos \frac{2\pi t}{\tau}$ for $ t  \leq \frac{\tau}{2}$ $= 0$ elsewhere	$W(f) = \tau \frac{\sin \pi f \tau}{\pi f \tau} \frac{.54 - .05 (f \tau)^2}{1 - (f \tau)^2}$

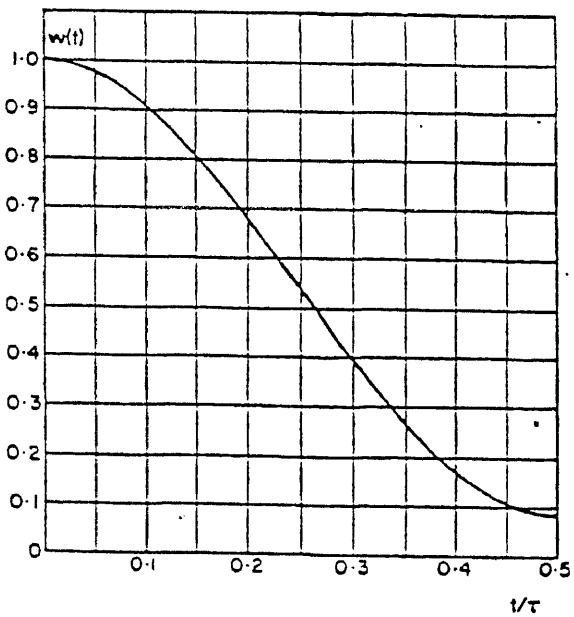


Hanning window function.

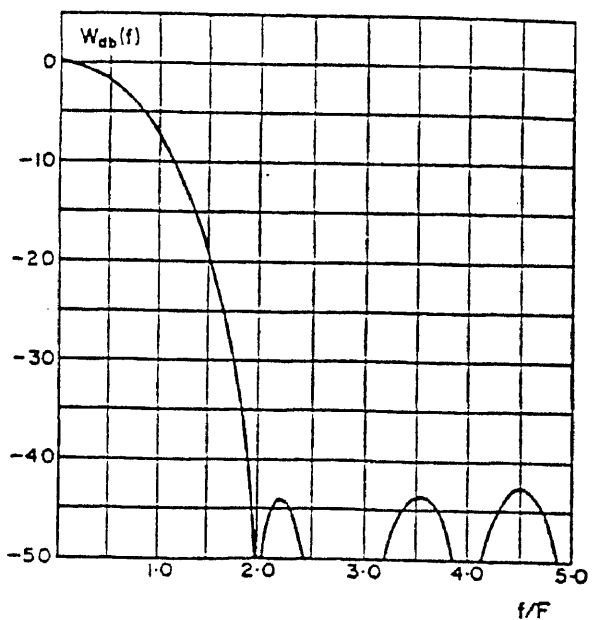


Decibel amplitude response of Hanning window function.

Figure 2.6 Hanning window and its decibel amplitude response



Hamming window function.



Decibel amplitude response of Hamming window function.

Figure 2.7 Hamming window and its decibel amplitude response



looking.

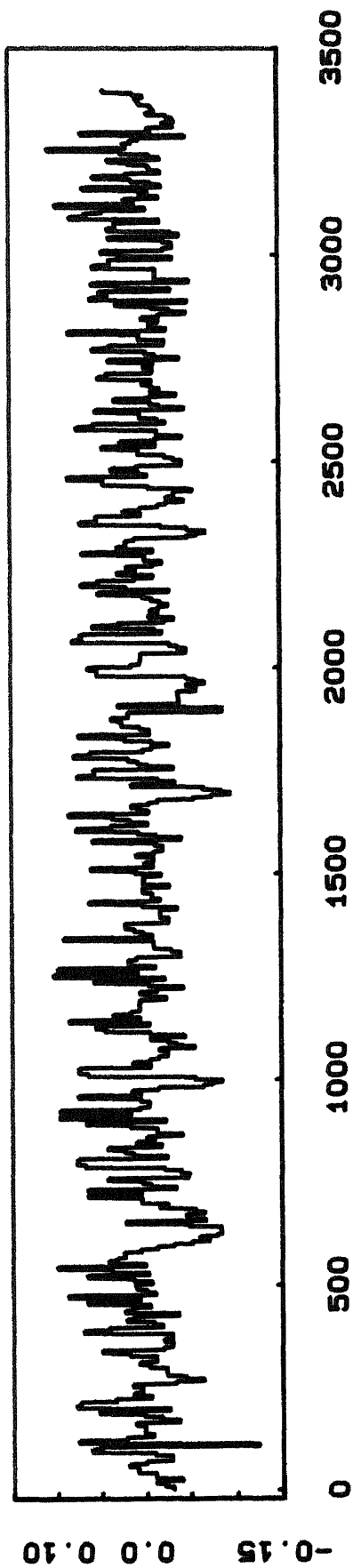
There are various types of windows depending on the application it is used for. The possibilities of windows<sub>14</sub> are endless. Using a window once produces some smoothness in the transfer function, applying it twice should produce a transfer function that has a continuous first derivative and hence more convergence in the resulting Fourier series. Applying the rectangular window twice, causes a wider transition band due to the double application. The result of convolving the window with itself and then applying the result once is like applying a triangular shaped window whose base is twice the original window width and whose apex is in the middle.

The data after detrending is tapered using a split cosine window to reduce the leakage in the spectrum. Typically the first 20% and the last 20% of the data will be tapered.

## 2.6 FOURIER TRANSFORM

The Fourier transform is then taken using the FFT. The Fast Fourier transform used implements the Sande-Tukey radix-2 fast Fourier transform. The Fourier transform of a signal can be expanded into the sum of an infinite number of harmonically related sine and cosine terms. The resulting periodogram is smoothed across blocks of 41 frequencies using a triangular window to produce a spectrum. Figure 2.8a shows detrended data and figure 2.8b shows the corresponding spectrum. Since we have data for several hours, we get

Detrended data



Spectrum

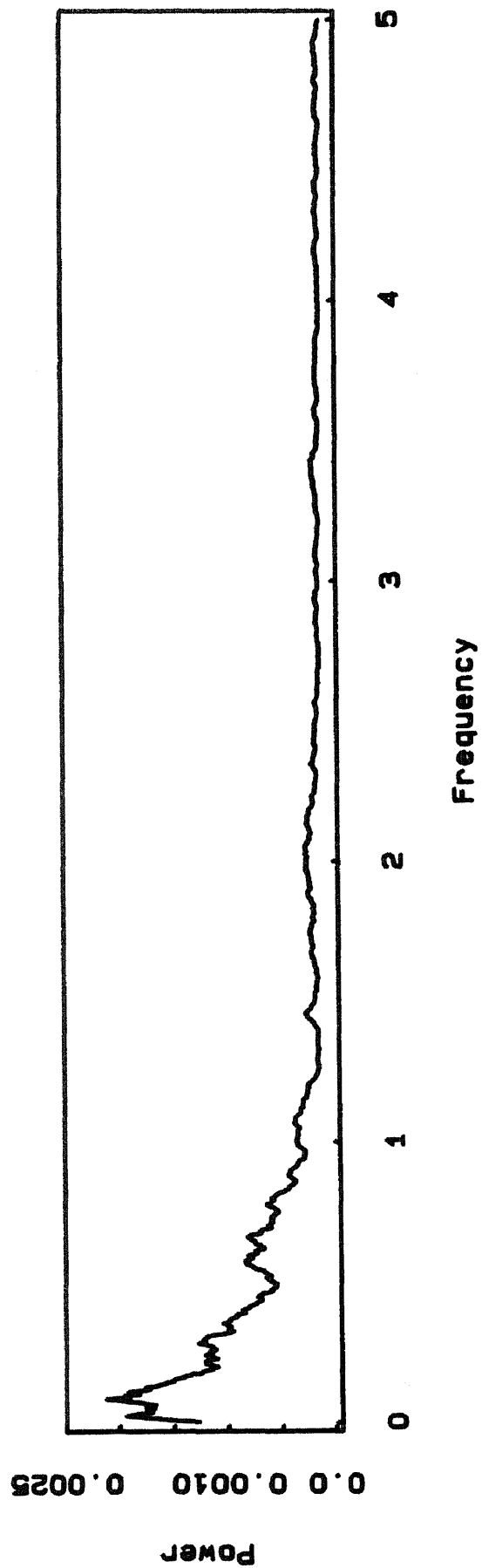


Figure 2.8a Detrended data

Figure 2.8b Spectrum

several spectra for each session. Finally the average spectrum is computed by averaging across the spectra of the individual 4096 point segments. Thus, the average spectrum shows only the features that are statistically consistent across the entire record. The same procedure is followed to compute the respiration spectrum, except that no interpolation is needed since respiration (unlike IBI) can be sampled at equidistant intervals from a continuous signal. Statistical techniques are then applied to analyze the data.

### 3. STUDIES PERFORMED

#### 3.1 INTRODUCTION

Heart rate variability due to autonomic nervous activity was studied using time series analysis. The work concentrated on the effect of the parasympathetic nervous system on the heart rate. In particular the work concentrated on the respiration peak because it is the best understood component of the heart rate spectrum and because it reflects the parasympathetic inputs that are the focus of this study.

Tests available to provoke changes of parasympathetic outflow in man are multiple and varied. They may be simple or complex, they may be noninvasive or highly invasive. Most analyses rely on changes of heart rate, few are based on changes of arterial pressure or its hemodynamic determinants. Most tests of autonomic function may provoke different responses in patients with cardiovascular diseases than in healthy volunteers. Eckberg<sup>14</sup> believes that to improve scientific credibility of tests used to assess human parasympathetic reflex responsiveness, the external particulars of each test should be controlled rigorously. Also the responses of two groups (patients with heart disease and healthy volunteers) should be compared when administered the same test.

The aim of this study however, is to get a better understanding of the effect of the parasympathetic input to the heart. The study was conducted on data collected from

three different experiments.

The first set of data was from an experiment conducted by the U.S. Army on helicopter pilots. These pilots were in excellent physical condition and their ECG and respiration was recorded for several hours while they flew a helicopter simulator. At some point in time on certain days they injected themselves with 2mg. or 4mg. of atropine. Atropine has the effect of inhibiting the parasympathetic nervous system. With this data the relationship between respiration and heart rate was studied and also the effect of atropine. The second experiment was conducted on five subjects, three men and two women in the age group 22 - 33. These subjects were all seemingly healthy, were not taking any medications except that one woman was taking oral contraceptives. Each subjects ECG and respiration was recorded on at least five different occasions at approximately the same time of day over a period of two weeks. Subjects were asked to sit quietly with their eyes open and to breathe spontaneously for about 10 mins while their measurements were taken. This data was used to study the stability of the heart rate spectrum.

The third set of data was collected from 8 subjects, all men, age group 23 - 44. These subjects were also seemingly healthy, non-smokers and were not taking any medication. They were first checked by a physician for any 'hidden' heart defects. At first the subjects were asked to sit quietly and breathe normally. Their ECG and respiration was

then recorded for 5 mins. Then they were asked to follow a display on a computer terminal which synchronized their breathing to a particular rate. Paced breathing at 10/min, 15/min and 20/min was then recorded. During paced breathing at 15/min, the subjects had to hold their breath every 1.5 mins for 6secs at different points in their respiration cycle as indicated by the display on the computer terminal. Data was also collected when the subjects performed the Valsalva maneuver and during a stress test. The Valsalva maneuver<sup>15</sup> comprises an abrupt transient voluntary elevation of intrathoracic and intra-abdominal pressures provoked by straining. The stress test consisted of 8mins of mental arithmetic performed by the subjects with a metronome clicking every second while the subject was constantly told to be quicker and more accurate. The effect of paced breathing and mental stress on the heart rate spectrum was studied using this data.

### **3.2 RELATIONSHIP BETWEEN RESPIRATION AND HEART RATE.**

The data from the study on the helicopter pilots was used to study this relationship. In healthy individuals heart rate increases and decreases cyclically during inhalation and exhalation. This "respiratory sinus arrhythmia" is vagally mediated and reflected in the respiration peak of the heart rate spectrum. The first practical problem faced was locating the respiration peak in the heart rate spectra especially when the magnitude of the peak is dramatically diminished, such as under the influence

of atropine. A plot of the frequency of the actual peak in the respiration spectrum (x-axis) versus the frequency of the respiration peak in the heart rate spectrum (y-axis) showed a linear one to one relation (see figure 3.1). The regression between the frequency of the respiration peak in the respiration spectrum and the frequency of the respiration peak in the heart rate spectrum was quite significant ( $p < 0.0001$ ). The slight discrepancies that do exist is because the heart rate signal used is not a continuous signal while the respiration is continuous. Since we have such a good fit in the relation between the frequency of the respiration peak in the respiration spectrum and the frequency of the respiration peak in the heart rate spectrum. It is felt that the respiration spectrum can be used to locate the respiration peak in the heart rate spectrum even when the peak is diminished or ambiguous.

It was also investigated, using the helicopter pilots data, if there was a relationship between the magnitude of the peak in the respiration spectrum and the magnitude of the peak in the heart rate spectrum. Figure 3.2 shows a plot of the magnitude of the respiration peak in the heart rate spectrum (y-axis) versus the magnitude of the respiration peak in the respiration spectrum (x-axis). It was found that there was no simple relation between the magnitude of the peaks at the respiration frequency in the two spectra. If such a relationship existed, it would be important because

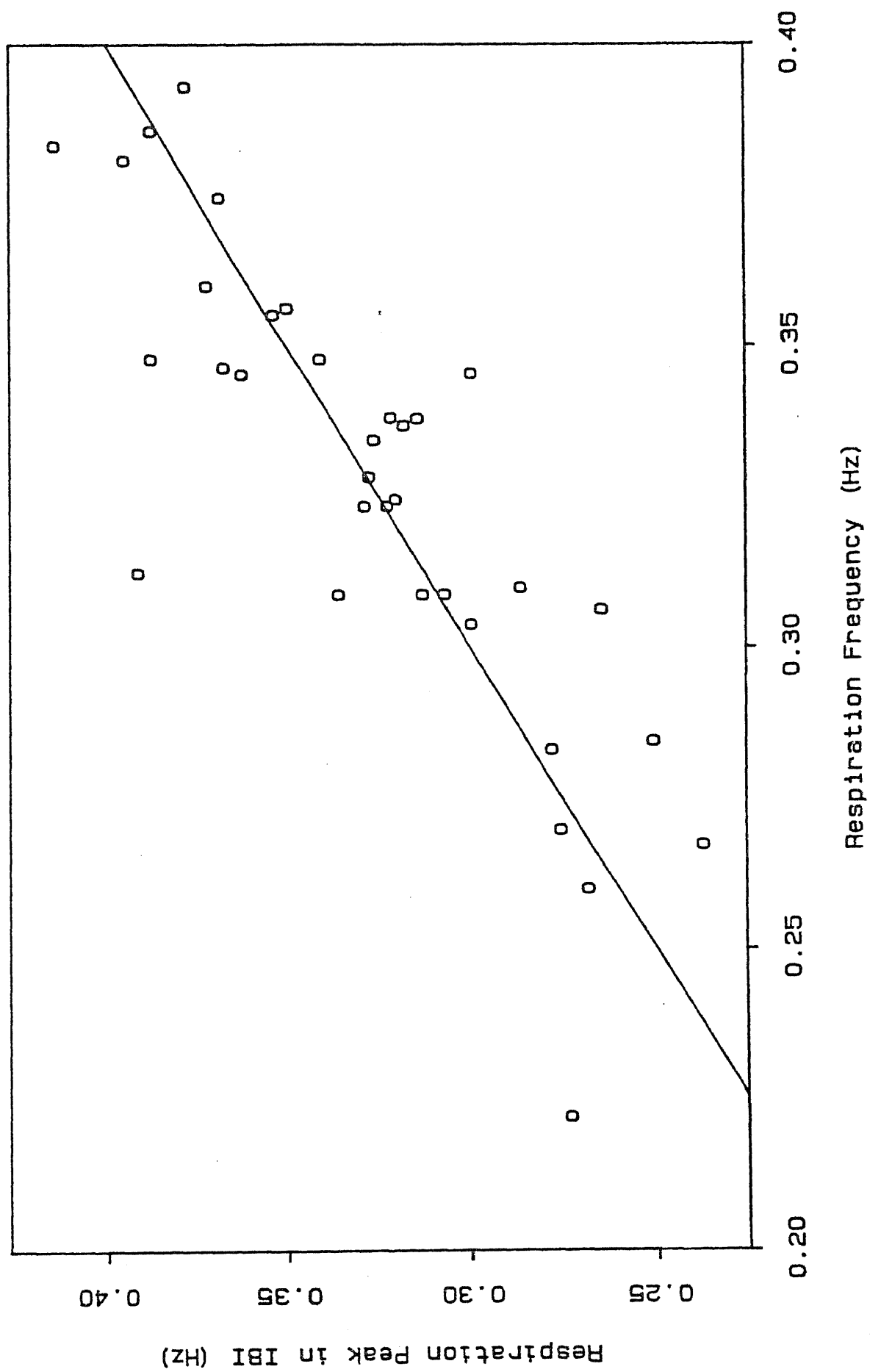


Figure 3.1 Freq. in Resp. spectrum vs. Freq. in Heart Rate Spectrum



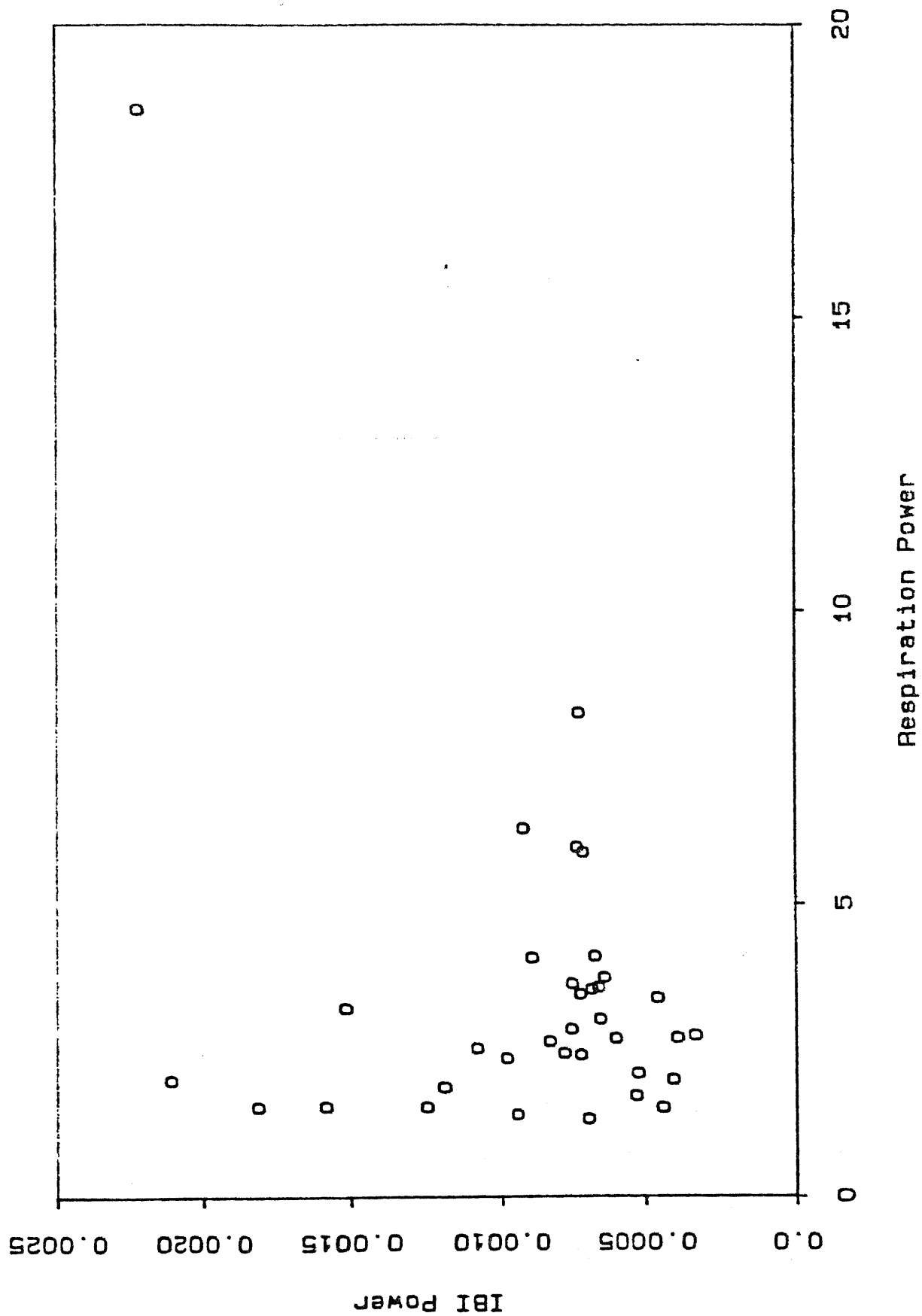


Figure 3.2 Magnitude of resp. peak in resp. spectrum vs. corresponding peak in heart rate spectrum

it would mean that respiration could be treated as an input with the respiration peak in the heart rate spectrum as its output, and the parasympathetic link between the two could be characterized as a transfer function. The data indicated that this is not the case. First of all the respiration changed dramatically over the course of the experiment, maybe due to talking. There were a lot of changes in the mode of respiration over the entire record, this is possibly due to the fact that the subjects were not just sitting quietly but flying a helicopter simulator and talking. Secondly, it is possible that the system mediating respiratory sinus arrhythmia may not be linearly superposable. Perhaps a study of the area under the respiration peak in the heart rate and respiration spectra would throw more light on this matter, or maybe the square root of the amplitude of the respiration peaks in the two spectra are related. More data should be collected under controlled conditions and further investigation in this regard needs to be carried out.

### 3.3 EFFECTS OF ATROPINE ON THE HEART RATE SPECTRUM

The helicopter pilots injected themselves on certain days with 2mg or 4mg of atropine. Atropine has rapid and profound changes on the heart rate spectrum. The respiration peak was visible around .25Hz and after the administration of atropine the peak diminished rapidly and was barely detectable. Figure 3.3 shows the heart rate spectrum and figure 3.4 the respiration spectrum for the

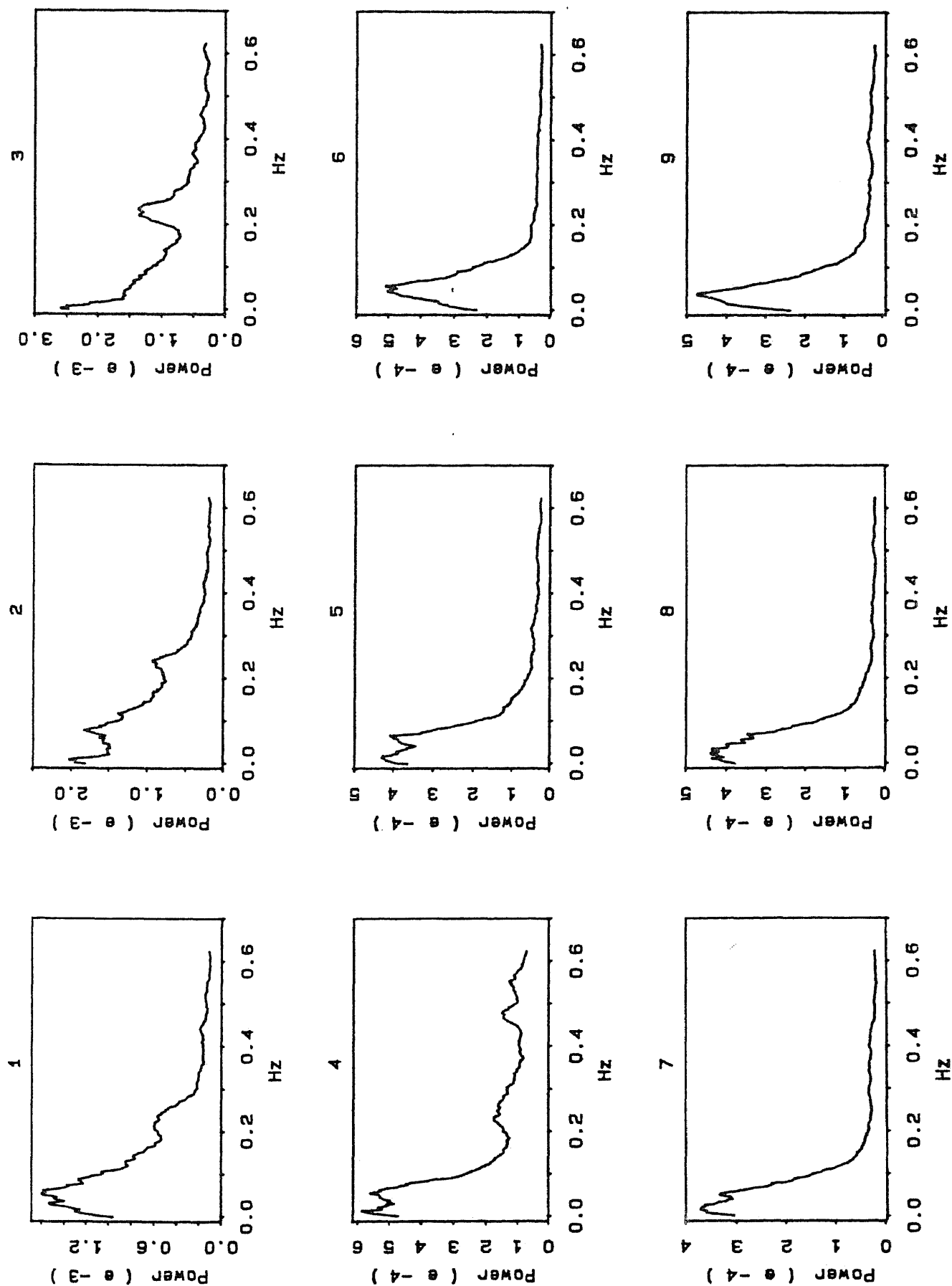


Figure 3.3 Heart Rate Spectra

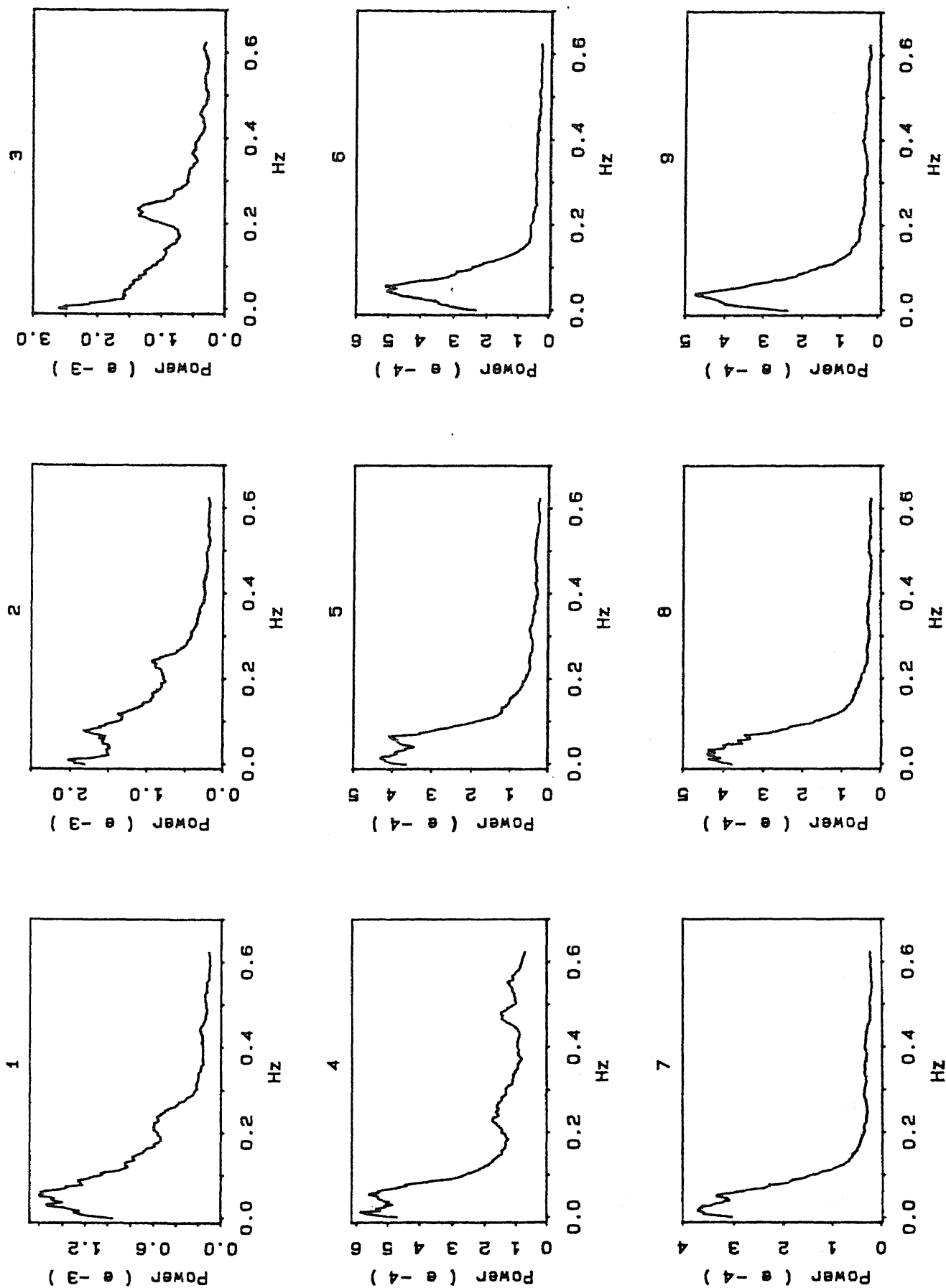


Figure 3.4 Respiration Spectra

same test on the same person. Each spectrum is for 6.8 minutes and is shown in order (according to numbers) during the course of the simulated flight. As can be seen the first three panels show the respiration peak quite clearly in the heart rate spectra. The pilot at some point in the third spectra injected himself with 2mg. of atropine. The following spectra show a rapidly diminishing respiration peak. It is to be noted that there is no change in the breathing of the subject, it continues at about .25Hz i.e about 15 breaths/min, but that the respiration pattern is not being transmitted to the heart. The respiration peak in the respiration spectra continues to be the same (magnitude and frequency) which proves a vital point that parasympathetic input to the heart can be severed by mucarinic blockade. Hence we can quantify parasympathetic input to the heart.

It was also noted that the total power in the heart rate spectrum decreased. However the decrease in total power was not as large as the decrease in the magnitude of the respiration peak. Atropine decreased the respiration peak in the IBI spectrum by an average of 74.3% ( $\pm .07$  SEM), but it only decreased total power by an average of 41.1% ( $\pm .09$ SEM), ( $p < 0.01$ ). The magnitude of respiration peak in the IBI spectrum is shown in figure 3.5. The mean level for all pilot's respiration peaks in the last three spectra of morning records are shown (error bars are SEM). Both doses of atropine 2mg. and 4mg produced similar dramatic ( $p <$

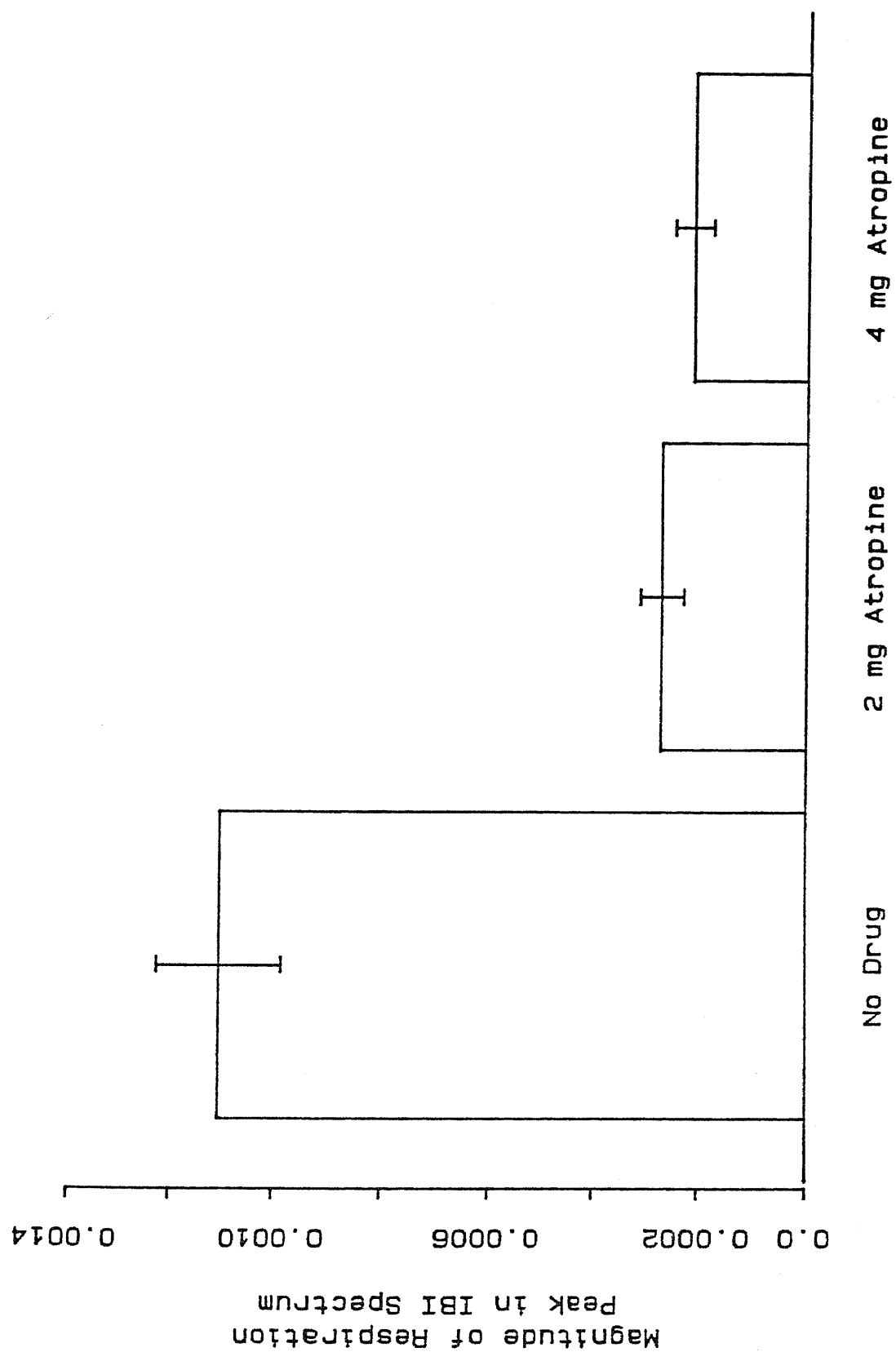


Figure 3.5 Magnitude of respiration peak in IBI spectrum with and without drugs

.000013) effects in the respiration peaks of the heart rate spectra. Calculated as percent decreases from baseline, these represented declines of 72.6% (2mg) and 76.04% (4mg). These data indicate that the doses of atropine used in this study effectively blocked parasympathetic input to the heart at least until the end of the morning flight. There was no significant difference between the doses at this point in the day suggesting that blockade of the parasympathetic input to the heart was essentially maximal at 2mg.

Another interesting observation was that the time course for the two dosages was different. Figure 3.6 compares the power in the respiration peak over the last 20 min of the morning and afternoon flight for the two doses. There is substantial recovery from both doses by the end of the afternoon flight. The 2mg dose was 30.1% below baseline and the 4mg dose was 39.8% below baseline. The difference between the two doses in the afternoon approached statistical significance ( $p < .09$ ). This may be more significant if we have more data for comparison.

The other concern investigated was whether the effect of atropine lasted into the following day. Therefore we compared the magnitudes of the respiration peak on the morning following drug days with the mornings with no drugs (and no drugs on the previous day). There was no significant difference between the average amplitude of the respiration peak on the morning after drug days ( $0.000956 \pm 0.000098$  SEM) and on other no drug mornings ( $0.00112 \pm$

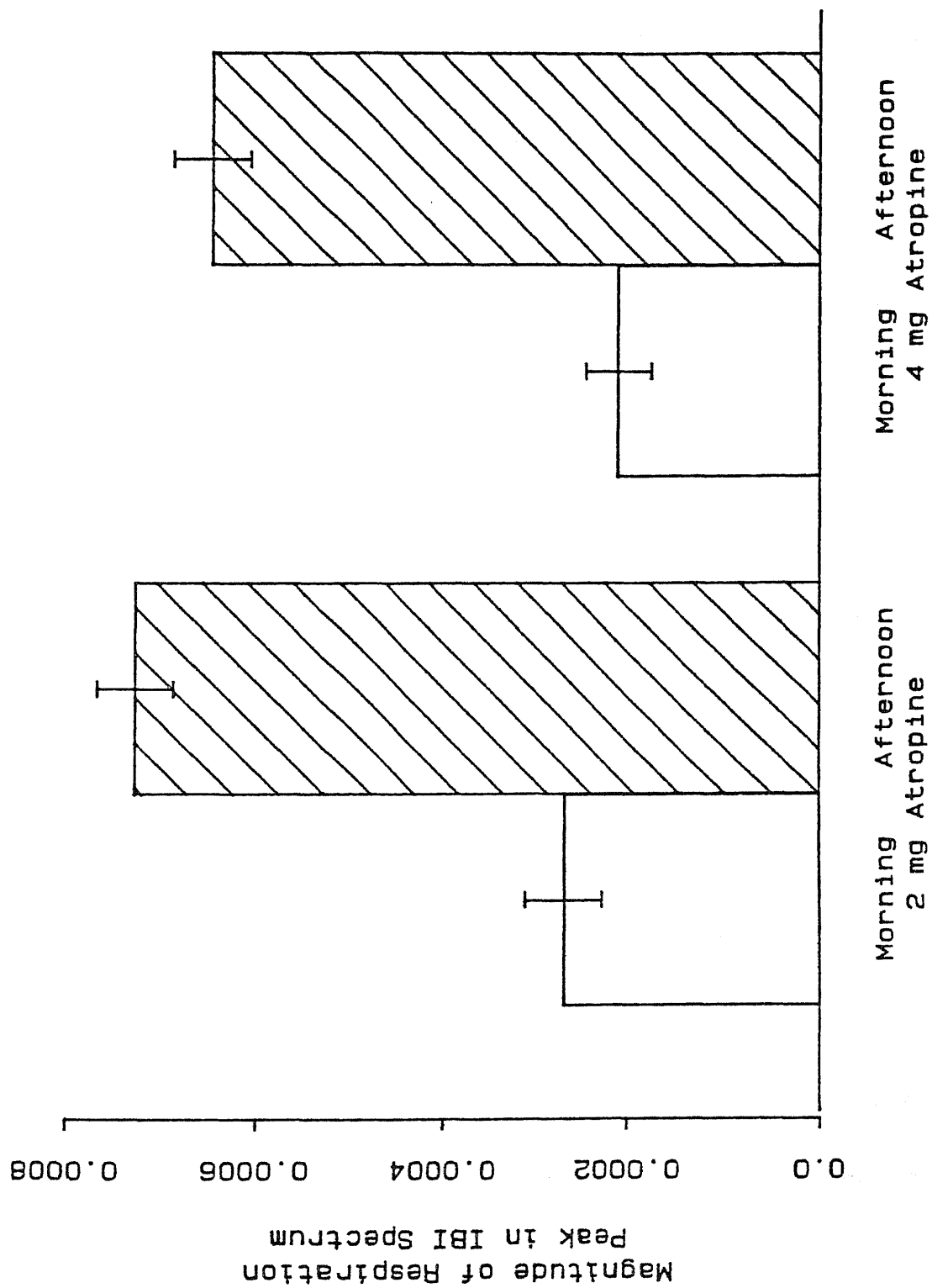


Figure 3.6 Comparison of the magnitude of respiration peak in IBI spectrum morning vs. afternoon



0.000199 SEM). This means that the effect of atropine of either 2 or 4mg does not persist to the following day.

### 3.4 STABILITY OF THE HEART RATE SPECTRUM

Stability of the heart rate spectrum from day to day for a given individual was studied. The data from the pilots study and the data from the second experiment using five subjects was used. This factor is quite crucial for understanding how the heart rate spectrum can be used. If the heart rate spectrum is stable from time to time under similar conditions then heart rate spectrum could be used to monitor changes in an individual's autonomic status due to pathology or the environment. The stability of the spectra was examined on the days the pilots were not given drugs. The magnitudes of the pilots respiration peaks ranged from 0.00076 to 0.00222. However, the magnitude of the respiration peak across days was very stable for each individual subject. This stability is shown by the coefficient of variability for flights ( $cv = \frac{\text{mean}}{\text{std. deviation}} * 100$ ) which expresses variability as a percent of the mean. The median cv was 5.4%. Five of the eight pilots had cv's less than 6%, and seven of the eight had cv's less than 10%. The maximum cv was 12%. Thus the normal variability in the magnitude of the respiration peak was typically about 5-6%. However, the possibility that the effect of atropine lasted more than a day could not be ruled out.

Additional data was then collected from five subjects. This experiment has been already described. It was found

that there was a remarkable consistency in the power of the respiration peak of the heart rate spectrum from measurement to measurement. Figure shows the data from the subject with the median coefficient of variation for the respiration peak(9.8%). Table 3.1 below shows mean power, standard deviation and coefficient of variation for the respiration peak of all 5 subjects

Table 3.1			
Subject	Mean power in Respiration peak of heart rate spectrum	Standard Deviation	Coefficient of variation
1.	.00457	.000447	9.8
2.	.00514	.000935	18.2
3.	.00361	.000491	13.6
4.	.00175	.000093	5.3
5.	.00413	.000337	8.2

There was more variability in the magnitude of the respiration peak in this study than there was in the pilots. There could be several explanations for this. Firstly the pilots were in a more controlled environment. Secondly the pilots data lasted several hours for each flight. On the other hand the data was collected for only 10 mins from the five subjects and also their diet,work,exercise was more variable than in the case of the pilots. The pilots had a much more dynamic environment . The pilots task loads, their physical movements, and the fact that they were talking all contribute to the variability of the heart rate spectrum. But, over long records involved in these studies the measures converge to yield consistent average parameters for an individual.

Finally it was noted that the records with greater power in their respiration peaks showed increased variability, which would explain the increased variability in the second study by the larger component of the respiration amplitude.

These studies show that the respiration peak in a persons heart rate spectrum is very stable. One can expect that most estimates of vagal tone (the respiration peak) will not deviate more than 5% to 10% from the average level.

### 3.5 EFFECT OF PACED BREATHING

In our analysis, we observed two consistent major spectral components, a low frequency component at about 0.1Hz and a high frequency component at about 0.25Hz. The high frequency component is synchronous with the respiration and has been considered as a quantitative evaluation of respiratory sinus arrhythmia. Since this high frequency component disappears after atropine , it could represent a clinically useful index of vagal activity.

Paced breathing is known to decrease the low frequency component and produce a more predominant high frequency component. The data from the third experiment was used for this analysis. Subjects were asked to follow a computer display which paced their breathing at 10, 15 and 20 breaths/min. All subjects showed a distinctly large and sharp peak at these frequencies 0.166666Hz, 0.25Hz and 0.3333Hz correspondin to 20 breaths/min, 15 breaths/min and 10 breaths/min.

See figure 3.7

The magnitude of the power in the respiration peak was seen to decrease as the respiration frequency was increased. Table 3.2 shows a very high negative correlation between the magnitude of the respiration peak and the frequency of respiration.

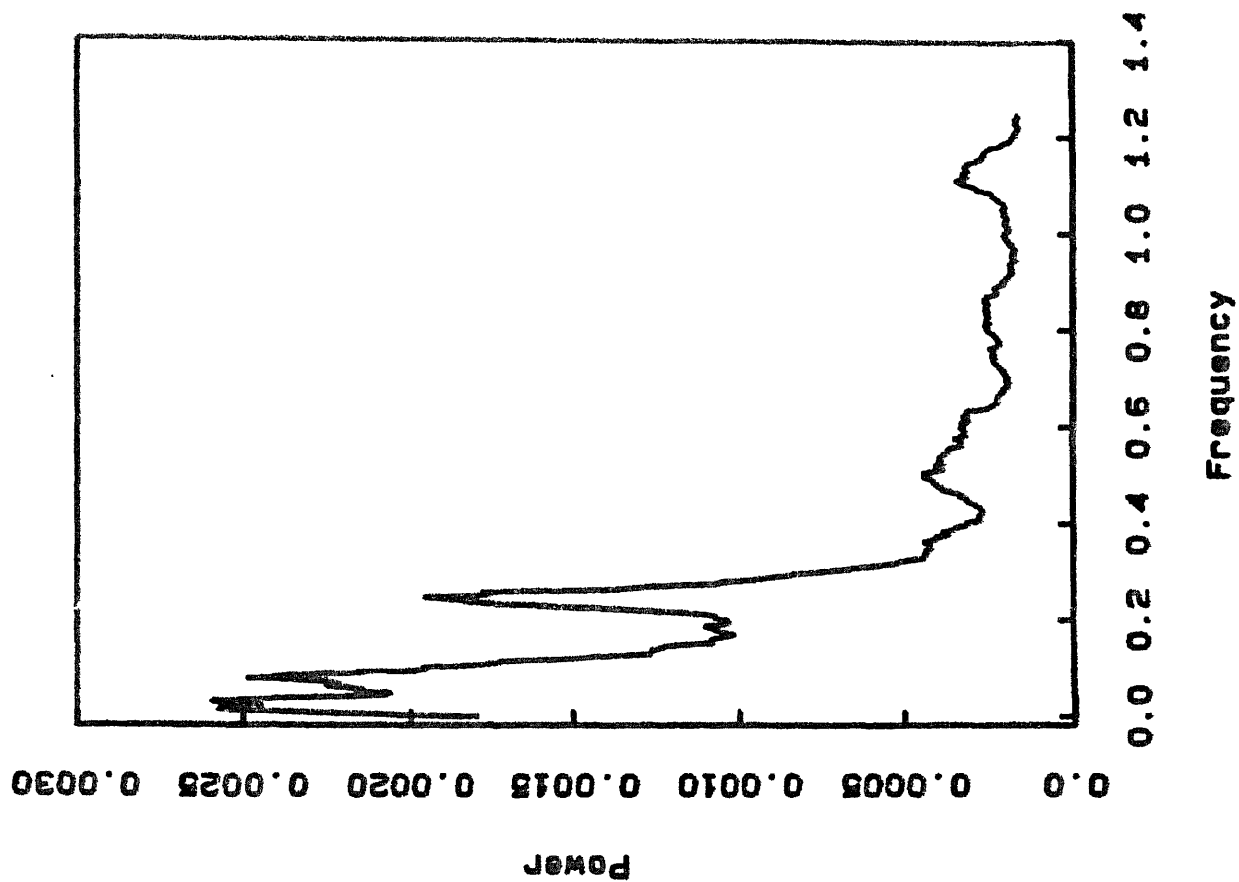
Table 3.2

Subjects	Correlation between magnitude of respiration peak and respiration frequency in	
	respiration spectra	heart rate spectra
1.	-0.97848	-0.99657
2.	-0.71018	-0.97143
3.	-0.99690	-0.97492
4.	-0.75708	-0.94059
5.	-0.95844	-0.97484
6.	-0.80698	-0.96965

Correlation from two subjects data has not been shown as the data was not good. These subjects were very fidgety and there was a lot of noise in the data.

Figure 3.8 shows the average value of the power in the respiration peak for all six subjects versus the nominal frequency. The data from the spontaneous breathing also conformed to this pattern. This was more true in the case of the heart rate data than in the respiration data. It would be interesting to investigate the relationship of the magnitude and frequency of the respiration peak in the respiration spectra and the magnitude and frequency of the respiration peak in the heart rate spectra and see how distinct or similar they are. The regression of these variables was taken as shown in fig 3.9. There is a possibility that the variation between peak amplitude and

Paced breathing at 15 breaths/min



Free breathing

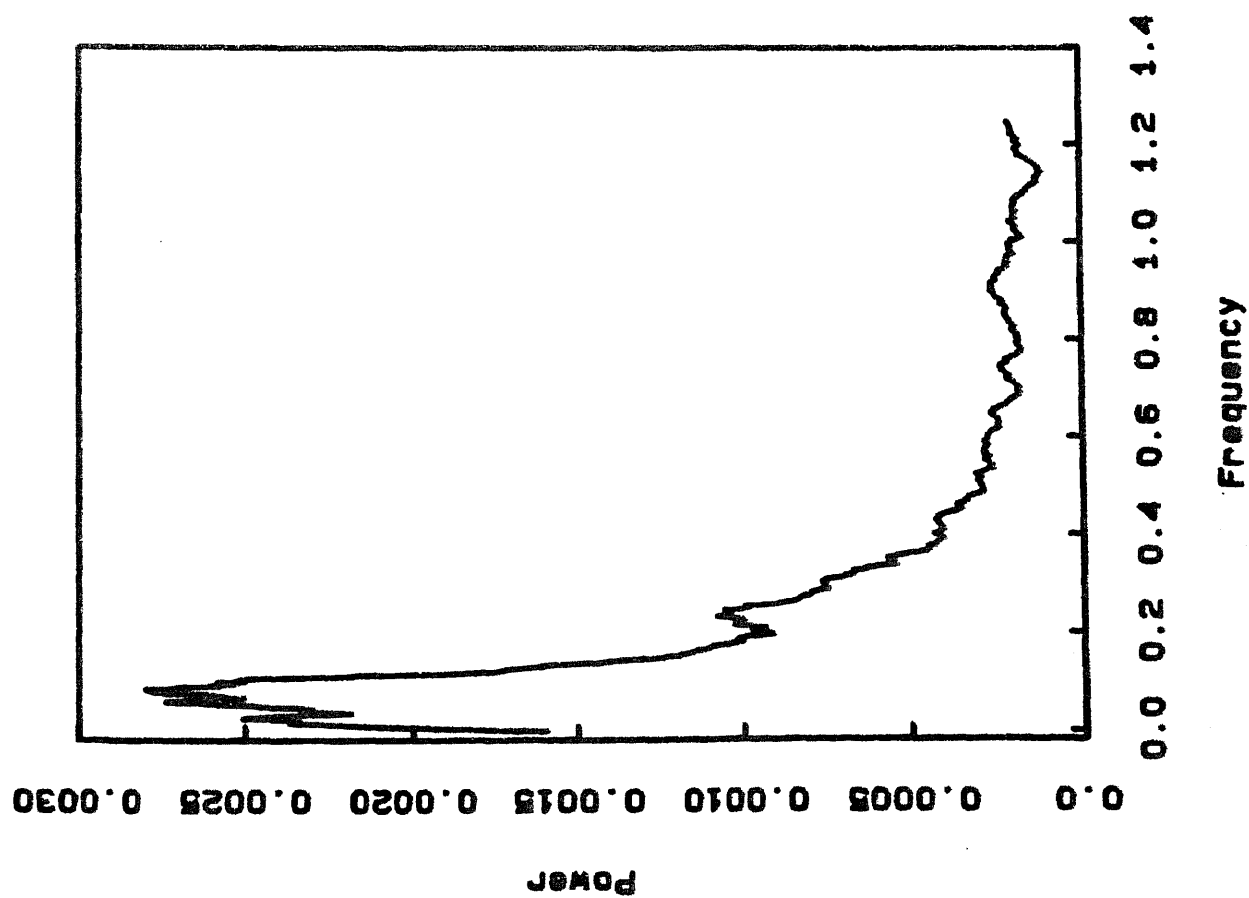
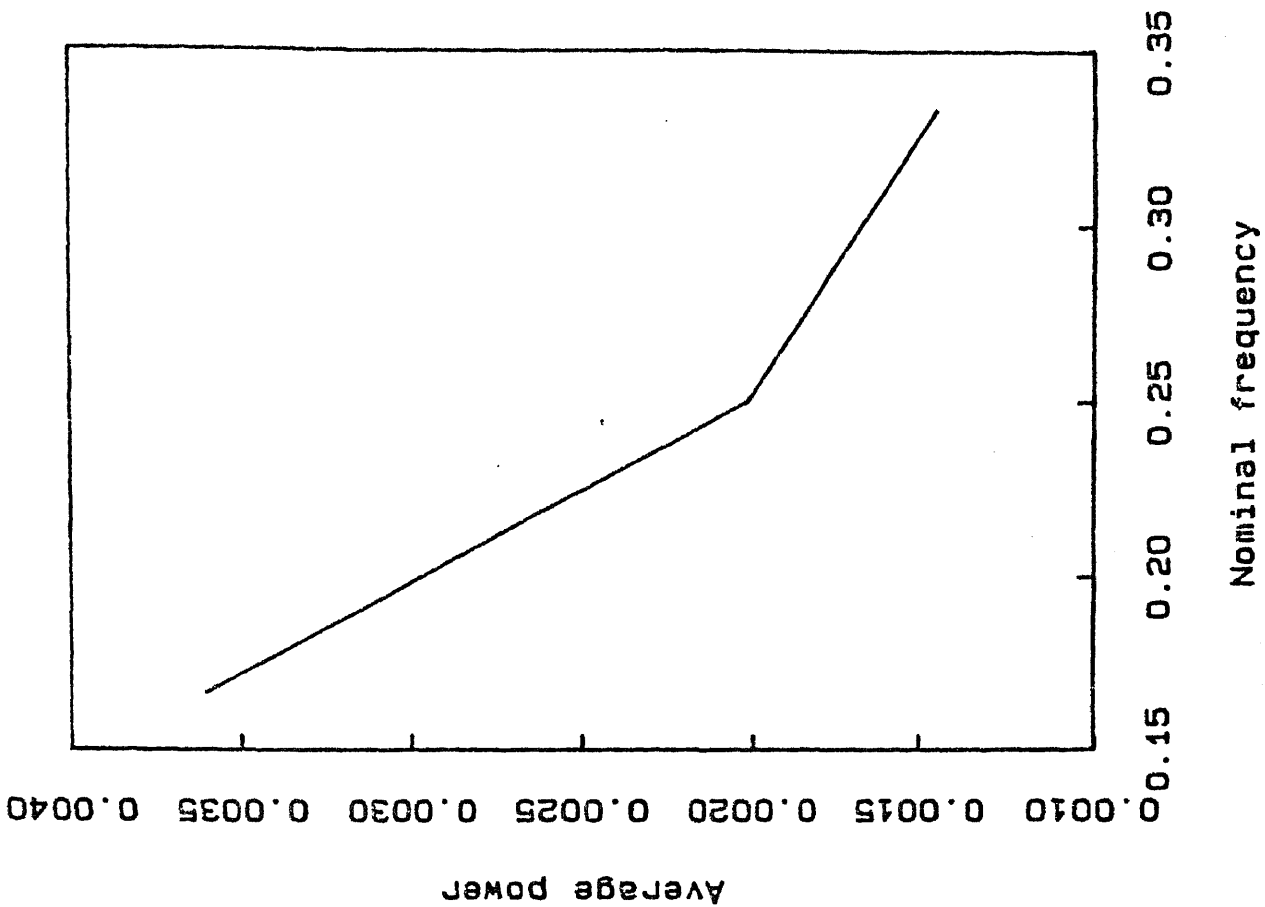


Figure 3.7 Spectrum showing paced breathing

Heart rate spectrum



Respiration spectrum

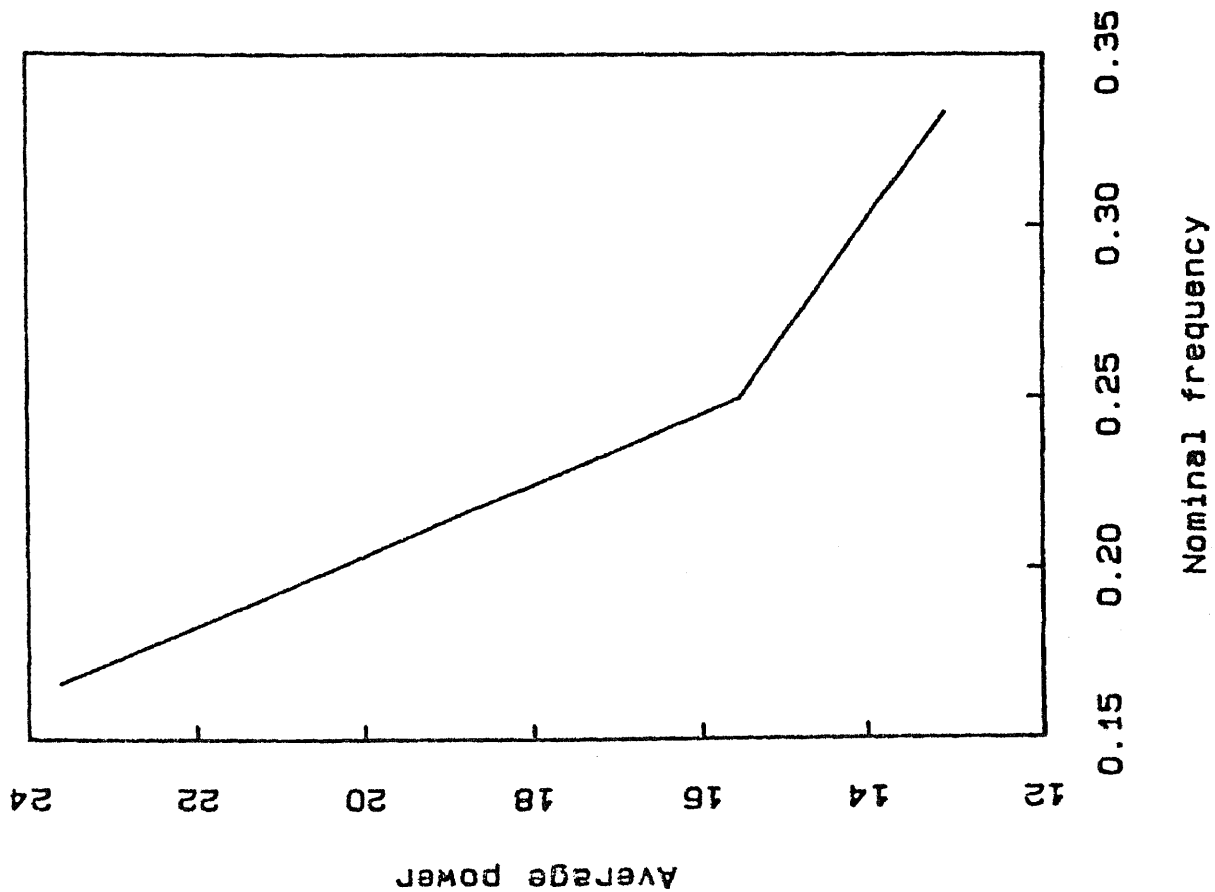


Figure 3.8 Average power vs. nominal frequency

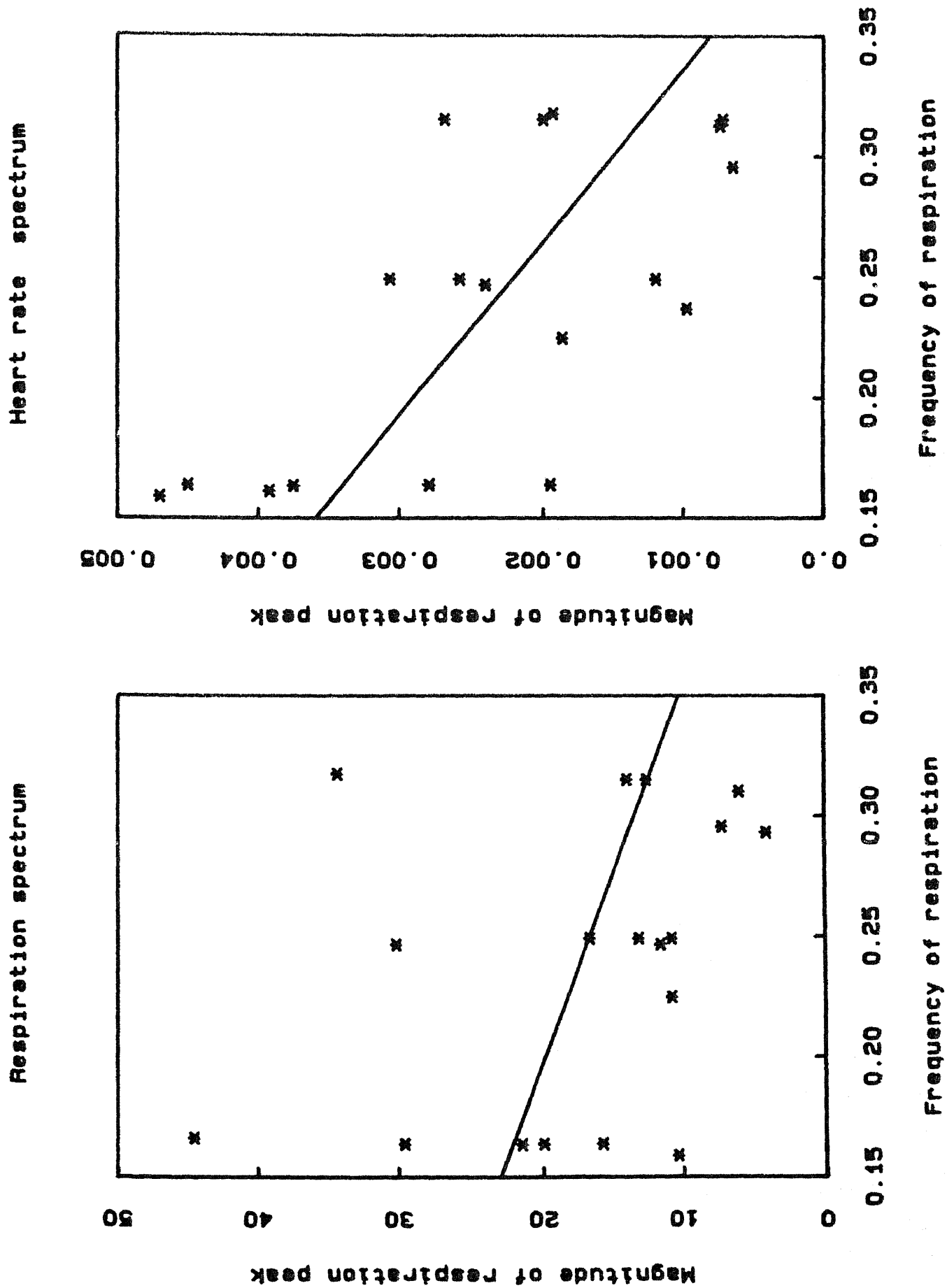


Figure 3.9 Regression between the frequency of the respiration peak and magnitude of respiration peak

respiration frequency in the respiration spectrum is related to the corresponding variation in the heart rate spectrum.

During the medium paced breathing ( 15 breaths/min i.e. 4 secs per respiration cycle) subjects were asked to hold their breath for 6 secs at different points in the respiration cycle. This introduces a  $180^{\circ}$  phase shift in the breathing pattern. It was observed in one subject, that his breathing slowly reverted to the original pattern, i.e. after the breath hold, the subject slowly got out of phase with the display and phase shifted another  $180^{\circ}$  to get to the original cycle. This was the only subject in which this behaviour was studied, and in the future the data for the other subjects should be examined.

### 3.6 EFFECT OF STRESS

While analyzing data from the first two experiments it was noticed that the pilots had less vagal tone during simulated flights than the subjects sitting quietly in the laboratory. The size of the average respiration peak of subjects in the second study (0.00358) was more than three times the size of the pilot's average respiration peak (0.00109) ( $p < 0.001$ ). This interpretation is strengthened by the observation that the pilots also had significantly higher average respiration rates (0.3514Hz or 21.08 breaths/min) than the subjects in the laboratory (0.1846 Hz or 11.08 breaths/min) ( $p < 0.00015$ ). These data suggested that the pilots may be aroused or stressed during flight simulation and this arousal is detected as decreased vagal



tone by the heart rate spectrum. On further examination of the respiration peak it was found that the amplitude did not increase over the course of the flight. There was no significant differences in amplitude of the respiration peak in non-drug sessions.

These findings suggest that the heart rate spectrum can be useful for detecting arousal or stress related to performance or workload. We then formulated a stress test which required subjects to perform simple mental arithmetic. They had to serially subtract a large prime # like 17 from a 4 digit number and speak the answer out loud. A metronome was clicking every second and the subject was constantly told to be quicker and more accurate and to put in greater effort.

The respiration peaks were not very distinct in the spectra to pursue this analysis. It is felt that the experiment should be modified to keep movements of subjects and talking to a minimum, perhaps a quiz/game on a computer terminal with the subject pressing buttons. In two subjects it was possible to detect a distinct respiration peak and the magnitude of this peak was less than the magnitude of the respiration peak when the subject was breathing spontaneously.

The data collected from the Valsalva maneuver is not sufficient or clear enough to signify anything at this time. A lot of noise was found in this data (mostly due to muscular activity). The respiration peak was not distinct

in either the heart rate or respiration spectra.

#### 4. CONCLUSIONS AND SUMMARY

All the data analyzed so far, supports the idea that the heart rate spectrum can be used as a noninvasive means to monitor autonomic changes. Currently, there is no other method that allows one to quantify autonomic changes.

##### 4.1 ATROPINE STUDIES

The atropine studies showed that the effect of respiration on heart rate is vagally mediated and can be severed by muscarinic blockade. It was also noted that pilots with the smaller dosage of 2mg of atropine recovered quicker than those with 4mg. It would be interesting to compute detailed time courses of the loss of parasympathetic input to the heart, so that, this effect of atropine can be compared with other functional compartments and with the known kinetics of the drug.

The pilots study showed the power in the respiration peaks to be nearly a third less than the power in the respiration peaks in our experiment with the five subjects. It was felt that as the pilots were flying a helicopter simulator, the stress decreased the parasympathetic component. This observation suggested that the heart rate spectrum is able to detect diminished vagal tone due to arousal or stress associated with the simulated flight.

##### 4.2 HEART RATE STABILITY

The heart rate spectrum was found to be very stable and consistent, when measured under similar conditions, which implies that it could be used to detect changes due to

pathology. The variability present was very small as compared to the variability caused by drugs such as atropine. Analysis on data, indicate that it will be possible to use the heart rate spectrum to detect changes in an individuals autonomic status or difference between individuals as well as group changes due to an experimental treatment. It was also found that the variability of the respiration peak was greater in records whose respiration peaks had larger magnitudes.

#### 4.3 RELATIONSHIP BETWEEN HEART RATE AND RESPIRATION

The respiration peak in the heart rate spectra can be located using the respiration spectra. The plot of the frequency of the respiration peak in the respiration spectrum versus the frequency of the respiration peak in the respiration spectrum showed a very linear relationship. The regression line was along  $x = y$  and the regression between the two was  $p < 0.0001$ . The respiration peak in the heart rate spectra can be located even if it is small or ambiguous.

#### 4.4 PACED BREATHING

Analysis of paced breathing tackled two questions. Firstly how well does heart rate frequency match respiration frequency in each condition. Secondly, whether there was a difference in amplitude during paced breathing as compared to free breathing. Also does the magnitude of the respiration peak in the heart rate spectra vary in the same way as the magnitude of the respiration peak in the

respiration spectra with frequency. These questions were not fully investigated and nothing definite can be said at this point.

#### 4.5 STRESS

Data was collected to study the effect of stress on the heart rate spectrum, on noting the diminished vagal tone of the helicopter pilots while flying their simulator. Unfortunately the data collected was very noisy. The stress made the subjects agitated and their movements caused a lot of noise in their measurements. A good experiment needs to be designed to investigate the decrease in magnitude of the respiration peak in the heart rate spectrum.

The same problem was encountered with the measurements of the Valsalva maneuver. The respiration peak could not be distinctly picked out in their respiration or heart rate spectra.

These experiments have shown that the heart rate spectrum is a very useful and quantitative tool in examining the autonomic nervous system input to the heart.

## A. OPERATIONS MANUAL

This chapter covers the procedures, equipment and programs used to collect data in this thesis.

### A.1 DATA COLLECTION

Respiration is measured using the principles of electrical impedance plethysmography. A constant current source is used to apply a low intensity, high frequency constant amplitude sinusoidal current to the body surface. It is desirable to use frequencies above 20KHz to avoid perception of the current by the patient and to lower the skin electrode impedance. In this application a frequency of 50KHz was chosen.

Four electrodes are used in this application, two electrodes to apply the current to the body and two different electrodes to sense the resulting voltage and ECG. Using two electrodes (applying the current and sensing the voltage with the same electrode pair) causes several problems. One problem is that the current density is higher near the electrodes than elsewhere in the tissue causing the measured impedance to weight impedance of the tissue more heavily near the electrodes than elsewhere. A four electrode system where the current is applied through two outer electrodes, causes a more uniform current density in the region sensed by the two inner electrodes.

A block diagram of the equipment used to collect the data from the subjects is shown in figure A.1. The electrodes are applied to the subject, two on either side

below the collar bone. The respiration signal is a measure of the resistance between the electrodes as the subject breathes.

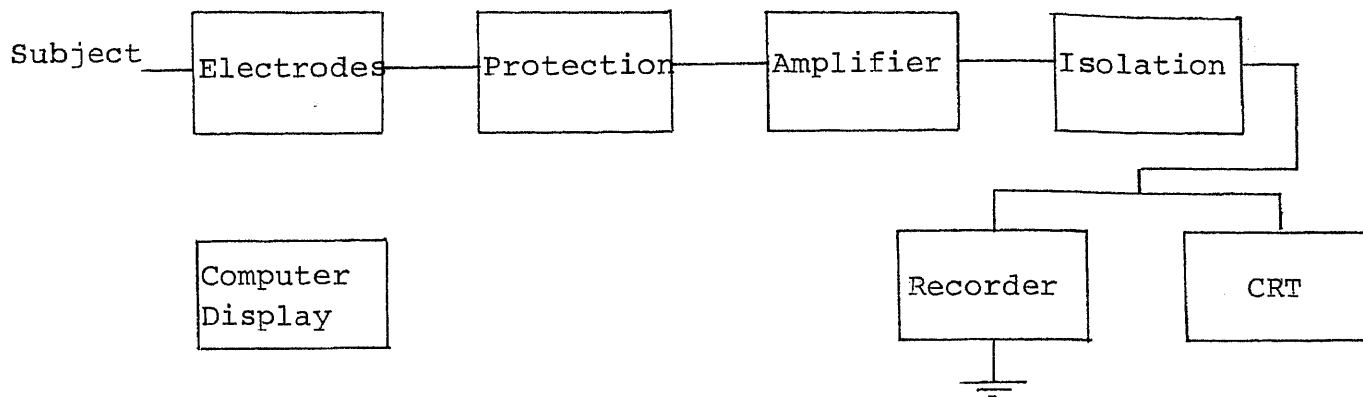


Figure A.1 Data collection equipment

The protection circuit blocks any high voltages from reaching the subject. The combined ECG and respiration signal is fed to a differential amplifier with an overall gain of 500, to provide a good common mode rejection ratio. The differential amplifier amplifies the ECG and rejects electrical interference. The single ended output is then applied to two filters to separate the low frequency ECG signal from the 50KHz respiration signal. A 100Hz low pass filter is used for the ECG channel and a 30KHz-70KHz band pass filter for the respiration signal.

The respiration signal must now be processed to remove the signal component from the 50KHz carrier. The respiration signal sensed by the pick-up electrode is the voltage resulting from the application of a constant current

voltage resulting from the application of a constant current source to a trans-thoracic impedance which varies with respiration. The amplifier bandwidth is limited just enough to adequately pass the ECG. This procedure results in the optimal signal-to-noise ratio, because artifacts(undesired signals) such as electrical voltages generated by muscle activity (which fall in a range from 30 to 2000Hz) is greatly reduced.

Amplifiers for use with human subjects require isolation circuits. These circuits isolate the subject and the amplifier from the recorder ground and prevent currents larger than 10 Ua from flowing through the subject. The data is recorded on two channels on a cassette tape.

## A.2 DATA ACQUISITION

The data is then transferred to the computer. The data acquisition equipment is shown in figure A.2

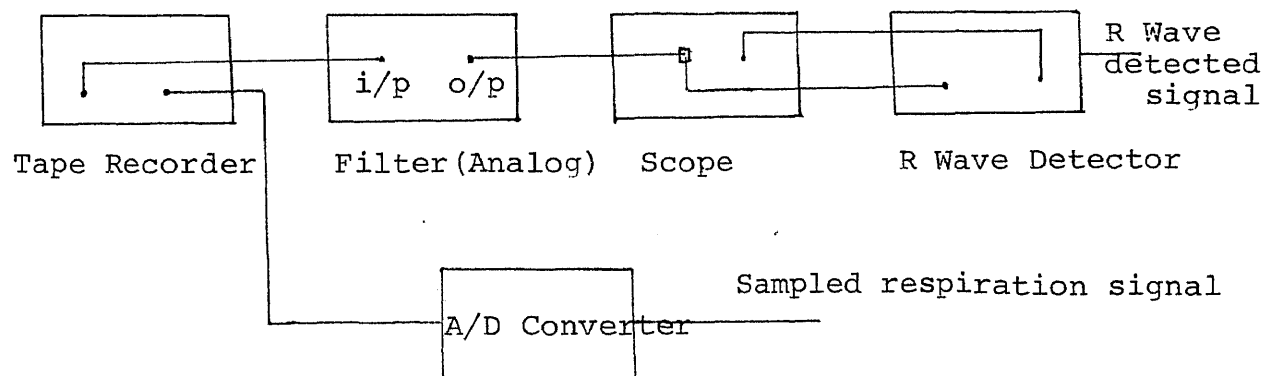


Figure A.2 Data Acquisition Equipment

The respiration signal is fed directly to the A/D



fed to a low pass filter. This filter reduces the noise in the signal and the data is then fed into an R wave detector. This is a variable thresh hold level R wave detector and the setup is such that the computer times the intervals between the R waves detected and records it. The data once on the VAX11/750 computer is then ready for analysis. The respiration and IBI's are stored in separate files. The IBI files need to be interpolated before any further analysis is done.

### A.3 DATA ANALYSIS

The entire data was analyzed in an 'S' environment. S is an interactive environment for data analysis and graphics on UNIX operating system. It has two components, a language and a support system. The data is first put in matrix form with 4096 values per column. The sequence of steps for analysis is as follows.

- i, The data is first clipped to remove any outliers. This stems values in the data set which are statistically far out.
- ii, The data is then tapered, i.e. the first 20% and the last 20% of the data will be tapered. This is to reduce the leakage in the spectrum. A split cosine bell window is applied.
- iii, The fourier transform is then taken. The radix-2 FFT employed in this analysis requires that the series length be a power of two. Because this affects the spacing of frequencies in the spectrum, it is useful to

be able to contro the length of the series to be transformed. The series can be extended by padding with zeroes and this only lengthens the transform and does not change the transform.

The program to regulate the breathing rate was written in Pascal. It makes use of the delay function to adjust the timing of the display. Different delays produce different breathing rates. In one session the subject is required to hold his/her breath to introduce a phase shift. This is the program hold.pas, in this program the complete respiration cycle is split into four procedures : for the first half of the inhalation , the second half of the inhalation, the first half of exhalation and the second half of exhalation. In this way it would be easy to introduce the phase shift at different times in the breathing cycle. The time for the breath hold can be adjusted easily. In this experiment, the breathing was regulated to fifteen times per minute, which is a complete breathing cycle every four seconds. The breathe hold was for six seconds which would introduce a phase shift of 180 degrees. The breathing rate and the length of breathe holding can be varied very easily in the program. All the programs display increasing and decreasing number of points during inhalation and exhalation which facilitates the subject in following the display to synchronize his/her breathing rate.

A script was written to ensure that outside factors would have minimal variation. This is to prevent the person

running the experiment from having biased data depending on the choice of words used on a particular day while collecting data. A copy of the script is shown in Appendix B. At the start of this experiment, the NJIT committee for the protection of human subjects, asked that each subject be checked by a physician for 'hidden' heart defects'. A consent form was filled out by the volunteer subjects before the experiment.

## APPENDIX B

{ This was the script used for the third experiment. The experiment consisted of measuring data while the subjects were breathing freely, while their breathing was paced, during the Valsalva maneuver and during the mental stress test. }

I'm studying the effect of respiration on heart rate. The purpose of this experiment is to see how your heart responds to certain simple tasks, like breathing at different rates and doing some simple arithmetic.

The equipment is completely safe. These instruments are totally isolated from you, so you can't get a shock. I'll be placing electrodes over here [show position] to measure your heart rate and respiration.

First I need to get a measure of your normal breathing and ECG. I want you to relax and breathe freely and I'll measure your heart rate for 5 mins.

I'm going to take your blood pressure now. Please stretch out your left arm. [after b/p] Fine

Now to see how paced breathing affects the heart rate. The display will tell you to breathe in and out at a fixed rate I'd like you to breathe according to the display on the screen. Try to breath as normally as you can and keep up with the display. Try and follow as best as you can. You can practice a bit before we record. You may find yourself breathing more deeply than normal.

Just as before I want you to breathe in and out. This time you will be asked to hold your breath at certain times. That is, the display will show IN and then OUT, etc. at a fixed rate and at some point it will show HOLD. No matter at what point of breathing in or breathing out you were at, hold your breath. It will only be for a few seconds. The display will complete that respiration cycle. For example, if you were breathing IN and the computer asked you to HOLD your breath in the middle, after breath holding the computer will ask you to continue breathing IN. Synchronize your breathing as best as you can. And remember to breathe in and out as indicated by the computer. Breathe at normal depth at the rate shown on the display.

I'd like to do another paced breathing trial at a different rate. We will not have any breath holding this time. follow the display just as before. This will be shorter.

I want you to relax, take it easy and when you are ready I want you to take a deep breath and bear down and strain as though you were lifting a heavy load and hold your breath for about 10 secs. Like this [demonstrate] I'll tell you when to stop. I want you to do it once again but this time hold your breath for 15 sec. I'll tell you when 15 secs are up.

Relax take it easy, OK I want you to do some simple arithmetic. This is called serial subtraction. I'll give you two numbers, I want you to subtract one from the other and tell me the answer. Like this subtract 13 from 7885 that gives me 7872, subtracting 13 once again from the remainder I get 7859, 7846, 7823 etc. If you get stuck anywhere I'll help you along, but I want you to do it as accurately and as fast as you can. This is to see how mental processing affects the heart rate. Most people can give me a difference every two seconds. I'll set this metronome at that rate.

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I'm sorry you're falling behind, please try and give me an answer with the metronome.

Most people can do better than you are doing now.

Please try harder, you're really not keeping up.

Your accuracy is slipping.

You really can do better if you try harder.

## APPENDIX C

```

{
    This program regulates the breathing to 15 breathes/min.
    i.e., 4 secs per cycle. Approximately every one and
    half minutes a phase shift is introduced by displaying a
    HOLD signal for 6 secs. Since 1 cycle is 4 secs, this
    would introduce a 180 degree phase shift. This phase
    shift is introduced every one and a half mins at
    different points in the complete breathing cycle.
}

program resp(input, output);
var
    i, n, d, j, k : integer;

procedure brehalfin(var d : integer); { First half of inhalatio
begin
    clrscr;
    writeln('IIIII  N  N');
    writeln('  I    NN  N');
    writeln('  I    N N N');
    writeln('  I    N N N');
    writeln('  I    N N N');
    writeln('  I    N  NN');
    writeln('IIIII  N  N');
    delay(d);
    gotoXY(9, 9);
    writeln('*');
    delay(d);
    gotoXY(7, 11);
    writeln('* * *');
    delay(d);
    gotoXY(5, 13);
    writeln('* * * * *');
end;

procedure brefullin (var d : integer); { Complete inhalation }
begin
    delay(d);
    gotoXY(3, 15);
    writeln('* * * * *');
    delay(d);
    gotoXY(1, 17);
    writeln('* * * * *');
    delay(d);
end;

procedure brehalfout (var d : integer); { First half of exhalat
begin
    clrscr;
    gotoXY(1, 19);

```

```

        writeln(' 000      U   U   TTTTT');
        writeln('O   O   U   U   T');
        writeln('O   O   U   U   T');
        writeln('O   O   U   U   T');
        writeln('O   O   U   U   T');
        writeln(' 000      UUU   T');
        delay(d);
        gotoXY(1, 15);
        writeln('* * * * *');
        delay(d);
        gotoXY(3, 13);
        writeln('* * * * *');
        delay(d);
        gotoXY(5, 11);
        writeln('* * * * *');
    end;

    procedure brefullout (var d : integer);    { Complete exhalation }
    begin
        delay(d);
        gotoXY(7, 9);
        writeln('* * *');
        delay(d);
        gotoXY(9, 7);
        writeln('*');
        delay(d);
    end;

    procedure hold (var x : integer);    { procedure to cause breath h
    begin
        for i := 1 to x do
        begin
            gotoXY(40, 10);
            writeln('H   H   000   L   DDD');
            gotoXY(40, 11);
            writeln('H   H   O   O   L   D   D');
            gotoXY(40, 12);
            writeln('H   H   O   O   L   D   D');
            gotoXY(40, 13);
            writeln('HHHHH   O   O   L   D   D');
            gotoXY(40, 14);
            writeln('H   H   O   O   L   D   D');
            gotoXY(40, 15);
            writeln('H   H   O   O   L   D   D');
            gotoXY(40, 16);
            writeln('H   H   000   LLLL   DDD');
            delay(820);
        end;
    end;
end;

```

```

procedure fullcycle(var n, d : integer);    { procedure for 1 enti
begin
    for i := 1 to n do
        begin
            brehalfin(d);
            brefullin(d);
            brehalfout(d);
            brefullout(d);
        end;
    end;

begin
    j := 3;
    for k := 1 to j do
        begin
            n := 22;
            d := 318;
            fullcycle(n, d);
            brehalfin(d);
            brefullin(d);
            brehalfout(d);
            i := 6;
            hold(i);
            brefullout(d);
            fullcycle(n, d);
            brehalfin(d);
            brefullin(d);
            i := 6;
            brehalfout(d);
            brefullout(d);
            fullcycle(n, d);
            brehalfin(d);
            i := 6;
            hold(i);
            brefullin(d);
            brehalfout(d);
            brefullout(d);
            fullcycle(n, d);
            i := 6;
            hold(i);
        end;
        fullcycle(n, d);
    end.

```



```

{
  This program runs for 10 mins regulating the breathing
  rate to 10 times a minute, i.e., 6 seconds/cycle (3 secs
  inhalation, 3 secs exhalation)

  This program can also be used to regulate breathing at
  20 times a minute by changing the delay to 208.
}

```

```

program resp(input, output);
var
  i, n, d : integer;
begin
  n := 100;    { data for 10 minutes }
  d := 458;    { delay (in mS) for breathing }
  for i := 1 to n do
    begin
      clrscr;
      writeln('IIIII  N  N');
      writeln('  I    NN  N');
      writeln('  I    N N N');
      writeln('  I    N N N');
      writeln('  I    N N N');
      writeln('  I    N  NN');
      writeln('IIIII  N  N');
      delay(d);
      gotoXY(9, 9);
      writeln('*');
      delay(d);
      gotoXY(7, 11);
      writeln('* * *');
      delay(d);
      gotoXY(5, 13);
      writeln('* * * * *');
      delay(d);
      gotoXY(3, 15);
      writeln('* * * * * * *');
      delay(d);
      gotoXY(1, 17);
      writeln('* * * * * * * * *');
      delay(d);
      clrscr;
      gotoXY(1, 19);
      writeln(' 000    U  U  TTTTT');
      writeln('O  O    U  U  T');
      writeln('O  O    U  U  T');
      writeln('O  O    U  U  T');
      writeln('O  O    U  U  T');
      writeln(' 000    UUU  T');
      delay(d);
    end
  end
end

```

```
gotoXY(1, 15);  
writeln('* * * * * * * * *');  
delay(d);  
gotoXY(3, 13);  
writeln('* * * * * * *');  
delay(d);  
gotoXY(5, 11);  
writeln('* * * * *');  
delay(d);  
gotoXY(7, 9);  
writeln('* * *');  
delay(d);  
gotoXY(9, 7);  
writeln('*');  
delay(d);  
end. end;
```

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