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# INTRASUBJECT VARIATION OF CERTAIN SPATIAL CARDIAC VECTORS

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INTRASUBJECT VARIATION OF CERTAIN

SPATIAL CARDIAC VECTORS

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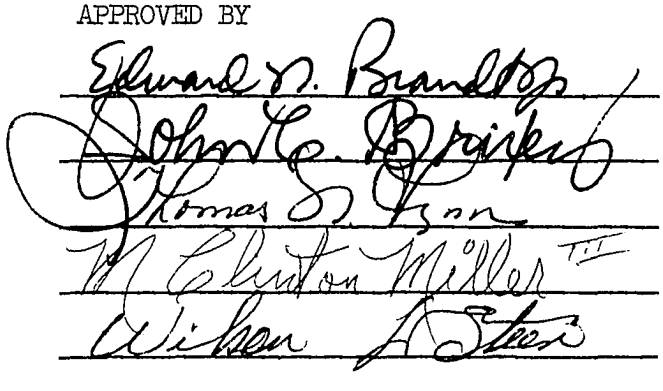

DISSERTATION COMMITTEE

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# INTRASUBJECT VARIATION OF CERTAIN SPATIAL CARDIAC VECTORS

## CHAPTER I

## INTRODUCTION

Several recent papers have reported the study of intrasubject variation of electrocardiographic and vectorcardiographic quantities. This subject is of interest for two basic reasons. The first of these is that knowledge about the variation is potentially useful in measuring average electrocardiographic values on individuals with the precision desired. For example, this basic knowledge should be useful in decisions about how many heart beats should be analyzed on each subject. Secondly, just as the variance of a sample of observations helps describe the sample, it seems likely that a measure of the variation of measurements on samples of heart beats from an individual may be in some way characteristic of the individual and therefore useful in describing him.

Cady and Mitchell (1966) have developed a method which reduces the variation in electrocardiographic wave form in successive heart beats within an individual. They were concerned primarily with the variation due to low frequency baseline drift and 60 cycle per second noise. Successive heart beats were averaged with the goal of obtaining

a wave form for the heart beat which was typical of the individual subject. The processing done by Cady and Mitchell used a hybrid computer. The electrocardiograms used were recorded on analog magnetic tape and used the lead system described by Frank (1956). To obtain a point by point average of successive cardiac cycles, a reference point was needed for each cycle. The point of maximum negative derivative, which occurs on the trailing side of the R wave, was chosen. Caceres, et al. (1962) also used the point of maximum negative derivative as a reference point in their digital computer programs to recognize electrocardiographic wave forms. An analog derivative circuit determined this point for each heart cycle. The analog record was digitized at a sampling rate of 1000 points per second. To obtain an average wave form, points on successive cycles which were equally distant from the reference points were averaged. This work used samples of 8 or 32 heart beats. The distortion of wave form due to low frequency baseline drift and high frequency noise was greatly reduced in the averaged wave.

A measure of heart beat cycle time is called an RR interval. Cady and Mitchell (1966) used the variance of RR interval among successive heart beats within subjects as a measure of the degree of irregularity in heart beat cycle times. This variance was computed using analog circuitry and was exponentially weighted in time so that sudden changes in heart rate contributed more than did smooth gradual ones. Large values of RR interval variance were taken as indicative of cardiac ventricular arrhythmias. They used the means and variances of PR and QRS intervals to help specify the diagnostic type of arrhythmia.

Downs and Liebman (1966) have developed a measure of the

precision of the angular data from cardiac vectors whose components are in spherical coordinates.

Cosma, Levy, and Pipberger (1966) investigated the beat-to-beat variability in the ventricular gradient vector in samples of three consecutive beats for which there was no baseline shift. This was done for 10 subjects. The object of this work was to reduce the variation due to respiration, which was said to be the main cause of variability among the three beats. For the heart and respiratory rates encountered, a complete respiratory cycle covered from 3 to 6 cardiac cycles. Therefore, it was concluded that three consecutive beats would cover one transition from inspiration to expiration and satisfactorily reduce the variation in the ventricular gradient which was due to respiration.

Certain aspects of the variation among heart beats within subjects which were not discussed in the above papers were immediately suggested as being worthy of study in order to complement the work described above.

Cady and Mitchell looked at variances of time intervals between wave forms, but did not investigate variances of the components of the ventricular gradient, P, or QRS vectors. These components are the time integrals of the electrocardiographic record in the respective leads. They arrived at a wave form which was fairly typical of the individual subject by averaging out much of the variation among that subject's heart beats. They did not, however, attempt to describe or measure the variation itself, except for that in the time intervals mentioned above.

Downs and Liebman studied variation among angular vector

components for heart beats within subjects, but did not discuss the situation when the vectors were represented in rectangular cartesian coordinates.

Cosma, Levy, and Pipberger concluded that variation in the ventricular gradient which was due to respiration could satisfactorily be reduced by averaging vector components for 3 consecutive heart beats. They did not study the variation due to causes of lower frequency than that of respiration. Such a study would require the use of larger numbers of consecutive heart beats. Neither did they investigate the variation in any of the other vectors.

To bridge some of the gaps among the above studies, it was decided to investigate electrocardiogram wave forms other than the ventricular gradient, to use larger numbers of consecutive beats, and to examine vectors whose components were in rectangular cartesian coordinates.

It was thought that the study of the variability with such factors as pulse rate, age, and sex, might lead to better understanding of the interrelationships of the vectorcardiogram and these factors. The variabilities of other quantities besides the RR interval might be found to differ among different pathological classifications, in which case they would be useful in diagnosis, too. This paper will examine the variability of certain spatial vectors in healthy subjects. This will therefore be a basis for later studies of other pathological groups.

The nature of the variation was of interest also. In particular, it was desired to investigate whether there might be periodic variation among the components of successive beats other than

that due to respiration.

The goals of this study are now defined. CHAPTER II will discuss the acquisition of the data. CHAPTER III will discuss periodic variation in the ventricular gradient components. CHAPTER IV will investigate the variation in the gradient, P, and QRS vectors in relation to sex, age, and pulse rate. CHAPTER V will summarize the results of this investigation.

# CHAPTER II

## METHODS

A research project, described by Bayley (1966), at the University of Oklahoma Medical Center has resulted in a library containing electrocardiograms of approximately two hundred subjects. The subjects were adult volunteers who were judged as having healthy hearts after careful histories, physical examination, and chest x-ray. Certain other information was available on the subjects for whom recordings existed. This information included age, sex, and pulse rate computed from the recording itself. At least two minutes or approximately one hundred fifty heart beats of recording were taken for each subject. All of these records were made available through the generosity of Dr. R. H. Bayley.

The axial lead system, described by McFee and Parungao (1961), was used in recording these electrocardiograms. The axial lead system uses three orthogonal leads. The X or transverse axis is from left to right, with right being positive. The Y or longitudinal axis is from head to toe, with the toe direction being positive. The Z or sagittal lead is from front to back, with back being positive. The three leads were simultaneously recorded onto separate channels of seven-channel FM analog magnetic tape by a CP-100 Ampex tape recorder. A fourth tape

channel was used for voice identification of each subject. The ECG signal from each lead was amplified by a Tektronix amplifier which had been modified to have a maximum low frequency response of approximately 0.04 cycles per second.

Four vectors of current interest in vectorcardiography are the ventricular gradient, the P, QRS, and the T. One obtains a particular component of a specific vector by finding the time integral of the electrocardiogram over the duration of the specific wave form of interest in that lead. The recorded electrocardiogram is a time-varying voltage which has both positive and negative values within a specific wave. Accurate determination of a vector component requires a knowledge of the location of the zero line, the baseline. The baseline can be accurately determined only before the beginning or after the termination of a heart beat, not during the beat. The baseline varies with time, for such reasons as respiration and muscle tremor, and behaves differently in the three leads, because of their different spatial orientations. To perform the integration, some assumption must be made about the form of the baseline during the heart cycle.

An analog computer which was especially constructed by Labko Scientific, Inc. for the computation of vectorcardiogram components was also made available by Dr. Bayley. This computer can integrate on one channel at a time. The baseline assumption used by the computer in its integration is that the baseline value at the beginning of the P wave remains constant throughout the duration of that heart cycle. The baseline is again determined at the end of the T wave for each heart beat. The voltage difference, or baseline shift, during the heart

cycle is computed and stored. Provision is made so that one can instruct the computer to bypass the print out of components for heart beats in which the baseline shift was large. The amount of baseline shift to be accepted is determined by the computer operator by the use of a dial which is set before the computation. The dial determines the maximum percentage of the baseline reading at the beginning of the heart beat which will be acceptable as baseline shift. For instance, suppose the baseline rejection dial were set on 5%. If for a particular heart beat the initial baseline were 1 millivolt and the terminal baseline were 1.06 millivolt, the vector component for that heart beat would not be printed out, since $(1.06 - 1.00)/1.00 > 0.05$. The shift may be either positive or negative, but its magnitude must be less than the indicated percentage of the initial baseline value. The dial has a continuous range from 0 to 100%, and thus allows for any desired rejection percentage in this range. There is also a toggle switch which can be set so that no baseline test is made, thus accepting every beat. The components obtained by the computer are time integrals of a voltage curve and have the units of microvolt-seconds ($\mu$vs). The computer can provide the net area under the chosen complex for any beat which is not rejected on the basis of baseline shift. It operates on one lead at a time. It can also provide the average of nine non-rejected beats for the given complex, but is not able to compute variances. The only output form available is printed paper tape. This output was keypunched into cards as was the identifying information for each subject, and all further processing and computations were done on digital computers.

There are two routine procedures which are used to guard

against error which might be introduced into the calculations by machine variation. The first of these is preventive. It consists of allowing the computer to warm up for at least one hour before any computation is done. The computer is normally not turned off until the end of the work day. The warmup period provides an opportunity for the electronic components to stabilize and thus helps insure constancy of the computer's operating characteristics. The second procedure has as its purpose the detection of changes in machine performance. It involves the use of a calibration signal which is a square wave, precisely generated to have a known area of 100 μvs. At least two calibration signals, one at the beginning and one at the end, are recorded on each reel of tape. The calibration signal is integrated at the beginning and end of each computation session, and the computer is adjusted to give the correct value when the computed area for the calibration signal fails to agree with the known value of 100 μvs within 1%. When the computer was first installed, the calibration signal was integrated several times daily, but since no change as large as 1% was ever found in as short a time period as one day, the operation procedure was modified. Over a year's operating experience indicates that changes are so slow that adjustment is necessary only every 10 days to two weeks. It seems likely that such changes as do occur are due to aging of electronic components. It is believed that these two procedures are adequate safeguards against the introduction of errors by machine variation.

## CHAPTER III

## PERIODIC VARIATION IN THE VENTRICULAR GRADIENT

Pipberger (1965), and other authors have noted the problems arising in the computer processing of ECG records from baseline shift. Two general areas of difficulty occur. Respiration effects can be produced both by disturbing the electrode contact by skin stretch and chest wall movement, and by changing the position of the heart. Longer term baseline drift is the second. This may be due to muscle and skin tremor, Caceres, et al. (1962). Various methods have been suggested to deal with the baseline problem, including the visual selection of heart beats for which baseline drift is negligible, Pipberger (1965), the averaging of several beats to reduce the variation, Cosma, et al. (1966), and the use of linear extrapolation of the baseline across the heart beat, Caceres, et al. (1962). Since respiration is a periodic phenomenon, it was anticipated that the variation due to respiration would be periodic. Cosma, et al. (1966), have reported respiration effects of period lengths of from 3 to 6 heart beats. No information was available on whether long term baseline drift is periodic or whether there might exist other periodic components of the variation of cardiac vectors among serial heart beats. Therefore, these areas are discussed here.

The analog computer uses a flat baseline for computation, therefore the computed area is too large for a beat during which the true baseline increases, and too small for a beat during which the true baseline decreases. Baseline shift is usually slow enough that the baseline may be regarded as effectively monotonic during one heart beat. If the true baseline is flat, then the computer makes no error due to baseline shift. Thus it may be seen that if the baseline is truly periodic, then the computer introduces a computational error which is periodic with the same frequency as the baseline and out of phase with it by 90 degrees. This means that if one computes areas from consecutive heart beats without rejecting those for which the baseline shifts, the successive areas will have a periodic component. An analysis of the frequencies present in the computed areas should therefore reveal the frequency of the baseline shift. If other frequencies are present, it may not be possible to identify the frequency which orginated in the baseline shift, but it will be present if the baseline is periodic. In order to study the effects of baseline drift and respiration, and to see whether other periodic components of variation could be detected, the decision was made to perform a spectral analysis on the vector components of consecutive heart beats. Jenkins (1961) recommends the use of spectral analysis in this fashion, i.e., for suggesting possible time series models.

According to Tukey (1961), spectral analysis estimates the components of variance due to various frequency bands. A frequency band is composed of all possible frequencies between the two extremes of the band. It consists of a continuous frequency range of finite

length. For example, the frequency interval between 0 and 3 cycles per second (cps) could be divided into 3 frequency bands, each of length 1 cycle per second, by defining the lowest frequency band as being from 0 to 1 cps, the middle as 1 to 2 cps, and the high band as being 2 to 3 cps. In this paper, all the frequencies of interest will be between 0 and 0.5 cycles per heart beat. This frequency unit will be discussed later.

The form of the variation among the observations in a time series, or in this instance, a sample of consecutive heart beat spatial vector components, may conveniently be classified into three types, trend, random, and periodic. Trends can be detected and treated by the methods of curvilinear regression. In practical situations there will always exist some variation which can be regarded as random, i.e., as having a mean of 0. Periodic variation, of course, may be present or absent, and if present may be weak or strong. There are three purposes of the spectral analysis of a time series. The first is to determine whether periodic variation exists. The second is to determine the strength, relative to the random variation, of any periodic variation which exists. The third is to determine the frequencies of whatever periodic variation has been found.

The purposes of spectral analysis are accomplished in the following way. Spectral analysis produces a spectral density, which is, practically speaking, the sample variance as a function of frequency. The density gives the amount of the variance due to each of the possible frequency bands. If all of the variation is random, then all frequencies contribute equally to the sample variance. This results in a flat

spectrum, or spectral density. Sampling variation tends to produce some fluctuation in estimated spectra, even when the variation is predominately random. To minimize this problem, it is common practice to smooth spectral densities before using them for inference purposes. This is usually done by replacing each raw spectral point by some sort of weighted average of several raw spectral points. These averages compose the smoothed spectral density. The smoothed spectral density has one or more peaks when periodic variation existed in the sample. The sum of the heights of these peaks indicates roughly how much of the sample variance was periodic. The peaks occur at the frequency bands which include the frequencies of the periodic variation.

It is often of interest to compare the general shapes of spectral densities from several time series. Such a comparison typically involves consideration of whether peaks occur in the same frequency bands in different spectra, whether the same numbers of peaks occur, and the relative sizes of peaks. Normalization facilitates comparison of several spectra. Normalization consists of dividing each of the smoothed spectral density points by their sum, which is the sample variance. A normalized spectral density gives the fraction of the sample variance due to each frequency band.

The theory of spectral analysis requires that the observations have 0 mean. This can be accomplished by subtracting the sample mean from each of the sample observations. Spectral analysis can then appropriately be performed on the deviations from the sample mean.

The method of computing the spectral density is given below. Given a set of N equally spaced observations, $X(I)$, $I = 1, 2, \ldots, N$,

the lag between any two specified observations, say X(K) and X(L), where L > K, is defined to be L - K. In other words, the lag is the difference in index numbers. The method for obtaining the spectral density uses lags, but the results can be immediately expressed in terms of frequencies. When there is only 1 observation per time unit, or as in the present case, one per heart beat, the frequency f, corresponding to lag P, is f = P/2M, where M is the maximum lag used in the computations. The spectral density gives a value for each frequency band (f - 1/4M, f + 1/4M) whose midpoint frequency, f, corresponds to lag P, P = 0, 1, ..., M. For convenience, the spectral points are usually referred to as occurring at the midpoints of the frequency bands. The lag product average, W(P), corresponding to lag P, is given by

$$W(P) = \frac{1}{N-P} \sum_{I=1}^{N-P} X(I)\, X(I + P).$$

The raw spectral density A(P), corresponding to lag P, where P = 0, 1, ..., M is computed according to

$$A(P) = \frac{2}{M} \left[ \sum_{I=1}^{M-1} W(I) \cos (PI\pi) \right] + W(M) \cos (P\pi) + W(0),$$

where M is the total number of nonzero lags. There are various methods of smoothing spectral densities. The one to be presented here uses the "hamming" (after R. W. Hamming) weights of 0.23, 0.54, and 0.23 for smoothing the raw spectral density, as described by Blackman and Tukey (1958). The smoothed spectral density S(P), corresponding to lag P, is a weighted average of the raw spectral density values for P-1, P,

and P+1, and is given by

$$S(P) = 0.23A(P-1) + 0.54A(P) + 0.23A(P+1),$$

for P=1, 2, ..., M-1, with

$$S(0) = 0.54A(0) + 0.46A(1), \text{ and}$$

$$S(M) = 0.54A(M) + 0.46A(M-1).$$

The smoothed spectral density thus obtained is the part of the variance among the X(I) which is due to frequencies in the interval (f - 1/4M, f + 1/4M) where f is the frequency corresponding to P. Division of each of the smoothed spectral density points by the sum of all of them produces the normalized spectral density.

It should be mentioned that when T observations per time interval are taken, the highest frequency for which the spectral density can be determined is T/2 cycles per time unit. This is called the folding, or Nyquist, frequency. In the present situation, with observations on consecutive heart beats, i.e., having taken one observation per heart beat, the highest frequency we can investigate is 0.5 cycles per heart beat. This corresponds to a periodicity of cycle length of two heart beats.

It should be noticed that the frequencies in this study are in cycles per heart beat, not in cycles per time unit. To obtain the cycle length in heart beats for a periodic component of particular frequency, one inverts the frequency. Even though it is known that the pulse rate is not constant, the heart beat is a convenient measure for periodic components whose cycle length is longer than two beats. This is somewhat analogous to the time normalization procedure used by Pipberger (1965), in which he computed a vector for each one-eighth

of the duration of the QRS complex. He then compared the first vector among subjects, then the second, etc., although the wave forms which generated the vectors were known to be of unequal durations.

Because of its longer duration, the ventricular gradient vector is most subject to baseline shifts. Since it was desired to view the frequency pattern of baseline, the gradient was the vector selected for spectral analysis. In an attempt to obtain a group of subjects which was homogeneous relative to pathology, age, sex, and race, recorded electrocardiograms of 8 healthy white males between the ages of 35 and 38 years were selected. Using no baseline rejection, the three components of the gradient were computed for each of 100 serial heart beats for each subject. The maximum lag, M, was selected to be 12 in keeping with the recommendation of Blackman and Tukey (1958) that M be a small fraction of N, the sample size. The normalized spectral density was then computed as outlined above for each component for each subject. The consequences of having M equal 12 are that spectral values will be computed for 12 frequency bands besides the 0 band and that the band width for each spectral value is 1/2M, or 1/24 cpb, where cpb will be adopted as notation for cycles per heart beat. The normalized spectral densities are given in Table 1. For purposes of locating important frequencies, values of the normalized spectral densities which are equal to or greater than the arbitrary value 0.11 and larger than either of the adjacent values will be referred to as peaks or peak values. They are indicated in Table 1. Table 2 gives the subjects, leads, and frequencies for which peaks occurred. Table 3 presents the component averages, variances, and

TABLE I

NORMALIZED SPECTRAL DENSITIES OF VENTRICULAR GRADIENT COMPONENTS

| Subject 107 | | | | Subject 121 | | | |
|---|---|---|---|---|---|---|---|
| f (cpb) | X | Y | Z | f (cpb) | X | Y | Z |
| 0 | .121[a] | .082 | .047 | 0 | .029 | .073 | .077 |
| 1/24 | .087 | .079 | .056 | 1/24 | .058 | .103 | .125 |
| 2/24 | .067 | .085 | .082 | 2/24 | .101 | .141 | .185 |
| 3/24 | .063 | .113 | .094 | 3/24 | .113[a] | .147[a] | .187[a] |
| 4/24 | .085 | .122[a] | .083 | 4/24 | .095 | .117 | .147 |
| 5/24 | .101 | .115 | .091 | 5/24 | .094 | .067 | .098 |
| 6/24 | .074 | .069 | .080 | 6/24 | .091 | .065 | .065 |
| 7/24 | .056 | .047 | .058 | 7/24 | .077 | .067 | .044 |
| 8/24 | .061 | .051 | .057 | 8/24 | .064 | .049 | .029 |
| 9/24 | .075 | .062 | .060 | 9/24 | .067 | .041 | .017 |
| 10/24 | .070 | .078 | .055 | 10/24 | .069 | .053 | .010 |
| 11/24 | .065 | .058 | .089 | 11/24 | .070 | .046 | .009 |
| 12/24 | .075 | .037 | .149[a] | 12/24 | .071 | .030 | .008 |

[a]Peak value.

TABLE 1--Continued

| Subject 125 | | | | Subject 138 | | | |
|---|---|---|---|---|---|---|---|
| f (cpb) | X | Y | Z | f (cpb) | X | Y | Z |
| 0 | .070 | .080 | .096 | 0 | .070 | .075 | .072 |
| 1/24 | .069 | .070 | .103 | 1/24 | .070 | .112 | .084 |
| 2/24 | .074 | .089 | .094 | 2/24 | .075 | .127[a] | .082 |
| 3/24 | .069 | .080 | .072 | 3/24 | .081 | .106 | .056 |
| 4/24 | .078 | .063 | .074 | 4/24 | .077 | .166[a] | .037 |
| 5/24 | .094 | .070 | .060 | 5/24 | .078 | .089 | .043 |
| 6/24 | .094 | .077 | .057 | 6/24 | .085 | .045 | .082 |
| 7/24 | .094 | .109 | .079 | 7/24 | .078 | .033 | .106 |
| 8/24 | .061 | .094 | .076 | 8/24 | .072 | .034 | .088 |
| 9/24 | .054 | .071 | .078 | 9/24 | .076 | .037 | .062 |
| 10/24 | .063 | .070 | .079 | 10/24 | .078 | .054 | .074 |
| 11/24 | .081 | .064 | .069 | 11/24 | .078 | .086 | .104 |
| 12/24 | .099 | .063 | .064 | 12/24 | .082 | .085 | .111[a] |

[a]Peak value.

TABLE 1--Continued

| Subject 140 | | | | Subject 169 | | | |
|---|---|---|---|---|---|---|---|
| f (cpb) | X | Y | Z | f(cpb) | X | Y | Z |
| 0 | .130[a] | .046 | .091 | 0 | .086 | .097 | .048 |
| 1/24 | .100 | .085 | .073 | 1/24 | .067 | .072 | .064 |
| 2/24 | .075 | .114[a] | .077 | 2/24 | .059 | .057 | .064 |
| 3/24 | .179 | .093 | .114 | 3/24 | .052 | .091 | .060 |
| 4/24 | .238[a] | .083 | .124[a] | 4/24 | .095 | .121[a] | .082 |
| 5/24 | .099 | .077 | .093 | 5/24 | .157[a] | .113 | .093 |
| 6/24 | .041 | .064 | .071 | 6/24 | .121 | .101 | .114 |
| 7/24 | .033 | .052 | .054 | 7/24 | .112 | .076 | .156[a] |
| 8/24 | .022 | .072 | .047 | 8/24 | .086 | .074 | .101 |
| 9/24 | .023 | .088 | .053 | 9/24 | .061 | .066 | .060 |
| 10/24 | .029 | .089 | .059 | 10.24 | .047 | .049 | .055 |
| 11/24 | .019 | .078 | .068 | 11/24 | .029 | .044 | .049 |
| 12/24 | .013 | .061 | .076 | 12/24 | .027 | .037 | .054 |

[a]Peak value.

TABLE 1--Continued

| Subject 173 | | | | Subject 182 | | | |
|---|---|---|---|---|---|---|---|
| f (cpb) | X | Y | Z | f (cpb) | X | Y | Z |
| 0 | .036 | .151[a] | .193 | 0 | .096 | .082 | .233[a] |
| 1/24 | .065 | .112 | .199[a] | 1/24 | .169 | .077 | .179 |
| 2/24 | .115 | .102 | .112 | 2/24 | .172[a] | .075 | .111 |
| 3/24 | .117[a] | .180[a] | .033 | 3/24 | .074 | .101 | .072 |
| 4/24 | .105 | .148 | .022 | 4/24 | .078 | .153[a] | .055 |
| 5/24 | .106 | .060 | .044 | 5/24 | .096 | .150 | .056 |
| 6/24 | .111[a] | .068 | .064 | 6/24 | .065 | .093 | .056 |
| 7/24 | .088 | .047 | .048 | 7/24 | .043 | .057 | .055 |
| 8/24 | .061 | .023 | .039 | 8/24 | .039 | .037 | .039 |
| 9/24 | .065 | .019 | .057 | 9/24 | .037 | .029 | .030 |
| 10/24 | .050 | .023 | .062 | 10/24 | .042 | .041 | .042 |
| 11/24 | .038 | .032 | .057 | 11/24 | .045 | .055 | .041 |
| 12/24 | .043 | .035 | .069 | 12/24 | .046 | .052 | .032 |

[a]Peak value.

TABLE 2

SUBJECT, LEAD, AND FREQUENCY LOCATION OF SPECTRAL DENSITY PEAK VALUES[a]

| Lead | Subject 107 | Subject 121 | Subject 125 | Subject 138 | Subject 140 | Subject 169 | Subject 173 | Subject 182 |
|---|---|---|---|---|---|---|---|---|
| X | 0 | 3 | | | 0,4 | 5 | 3,6 | 2 |
| Y | 4 | 3 | | 2,4 | 2 | 4 | 0,3 | 4 |
| Z | 12 | 3 | | 12 | 4 | 7 | 1 | 0 |

[a]Table entries are frequencies in units of 1/24 cpb.

TABLE 3

PULSE RATE AND VENTRICULAR GRADIENT COMPONENT
MEANS AND VARIANCES

| | Subject 107 | Subject 121 | Subject 125 | Subject 138 | Subject 140 | Subject 169 | Subject 173 | Subject 182 |
|---|---|---|---|---|---|---|---|---|
| $\bar{X}$ | 50.3 | 75.5 | 126.0 | 111.3 | 92.1 | 67.8 | 62.2 | 49.6 |
| $\bar{Y}$ | 41.8 | 60.2 | 83.7 | 48.6 | 47.8 | 87.7 | 85.1 | 47.4 |
| $\bar{Z}$ | - 38.6 | - 81.4 | -105.7 | - 89.2 | - 44.4 | - 57.1 | - 36.1 | - 37.4 |
| $s_X^2$ | 90.8 | 377.0 | 147.6 | 545.2 | 146.4 | 249.0 | 100.7 | 204.3 |
| $s_Y^2$ | 178.1 | 191.3 | 315.9 | 91.8 | 707.7 | 195.6 | 183.2 | 243.3 |
| $s_Z^2$ | 90.8 | 198.4 | 105.5 | 120.0 | 116.7 | 151.2 | 206.6 | 223.1 |
| Pulse Rate (beats/min) | 82 | 68 | 68 | 68 | 73 | 63 | 67 | 80 |

the pulse rates for the subjects.

In the X lead, all peaks were at 6/24 cpb or lower, Subject 173 having the peak at 6/24 cpb. Subjects 125 and 138, however, had no definite peak in this lead. In the Y lead, all peaks were at 4/24 cpb or lower, except that Subject 125 had a doubtful peak at 7/24 cpb. Only one of the peaks in this lead, however, was in the lowest frequency band, 0 cpb. The Z lead evidenced considerable variety in the frequency locations of spectral peaks, in that peaks occurred both in the highest bands (definitely in Subject 107, and probably in Subject 138) and in the lowest frequency bands (Subject 182).

Comparison of the individual subjects reveals a rather diverse pattern. The spectral densities for Subjects 107 and 121 are graphed in Figures 1 and 2, respectively. In Subject 107, the three components had peaks at low, medium, and high frequencies in X, Y, and Z, respectively. The three peaks were all at the same frequency, 3/24 cpb, in Subject 121. Subject 125 had practically uniform spectra in all leads. Subjects 140, 169, and 182 each had peaks in the different components which fell within a frequency range of 5/24 cpb or less for each person. These clusters of peaks were all in the middle or low frequency areas of the spectra.

Even though the subjects were selected for their similarity in pathology, race, sex, and age, there was considerable variation of location of spectral peaks, both within subjects among the three leads, and among subjects. Since it was expected that the respiration effect would be strongly evident in all components, it is interesting that even when the subject had spectral peaks in all three leads in the respiration frequency range, the peaks themselves did not always occur

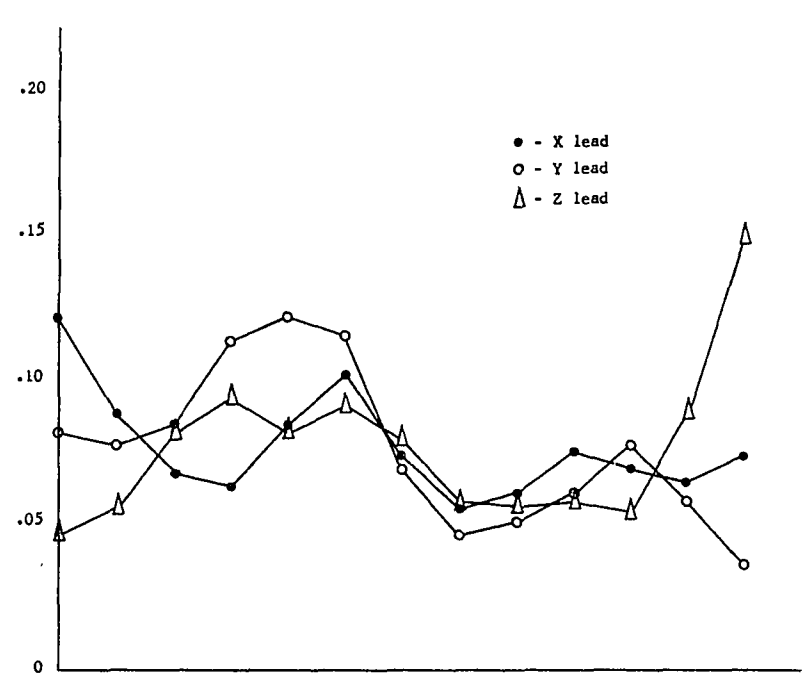


Figure 1. Normalized spectral densities of the ventricular gradient components, Subject 107.

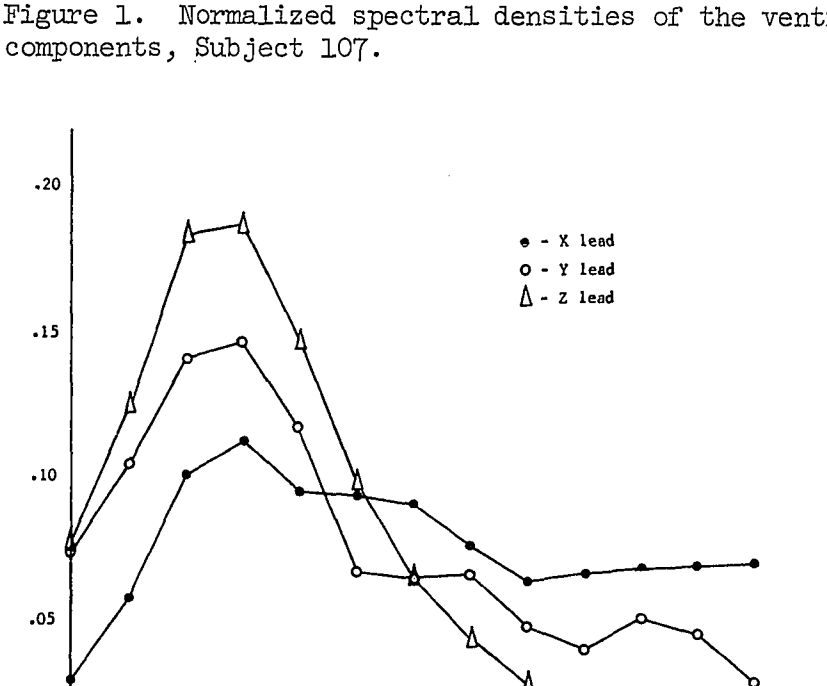


Figure 2. Normalized spectral densities of the ventricular gradient components, Subject 121.

at the same frequency. This was especially true in Subjects 140 and 169, although 121 was the exception. One can also note that when peaks came in Y, they fell in the respiration frequency range more often than did those peaks which occurred in other leads.

Longer term drift peaks, those for which the frequency is equal to or less than 2/24 cpb, occurred in each of the 3 leads at least once. These were in Subjects 107, 138, 140, 173, and 182. Moreover, the last three of the above subjects had low frequency peaks in two different leads.

There was some evidence for the existence of periods other than those previously expected, i. e., those due to baseline drift and respiration. In Subjects 138, 140, and 173 there was evidence of double spectral peaks in single leads, these being generally in the lower frequency half of the spectrum. It is believed that these double peaks correspond to baseline drift and respiration effect. It is interesting to note that there was no evidence that baseline drift and respiration effect peaks occurred together in the Z lead.

If spectral peaks had occurred in adjacent frequency bands, they could not have been successfully resolved. This creates some problem in searching for multiple spectral peaks. There are three reasons for the difficulty. The first is that only 100 heart beats were used for each subject. The second, a consequence of the first, is that only thirteen spectral points were estimated. Thirdly, the spectra were smoothed. In general, if the frequency of a periodic component is not constant relative to the heart beat, there is a smearing effect which makes it difficult to detect a small or minor

peak, since the estimate of the smoothed spectrum will attribute the variation due to that effect to more than one frequency band, thus reducing the spectrum value in each band.

However, the strong peak in the Z lead at the frequency 0.5 cpb in Subject 107 and the lesser peak in the Z lead of Subject 138 suggest the possibility of an occasional high frequency component in the ventricular gradient Z lead, which is certainly not the result of respiration effect or baseline drift. It is observed that Subject 107 had the highest pulse rate among the eight subjects, (Subject 138 however, had one of the lowest), but it is not known whether this fact is relevant.

A component of frequency 0.5 cpb or cycle length of two heart beats, alternates with every heart beat. This suggests the possibility of some relationship between the present observation in normal subjects and the pathological condition "electrical alternans", mentioned by Hurst and Logue (1966). In electrical alternans, spatial cardiac vector components increase and decrease on alternate heart beats. Further research is needed to explore this possibility. Such a study should probably involve more subjects than were used in this paper, and might well select subjects with higher than average pulse rates, or those in which higher pulse rates were induced by exercise or drugs.

Four results of the time series analysis of the ventricular gradient vector are apparent. The first is that respiration effect was not as strong or as consistent across leads within subjects as had been expected. Secondly, low frequency baseline drift did prove to be periodic but did not occur in all subjects. Thirdly, periodic

variation of a frequency too high (0.5 cpb) to be attributable to baseline drift or respiration effect was observed. Finally, there was the large variation in the frequency and lead location of peaks among subjects who were supposed to be a homogeneous group. This diversity precludes a precise description of periodic variation among heart beats until further research has been done. This large inter-subject variation indicates that the problem is complex and that larger numbers of subjects will be needed to overcome the variation.

In reference to the conclusion of Cosma, et al. (1966), the results obtained here seemed to indicate that because of the common occurrence of lower frequency periodic variation in the ventricular gradient, considerably more than three beats should be averaged when the baseline assumption described herein is used. It would seem that at least enough heart beats to cover one cycle of the lowest frequency component present should be averaged. Since some spectral peaks were found at 1/24 cpb and lower frequencies, it seems that at least 40 beats should be used when there is no baseline rejection.

# CHAPTER IV

## VECTOR COMPONENT VARIATION IN RELATION TO AGE, SEX, AND PULSE RATE

As was mentioned earlier, it was desired to investigate whether the amount of variation in the components of certain spatial cardiac vectors changes with other demographic factors. Since age and sex are among the most important of these, and because of the possibility suggested in CHAPTER III that pulse rate may have some effect on vector component variability, these three factors were selected for this study. The P and QRS vectors, in addition to the ventricular gradient, were considered.

To study the variability due to the heart alone, it was necessary to minimize the effects of low frequency baseline drift and respiration. This was done by utilizing the baseline rejection capability of the analog area computer as described in CHAPTER II. Thus the computer was caused to reject any heart beat for which the baseline shift in the lead being computed was greater than the amount determined by the dial setting. The normal dial setting was 5%.

Records for 99 subjects for whom the age, sex, and pulse rate information was complete were obtained. The subjects in the sample ranged in age from 22 to 67 years and were classified as being

above or below the median age of 37.5 years. The pulse rate median was 71.5 beats per minute and it was similarly used to divide pulse rates into low and high groups. The sex dichotomy completed the 2 by 2 by 2, or $2^3$, factorial arrangement into which the subjects were classified. Some information was lost, of course, by dichotomizing age and pulse rate, which are continuous variables. Table 4 gives the number of subjects in each classification group.

TABLE 4

CLASSIFICATION GROUP SAMPLE SIZE

| Age (yrs) | < 37.5 | | > 37.5 | | Total |
|---|---|---|---|---|---|
| Pulse Rate (beats/min) | < 71.5 | > 71.5 | < 71.5 | > 71.5 | |
| Male | 19 | 22 | 18 | 15 | 74 |
| Female | 3 | 5 | 8 | 9 | 25 |
| Total | 22 | 27 | 26 | 24 | 99 |

Averages for samples of 9 heart beats each were computed for the components of the gradient, P, and QRS vectors in these people. The number of such averages ranged from 4 to 14 in the various leads. Thus several averages were computed for each subject on 3 components for each of 3 vectors. These sample averages were assumed to be approximately normally distributed for two reasons. The first is the Central-Limit Theorem, which Mood (1950) states as follows, "If a population has a finite variance $\sigma^2$ and mean $\mu$, then the distribution

of the sample mean approaches the normal distribution with variance $\sigma^2/n$ and mean $\mu$ as the sample size n increases.". The second is that the baseline rejection helped remove the periodic variation due to baseline shift and respiration, and the spectral analyses in CHAPTER III indicate that these are the most common periodic disturbances, at least in the gradient vector. The P and QRS durations are much shorter than that of the gradient, so that baseline disturbances of frequencies of several cpb or lower should have even less effect on them. At this stage, the object was to compare the variability among the classification groups, the comparisons of prime interest being the main effects. The following measure of variability was adopted. For each of the 9 vector components the sample variance among the averages of 9 beats was computed, thus giving 9 sample variances of means for each subject. Next, following the recommendation of Bartlett (1947) these sample variances were transformed by taking their natural logarithms. Eisenhart (1947) and Cochran (1947) discuss the assumptions for the analysis of variance and the possible consequences when the assumptions do not hold. It was assumed that the new variables, the logarithm of sample variance of means of 9 observations for each component, were suitable for the analysis of variance. A $2^3$ factorial analysis of variance was then done on each of the 9 new variables. International Business Machines 1620 Users Group Library program 6.0.132, Analysis of Variance and Covariance - Unequal Subclass Frequencies, written by Rex L. Hurst, was used to perform the calculations. The results are given in Table 5.

All the F tests used 1 and 91 degrees of freedom. Only the mean square is given where the contrast has 1 degree of freedom.

TABLE 5

ANALYSIS OF VARIANCE OF TRANSFORMED SAMPLE VARIANCES

| | | Ventricular Gradient Vector | | | | | |
|---|---|---|---|---|---|---|---|
| | | X | | Y | | Z | |
| Source | df | M.S. | F | M.S. | F | M.S. | F |
| Sex | 1 | .016 | NS | .410 | NS | .211 | NS |
| Age | 1 | 1.466 | 2.55 | .150 | NS | .013 | NS |
| Pulse | 1 | 1.650 | 2.87[a] | 1.075 | 1.71 | .042 | NS |
| Sex x Age | 1 | .061 | NS | .756 | NS | .005 | NS |
| Sex x Pulse | 1 | 6.503 | 11.33[c] | .170 | NS | .465 | NS |
| Age x Pulse | 1 | .460 | NS | .165 | NS | .117 | NS |
| Sex x Age x Pulse | 1 | .257 | NS | 1.966 | 3.12[a] | .100 | NS |
| Error | 91 | .574 | NS | .630 | NS | .795 | NS |
| Error SS | | 52.259 | | 57.370 | | 72.375 | |

[a]Significant at the 0.1 probability level.
[b]Significant at the .05 probability level.
[c]Significant at the .005 probability level.

TABLE 5--Continued

| | | P Vector | | | | | |
|---|---|---|---|---|---|---|---|
| | | X | | Y | | Z | |
| Source | df | M.S. | F | M.S. | F | M.S. | F |
| Sex | 1 | 31.384 | 10.96[c] | 23.301 | 15.92[c] | 47.852 | 19.62[c] |
| Age | 1 | 2.018 | NS | 5.011 | 3.42[a] | .503 | NS |
| Pulse | 1 | .239 | NS | 1.571 | NS | .303 | NS |
| Sex x Age | 1 | 1.353 | NS | 1.235 | NS | 5.929 | 2.43 |
| Sex x Pulse | 1 | 1.476 | NS | .469 | NS | .438 | NS |
| Age x Pulse | 1 | .525 | NS | .058 | NS | 2.135 | NS |
| Sex x Age x Pulse | 1 | .307 | NS | .010 | NS | .009 | NS |
| Error | 91 | 2.864 | NS | 1.464 | NS | 2.439 | NS |
| Error SS | | 260.594 | | 133.251 | | 221.962 | |

[a]Significant at the 0.1 probability level.

[b]Significant at the .05 probability level.

[c]Significant at the .005 probability level.

TABLE 5--Continued

| Source | df | QRS Vector | | | | | |
|---|---|---|---|---|---|---|---|
| | | X | | Y | | Z | |
| | | M.S. | F | M.S. | F | M.S. | F |
| Sex | 1 | 4.613 | 2.93[a] | 6.609 | 5.03[b] | 13.768 | 8.86[c] |
| Age | 1 | .095 | NS | 4.584 | 3.49[a] | 1.387 | NS |
| Pulse | 1 | 4.386 | 2.79[a] | .945 | NS | 1.421 | NS |
| Sex x Age | 1 | .572 | NS | .169 | NS | .323 | NS |
| Sex x Pulse | 1 | .518 | NS | .297 | NS | 1.285 | NS |
| Age x Pulse | 1 | 1.030 | NS | .159 | NS | .415 | NS |
| Sex x Age x Pulse | 1 | .017 | NS | .523 | NS | .168 | NS |
| Error | 91 | 1.574 | NS | 1.315 | NS | 1.554 | NS |
| Error SS | | 143.22 | | 119.653 | | 141.39 | |

[a]Significant at the 0.1 probability level.

[b]Significant at the .05 probability level.

[c]Significant at the .005 probability level.

For the ventricular gradient 0.1 level significance was found for the pulse main effect in the X lead and the sex by age by pulse interaction in the Y lead. The sex by pulse interaction in the X lead was significant at the 0.005 level. In males, the low pulse rate group had the higher variation, while in females, the high pulse rate group had the higher variation.

The sex factor was significant at the 0.005 level for all three components of the P vector. Age was significant at the 0.1 level in the P vector Y component.

The sex factor in the QRS vector was significant at the 0.1, 0.05, and 0.005 levels in the X, Y, and Z leads, respectively. The pulse factor in the X lead and the age factor in the Y lead were significant at the 0.1 level.

No great weight should be given results which are significant at only the 0.1 level, especially when a large number of tests are done in one analysis. It is interesting, however, to note that in the Y component of both the P and QRS vectors the age factor was significant at this mild level. The highly significant sex by pulse interaction in the gradient X lead is difficult to interpret. The striking result of this study is the strong significance of the sex factors in the P and QRS vectors. This leads one to conclude that the males and females have different averages of the transformed variables in these vectors. To determine the direction of the difference, i.e., which sex has the larger variation, the antilog of the average of the transformed variables for each sex and vector component was taken. The antilog of an average of logarithms is the geometric mean of the

values whose logarithms were averaged. The geometric means for sexes and vector components are given in Table 6. Inspection of this table reveals that the females were more variable in all vector components in which there was a significant sex difference.

There are 4 important results of the study of ventricular gradient, P, and QRS vector component variation in relationship to age, sex, and pulse rate. First, differences did exist in the amounts of variation among the different subject groups. Second, the amount of variation differed strongly between the sexes in the P and QRS vectors, but not in the ventricular gradient. Third, females were the more variable when the sexes differed. Fourth, the amount of variation in the components of the 3 vectors was not found to differ significantly between low and high age groups, or between low and high pulse rate groups.

TABLE 6

GEOMETRIC MEANS OF SAMPLE VARIANCES

| | Gradient | | | P | | | QRS | | |
|---|---|---|---|---|---|---|---|---|---|
| Sex | X | Y | Z | X | Y | Z | X | Y | Z |
| Male | 8.337 | 8.472 | 7.464 | .393 | .472 | .377 | .738 | .653 | .637 |
| Female | 8.590 | 9.817 | 6.792 | 1.629 | 1.742 | 2.046 | 1.303 | 1.416 | 1.675 |

# CHAPTER V

## SUMMARY

The form of the variation among heart beats within subjects was investigated for the axial lead system X, Y, and Z components of the ventricular gradient vector. One hundred consecutive heart beats from each of 8 healthy white male subjects between the ages of 35 and 38 years were used. Spectral analysis was used to look for periodicities among the heart beats. No more than two spectral peaks were found in any one lead, and when double peaks occurred they were at frequencies of 6/24 cycles per heart beat or lower. Such double peaks are attributed to the joint occurrence of baseline drift and respiration effects. Double peaks were not observed in the Z lead. Considerable variation in the shape of the spectral density was found among subjects, and even among leads within subjects.

One subject had a definite spectral peak at 12/24 cycles per heart beat, but only in the Z lead. A periodic component of variation among heart beats of such high frequency was not previously expected and no explanation of its physiologic origin can yet be made.

Within individual subjects, spectral peaks in the baseline drift and respiration frequency ranges did not always occur at the same frequencies in the different leads. For this reason and because of the

common occurrence of low frequency periodic variation in the ventricular gradient, it was concluded that attempts to reduce this variation by averaging vector components for individual subjects should use samples of at least 40 heart beats when no form of baseline rejection is used.

Comparisons were made on the basis of age, sex, and pulse rate in the amount of intrasubject variation among heartbeats. This was done for each of the X, Y, and Z components of the ventricular gradient, P, and QRS vectors in 99 healthy adult subjects. Subjects were grouped into low and high ages, below and above 37.5 years, low and high pulse rates, below and above 71.5 beats per minute, and into sexes. This classification scheme resulted in a $2^3$ factorial arrangement where the factors were age, sex, and pulse rate. The measure of variation used was the natural logarithm of the sample variance among means of 9 heart beats. The analyses of variance did not indicate significant differences in amount of variability between the two age groups, or between the two pulse rate groups. Males and females did not differ significantly in the ventricular gradient components. Males and females did differ significantly in all components of P, and in the Y and Z components of the QRS vector. Females were the more variable in all components in which the sexes differed.

Thus, the investigation of the form of the intrasubject variation among heart beats revealed spectral peaks in the respiration frequency range, the long term baseline drift range, and, in one subject, in the highest frequency range. The shape of the spectral density varied widely both within and among subjects. Females were more variable in the P and QRS vector components than were males. Sex

differences were not found in the ventricular gradient. Neither the comparisons between low and high ages, nor those between low and high pulse rates revealed significant differences in amounts of variability.

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