AN AUTOMATED MUSCLE MOTOR UNIT COUNTING SYSTEM

AN AUTOMATED MUSCLE MOTOR UNIT COUNTING SYSTEM

By

RICHARD CAVASIN, B.ENG.

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AUTHOR: Richard Cavasin, B.Eng. (McMaster University)

SUPERVISOR: Dr. H. de Bruin

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ABSTRACT

A completely automated system for determining the number of motor units in a skeletal muscle has been developed and tested. It is based on the McComas incremental motor unit counting technique and eliminates the subjectivity introduced by the operator's judgement and addresses the problem of alternation which plagues manual estimation techniques.

The system, currently implemented using a PDP-11/34 mini-computer, uses silver strip electrodes to record the electrically evoked electromyographic responses which are amplified, filtered, and digitally converted for computer processing, display, and storage. The software uses digital signal processing, pattern recognition, and complex algorithms with well defined decision criteria to vary the stimulus amplitude, classify the responses, identify alternation, and estimate the motor unit count. The system was extensively tested on the thenar and extensor digitorum brevis muscles of numerous subjects. Its performance compared favourably with that of an experienced manual operator.

The speed, reliability, and objectivity of the system make it very useful clinically and promote the standardization of motor unit count estimation.

ACKNOWLEDGEMENTS

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LIST OF ACRONYMS

AMUAP = Average Motor Unit Action Potential

AP = Action Potential

CR = Composite Response

CV = Coefficient of Variation

EDB = Extensor Digitorum Brevis

EFI = Extrapolation Fit Indicator

MAMUCS = McMaster Automated Motor Unit Counting System

MEP = Maximum Evoked Potential

MN = Motor Neuron

MU = Motor Unit

MUAP = Motor Unit Action Potential

SPA = Stimulus Pulse Amplitude

CHAPTER 1

INTRODUCTION

1.0 Introduction

A motor unit (MU), the smallest unit of contraction in a skeletal muscle, consists of a motor neuron (MN) and all the muscle fibres innervated by it. Since a change in the number of MUs comprising a muscle is indicative of a neuromuscular disorder, a technique for reliably estimating this number would be a valuable tool in the diagnosis and monitoring of these disorders.

Currently, the only practical, non-invasive technique described in the literature for performing this estimation is the incremental motor unit counting technique proposed by McComas and his colleagues (1971) and several variations on it (Ballantyne and Hansen, 1974; Panayiotopoulos et al., 1974; Milner-Brown and Brown, 1976; Jasechko, 1987). This method uses surface electrodes to record the electromyographic responses evoked from a muscle by electrically stimulating its motor nerve. The operator performs the estimation based on measurements taken from these responses. One of the main criticisms levelled against this technique is that considerable subjectivity is introduced by the variability in the operator's judgement.

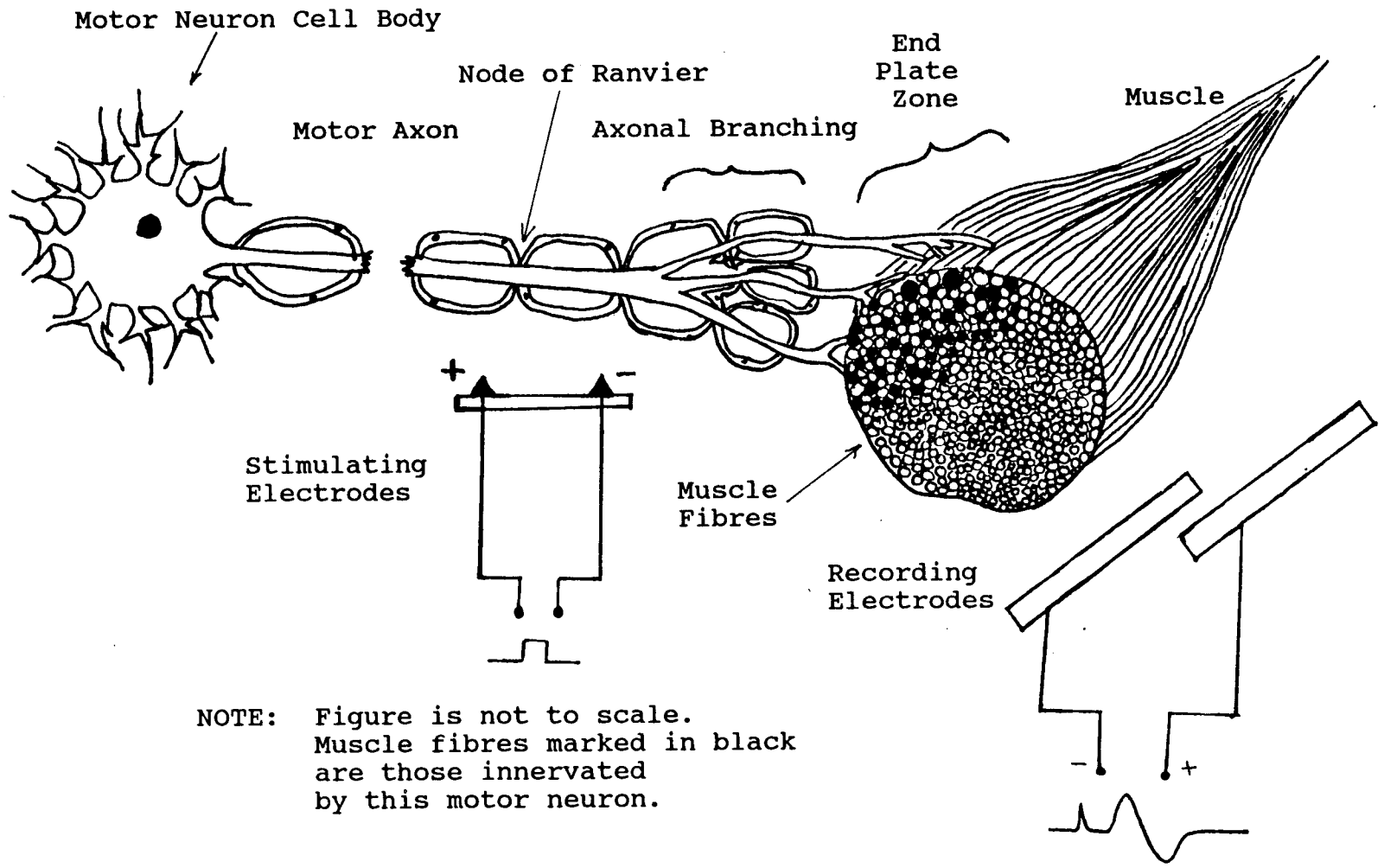
This thesis describes the automation of what will be referred to as the McComas technique. While other researchers such as Ballantyne and Hansen (1974) have used computers as aids in performing motor unit counts, Jasechko (1987) was one of the first to propose a completely automated system requiring virtually no operator input. The McMaster Automated Motor Unit Counting System (MAMUCS), which is based on this preliminary work, uses digital signal processing and pattern recognition to eliminate the subjectivity introduced by the operator's judgement in the estimation procedure.

1.1 The Motor Unit

Although a detailed discussion of the electrophysiological basis for motor unit counting is beyond the scope of this thesis, a brief overview follows. A more detailed description may be found in references such as Basmajian (1979).

Figure 1 summarizes the morphology of a typical motor unit. It includes the motor neuron and a number of muscle fibres that normally are randomly distributed within a segment of the muscle cross section. The terminal branches of the MN innervate the muscle fibres in what is called the end plate zone. The width and location of this zone along the muscle's longitudinal axis varies from muscle to muscle and across subjects. The number of muscle fibres within any particular motor unit can vary from a few to several hundred. In addition, the number of motor units within a particular muscle can vary over a similar range. In this

Figure 1 Motor Unit Morphology



NOTE: Figure is not to scale.
Muscle fibres marked in black are those innervated by this motor neuron.

way very fine control of muscle contraction can be achieved where needed.

The central nervous system controls the tension exerted by a muscle by varying the number of motor units being activated or 'recruited' and by modulating their individual firing rates. Each firing results in a brief contraction or 'twitch' of the muscle fibres. The summation of the individual asynchronous motor unit twitches results in the smooth contraction observed in the muscle.

The contraction of the muscle fibres of a motor unit is triggered by an electro-chemical event called the Action Potential (AP). In healthy nerve and muscle the AP is an all or nothing phenomenon in that once initiated it will propagate down the MN, across the synaptic gaps at the terminal branches, and down all the muscle fibres of that motor unit. In other words a MU either fires entirely or not at all depending on whether or not its stimulation threshold has been exceeded. The AP is a rapid depolarization/repolarization of the cellular membrane which when travelling the length of a muscle fibre appears as a moving dipole to a stationary recording electrode. Although the AP for a single muscle fibre has been calculated and recorded as a triphasic signal (Plonsey, 1969), the spatial dispersion of the terminal branches of the MN over the end plate zone results in a temporal dispersion of the individual muscle fibre APs that sum to form the Motor Unit Action Potential (MUAP). The shape of any particular MUAP will be a function of the dispersion of MN terminal branches, the number and arrangement of muscle fibres in the MU, the spatial relationship of the muscle fibres with respect to the recording electrodes, and the filtering properties of the tissues and

instrumentation. Once the recording electrodes are applied however, the all or nothing nature of the AP makes the shape of any particular MUAP relatively stable over time. It is this constancy of MUAP shape and size over the course of a test that makes the McComas technique possible.

When the muscle fibres of a MU are chronically deinnervated through the destruction or injury of a MN they will usually be captured by neighbouring MNs through collateral reinnervation. In this way the strength of the muscle can be maintained even though the number of MUs in the muscle may decrease. A certain amount of deinnervation and reinnervation is to be expected as part of the normal wear and tear in a healthy muscle and a significant reduction in the number of motor units of a muscle can be sustained without impairing the control of muscle contraction. This process, combined with the normal variation between individuals, accounts for the width of what is considered to be the 'normal' range of MUs for any particular muscle. It is not until chronic disease or permanent injury reduces the muscle to a small number of very large MUs that physical impairment is observed. One would record correspondingly large MUAPs in such cases.

If however, the pathology involves the destruction of muscle fibres one would expect to observe a normal number of MUs of reduced size with correspondingly decreased muscle strength. For these reasons, some method of estimating the number of MUs in a muscle would be useful for diagnosing and monitoring the progress of neuromuscular disorders.

Unfortunately, even dissection of the motor nerve cannot give an accurate count of the number of MUs in a muscle. Although several

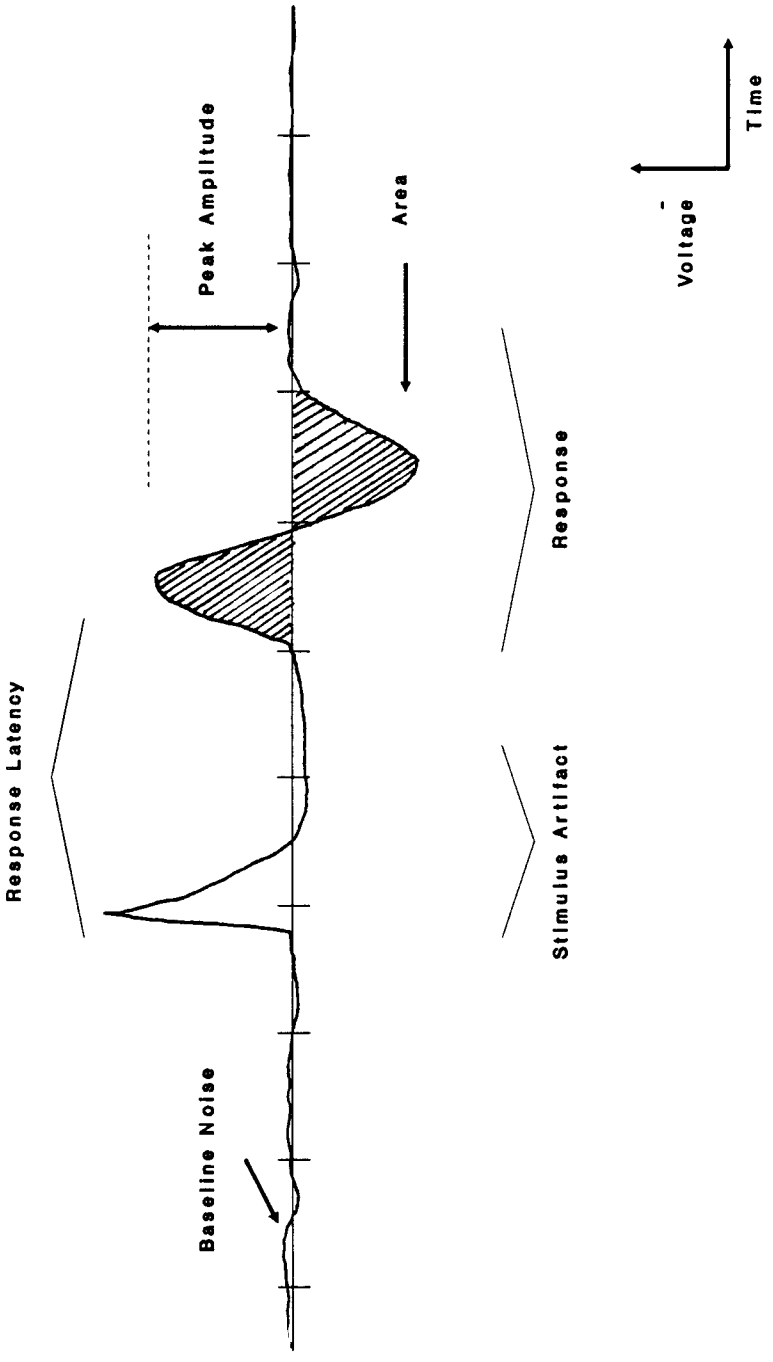
electro-myographic techniques for MU count estimation have been proposed using both voluntary and evoked potentials, the most common method currently used clinically is the McComas technique. A more invasive technique such as that proposed by De Koning et. al. (1988) does not easily lend itself to clinical implementation.

1.2 The McComas Technique

If a pair of electrodes are applied to the skin over a nerve bundle that runs near the surface, the application of an electrical pulse across them can induce an AP in some of the MNs within the nerve. These APs will travel down the MNs to the muscle fibres they innervate and evoke MUAPs which can be recorded by surface electrodes placed over the muscle belly. Figure 2 shows a typical response that consists of a stimulus artifact caused by the volume conduction of the stimulating pulse, a propagation delay as the AP travels down the MNs and across the synaptic gaps, and the summated MUAPs from all the MUs activated by the stimulus. Although the stimulating pulse is rectangular, the filtering properties of the tissues and electrodes results in an exponentially decaying artifact. By varying the stimulus pulse amplitude (SPA) the percentage of the total number of MUs in the muscle that are activated can be varied between zero and one hundred. Unfortunately, as will be explained later, there is not a one to one relationship between SPA and the number of MUs activated.

In order to use this technique the muscle under investigation must therefore be accessible for both stimulation and recording using surface

Figure 2 Signal Topology

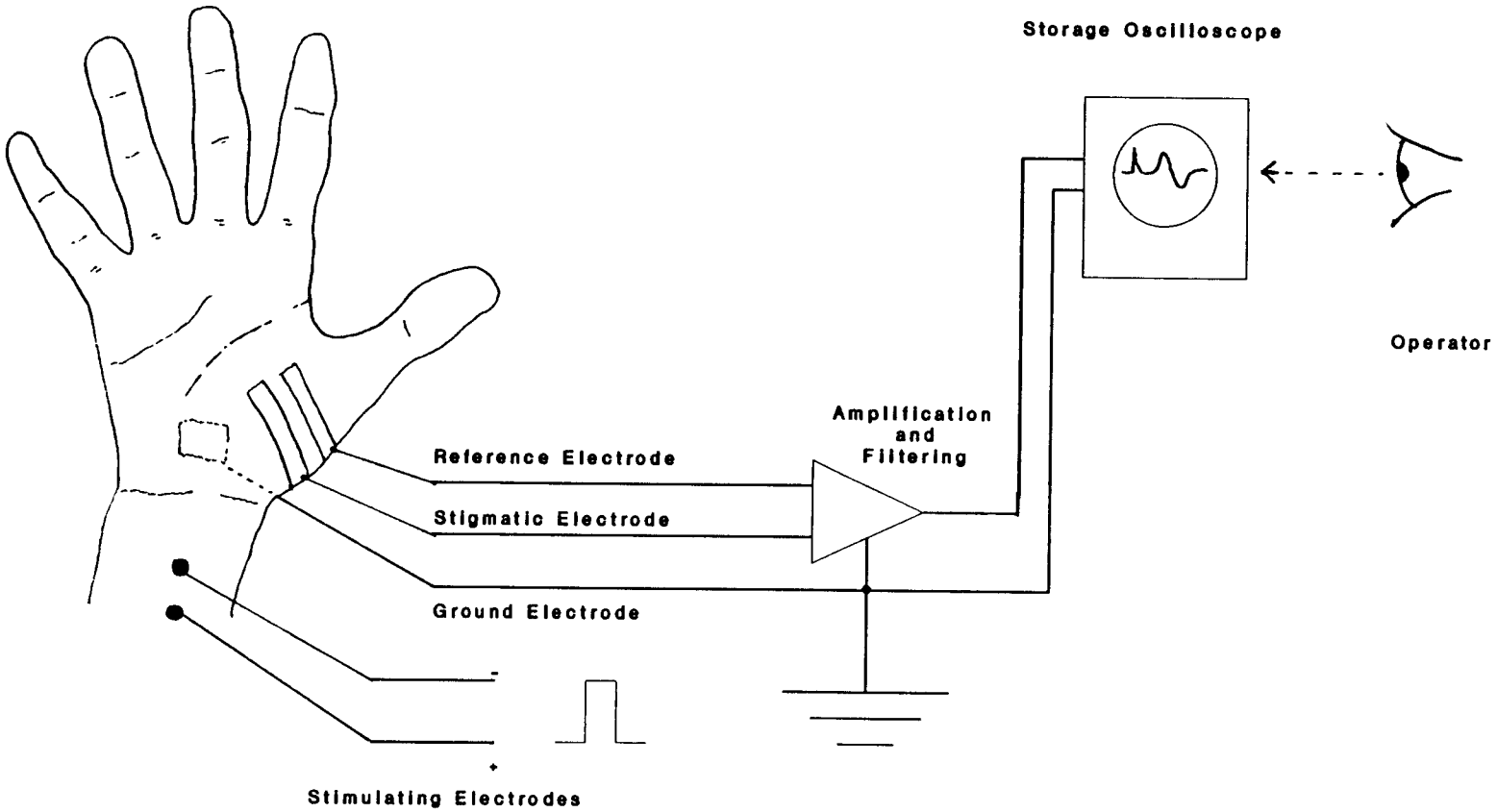


electrodes. Some of the muscles that are usually tested are the thenar, hypothenar, extensor digitorum brevis, soleus, first dorsal interosseus, and deltoid.

Figure 3 summarizes the hardware setup used in the McComas technique. The electrode placement depicted in this figure is used for performing MU count estimation on the thenar muscle group. Briefly, this technique consists of gradually increasing the SPA under manual control and displaying the evoked responses on a storage oscilloscope to obtain a composite response (CR) which is composed of a number of discrete gradations or increments (Figure 4). Due to resolution limitations the operator can rarely discriminate more than about fifteen gradations visually. Each successive increment in this CR is assumed to be the contribution of an additional MU that has been excited. Thus, by dividing the amplitude of the largest response in the CR by the number of increments, the operator obtains an estimate of the average MUAP (AMUAP) amplitude for that muscle. The operator then reduces the oscilloscope/amplifier gain and increases the SPA until the response displays no discernable increase in amplitude. This response comprises the summated MUAPs for all the MUs in the muscle. By dividing the amplitude of this Maximum Evoked Potential (MEP) by the AMUAP amplitude one obtains an estimate of the number of MUs in the muscle (N):

$$N = \frac{\text{MEP amplitude}}{\text{AMUAP amplitude}}$$

Figure 3 Instrumentation for the McComas Technique



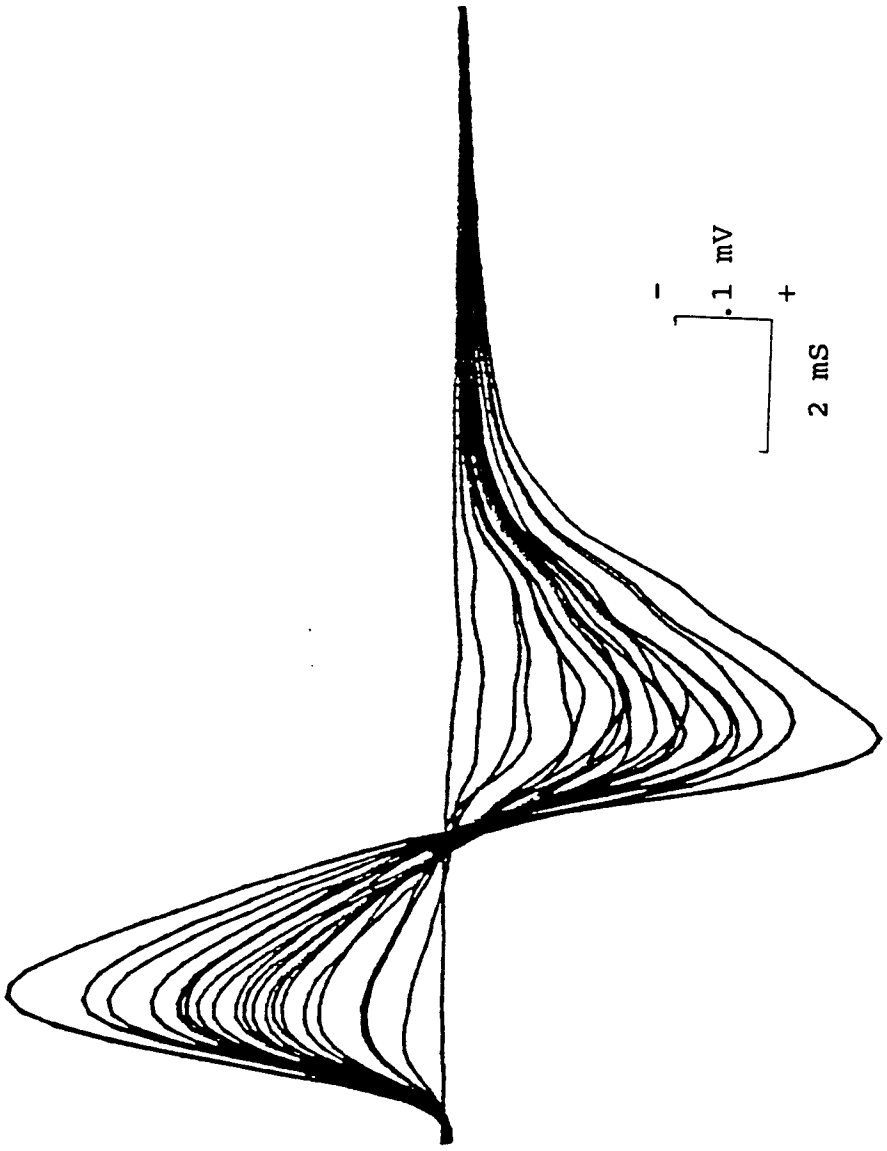


Figure 4 Typical CR (Thenar Muscle)

In other words, if there are k increments in the CR, we assume that k MUAPs have summed to produce the largest increment in the CR. Therefore we know that k MUs produce a response with a known amplitude and by assuming that zero MUs produce zero amplitude we can linearly extrapolate how many MUs it would take to produce the measured MEP amplitude (Figure 5).

1.3 Criticisms of the McComas Technique

Unfortunately, this technique suffers from several potential limitations, not the least of which is its dependence upon the operator's judgement in identifying the discrete increments of the CR. In addition, the method is based on the following three assumptions:

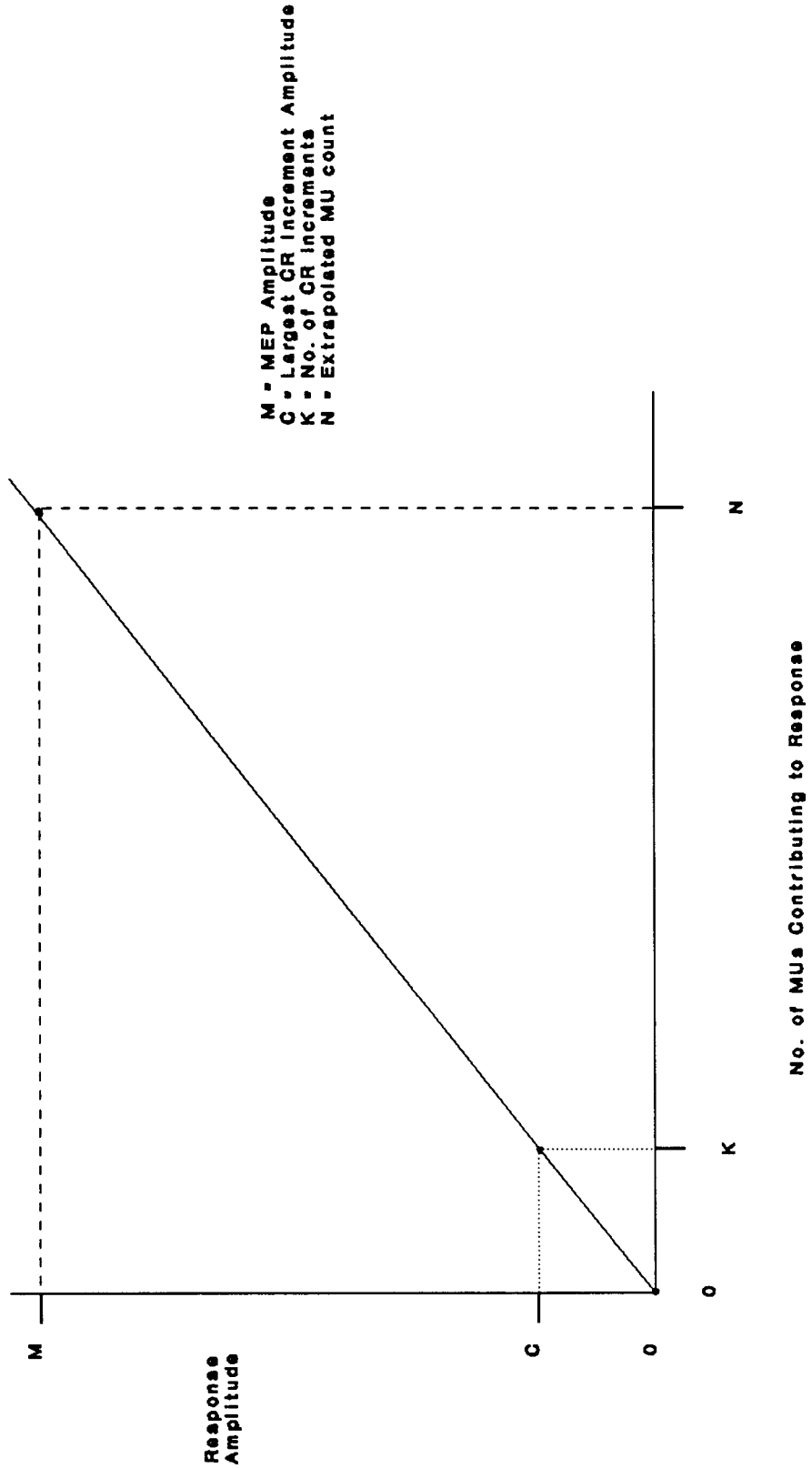
1) Each increment in the CR corresponds to the contribution of a single MU.

   Three conditions can potentially lead to a violation of this assumption:

   A) If very small or distant MUs produce small MUAPs that are of the same order of magnitude as the instrumentation noise it may be impossible to discriminate the resulting increments in the CR. This condition would lead to an over-estimation of the AMUAP and thus an under-estimation of N, the MU count.

   B) Two MUs may have similar stimulation thresholds and may therefore consistently fire in unison. Thus, two MUAPs will be mistaken for one and the AMUAP will again be over-

Figure 5 Motor Unit Count Extrapolation



estimated.

C) If the stimulation thresholds of several MUs are fairly close together they may fire in various combinations to produce more CR increments than there are MUs active. This phenomenon has been referred to as alternation (McComas et. al., 1971) and will lead to an under-estimation of the AMUAP and an over-estimation of the MU count. This phenomenon will be discussed in greater detail in Chapter 3.

D) If the motor axon branches proximal to the stimulation site, stimulating the branches individually will result in CR increments which correspond to subsections of MUs (Kadrie et. al., 1976).

2) The small number of MUs contributing to the CR are a representative sample of the entire population of up to several hundred MUs contributing to the MEP.

If, as mentioned earlier, the contributions of very small MUAPs are masked by noise, the sample of MUAPs will be skewed towards larger units. On the other hand, it has been claimed that MUs that are much larger than those sampled near the motor threshold exist and that MU count estimates obtained with this technique are therefore abnormally high (Feasby and Brown, 1974).

3) The way the MUAP amplitudes sum to form the CR amplitude can be linearly extrapolated to how the amplitudes of all the MUAPs sum to form the MEP amplitude.

Because the MUAPs vary in shape and latency their amplitudes do not sum linearly. The technique assumes that a piecewise nonlinear model for their summation will accurately predict the way they actually sum.

1.4 Improvements to the McComas Technique

Since the proposal of the McComas technique other researchers have suggested several enhancements to address its previously outlined shortcomings. Panayiotopoulos et al. (1974) have used a microfilm reader to perform signal averaging visually and extract small MUAPs normally masked by noise. Ballantyne and Hansen (1974) have suggested using the absolute area under the response curve as the feature upon which the extrapolation is performed since MUAP areas should tend to sum more linearly than the MUAP peak amplitudes. In addition, their system provides computer processing and enhanced displays to aid the operator in analyzing the responses. Milner-Brown and Brown (1976) have proposed a method for taking alternation into account based on the theoretical firing probabilities of the MUs and exhaustive stimulation to yield as many combinations of MUs as possible.

Jasechko (1987) took the computer processing proposed by Ballantyne and Hansen a step further by allowing the computer to control the stimulator and make the decisions in classifying the evoked responses. Responses were compared by calculating both the absolute area between response curves and by calculating the Euclidean distance between the vectors of time samples of the responses. In addition the stimulus

amplitude was also placed under computer control, shifting the operator to the role of a supervisor with little active involvement in the progress of the test. Compared to the manual technique, the finer control of the stimulus amplitude thus achieved, combined with the improved resolution in response classification, considerably reduced the chances of missing CR increments. Alternation was not directly addressed but it was felt that the additional CR increments produced by it would occur infrequently and that by requiring a large number of samples for each CR increment these irrepeatable responses would be ignored.

The question of whether or not the responses of the MUs sampled in the CR are representative of those of the entire population of MUs in the muscle was also not directly addressed aside from increasing the number of CR increments collected in order to increase the MUAP sample size used in calculating the AMUAP. The fact that Jasechko's studies showed no significant correlation between MUAP size and order of recruitment indicates that the criticism that there is a preferential early recruitment of either large or small MUs may not be valid.

The extrapolations of the MU counts were performed based on two features: peak amplitude (as done by McComas) and absolute area (as done by Ballantyne and Hansen). (It should be noted that all area calculations in MAMUCS are performed using simple rectangular integration). In addition, the extrapolation was performed in three ways for each of the two features. Firstly, the feature was calculated for each of the CR increments and the MU count extrapolated by performing linear regression of the CR increment feature against the number of MUs thought to

contribute to each increment. Secondly, the extrapolation was performed as done in the McComas technique by linearly extrapolating from the largest CR increment feature. Lastly, the individual MUAPs were extracted by successive subtraction of the ranked CR increments, their individual features calculated, and the features averaged to give an AMUAP feature which was then divided into the MEP feature.

The regression technique was suggested since it uses all the CR increments as opposed to only the largest response, as in the second method. The last method assumes a linear model for the summation of MUAP features as opposed to the piecewise nonlinear model assumed by the first two. Although Jasechko's system performed well under certain conditions, it proved unwieldy and extremely unreliable when tested on a range of subjects. The large number of samples required for each response made the test long and uncomfortable, and in cases where there were large degrees of overlap in MU stimulation thresholds the system would reject virtually every response due to the resulting lack of response repeatability. The system proved useful for the investigation of various aspects of the McComas technique but was impractical for longterm clinical or research use. A more streamlined system with a more powerful response classification algorithm was required. Although some of the basic structure of Jasechko's system has been retained in MAMUCS, there have been radical changes in the approach to the problem of automating the McComas technique. This thesis outlines these changes and describes the performance of the resulting system. The next chapter outlines the hardware used in the implementation of the system along with the

algorithms used in the first version of MAMUCS. Chapter three discusses the problem of alternation and the detection scheme devised to alleviate it. In addition the results of a single subject and a multi-subject study are discussed. Chapter four introduces the problem of latency shifting and the resulting need for the spectral response classification system implemented in MAMUCS II. The results of multi-subject studies that compare MAMUCS against an experienced manual operator are discussed in chapter five. Chapter six concludes by summarizing the work to date and suggests topics for further investigation.

CHAPTER 2

MAMUCS (version 1)

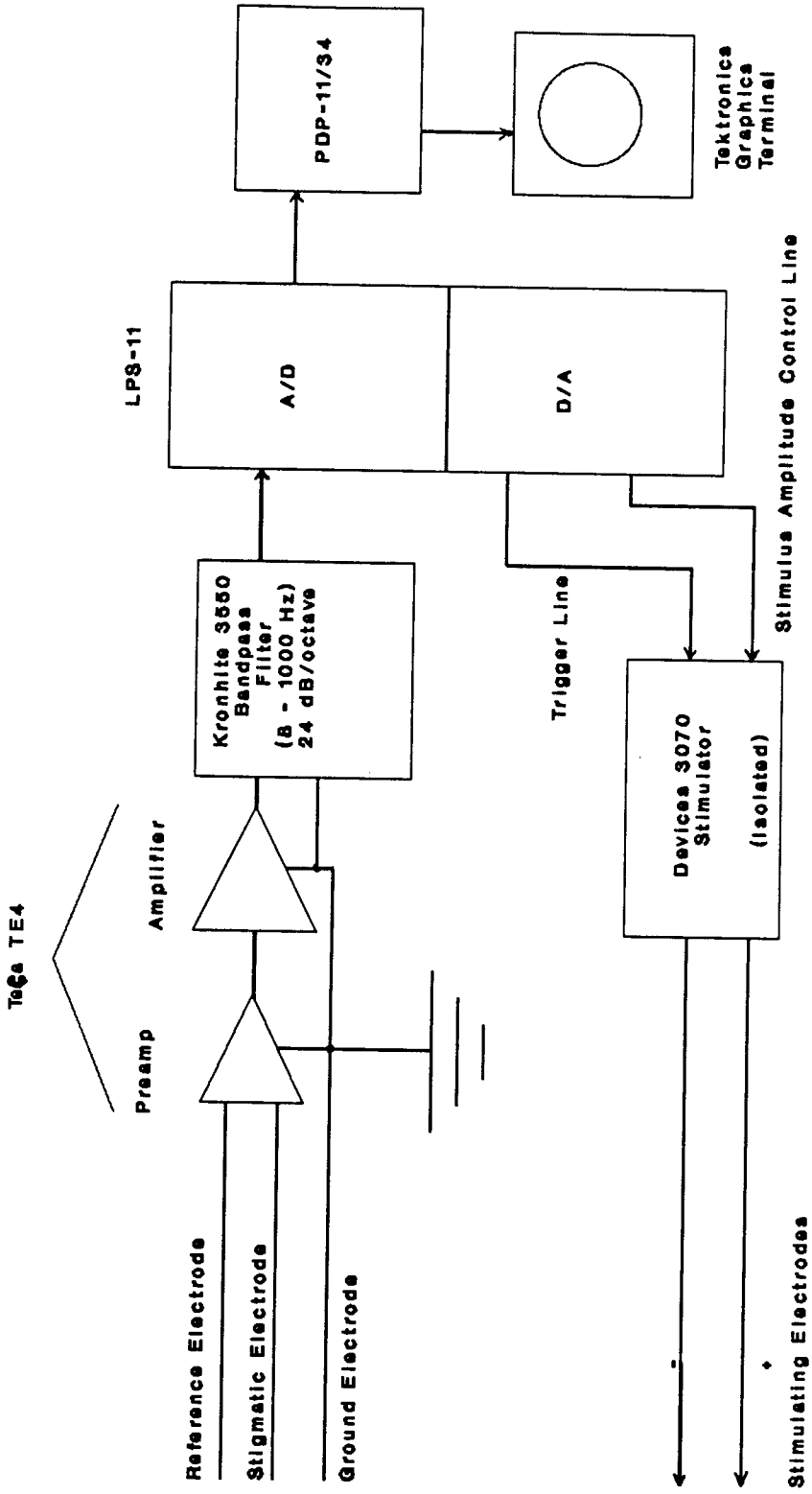
2.0 Hardware

MAMUCS is currently implemented on a PDP-11/34 mini-computer with a cache memory unit, a floating point processor, and an LPS-11 laboratory interface unit which provides analogue I/O for the instrumentation. The 12 bit analogue to digital converter of the LPS-11 provides a resolution of 2.44 mV. A summary of the hardware involved is provided in Figure 6.

Since the removal of operator intervention in the estimation procedure was one of the primary objectives in the design of this system, it was necessary to modify the Devices 3070 constant voltage stimulator so that it could be computer controlled. A detailed description of the modifications performed by Jasechko can be found in his thesis (1987). While one of the LPS-11 outputs is used to supply the trigger pulse for the stimulator, another output is used to control the SPA, bypassing the potentiometer used for manual control. A switch installed on the front panel of the stimulator allows the operator to switch from manual to computer control.

The width of the stimulating pulses was set to 50 μS to minimize stimulus artifact and subject discomfort. Initially, the pulses were applied via the commercially available silver disk surface electrodes used clinically for manual estimation. Experimentation revealed that in many

Figure 6 Hardware Configuration for MAMUCS



cases the application of pressure to the electrodes significantly reduced the stimulation thresholds for the MUs. Since the use of lower SPAs would in turn reduce the stimulus artifact and extraneous muscle stimulation, conical stimulating electrodes were designed to achieve the same effect. These 6 mm diameter stainless steel electrodes were mounted 1.8 cm apart on a plastic plate. The exact placement of these electrodes for a particular muscle varied from subject to subject and was arrived at by searching for the placement that gave the lowest stimulus threshold and minimum activation of adjacent muscles. No effort was made to selectively stimulate any particular muscle within the muscle groups tested.

In an effort to reduce biological noise, stimulus artifact, and crosstalk from neighbouring muscles a bipolar recording electrode configuration was adopted in lieu of the traditional monopolar configuration (reference electrode location is remote with respect to the stigmatic electrode). Silver strip electrodes (6 by .6 cm) were used for the stigmatic, reference, and ground electrodes. The stigmatic and reference electrodes were placed parallel to each other and approximately 1 cm apart over the end plate zone of the muscle and perpendicular to the axis of the muscle belly. The ground electrode was situated approximately equidistant from the stimulating and recording electrodes. All the electrodes were coated with electro-conductive gel prior to application and held in place with surgical tape.

Because the large artifacts produced by the stimulus pulses tended to saturate the preamplifier used by Jasechko, the clinically used Teca TE4 preamplifier/amplifier was substituted. The low pass and high pass

settings were set to 32 kHz and .8 Hz respectively. The signals were then filtered using a Kronhite 3550 bandpass filter with corner frequencies at 8 Hz and 1000 Hz and a roll off of 24 dB per octave. The frequency responses of the analogue filter are plotted in Figures 7 and 8. Software selectable gain settings allow the system to accommodate any analogue instrumentation with similar bandwidth characteristics. Although a tighter passband was desirable it lead to distortion of the stimulus artifact which then corrupted the desired responses. The signal is then fed into the LPS-11 where it is sampled and digitally converted. CR collections were typically performed with the amplifier gain set to 2500, giving the system a resolution of 1.0 uV. For MEP collection the gain was reduced by a factor of 10. For collecting the CR the stimulator resolution was set to 92 mV, which allows an SPA range of 0 - 174 V. The SPA resolution and range were doubled for MEP collection.

2.1 Software

The software is divided into 3 programs: MP, AP and EST. These programs collect the MEP, collect the CR and perform the MU count extrapolation respectively. A data acquisition routine (AQ) common to MP and AP has been retained from Jasechko's system. While most of the parameters used by AQ are software selectible, for the purposes of the studies whose results will be subsequently presented they were held constant at values that were empirically determined to work well on the average (normal) thenar. Minor adjustments were made when testing other muscle groups.

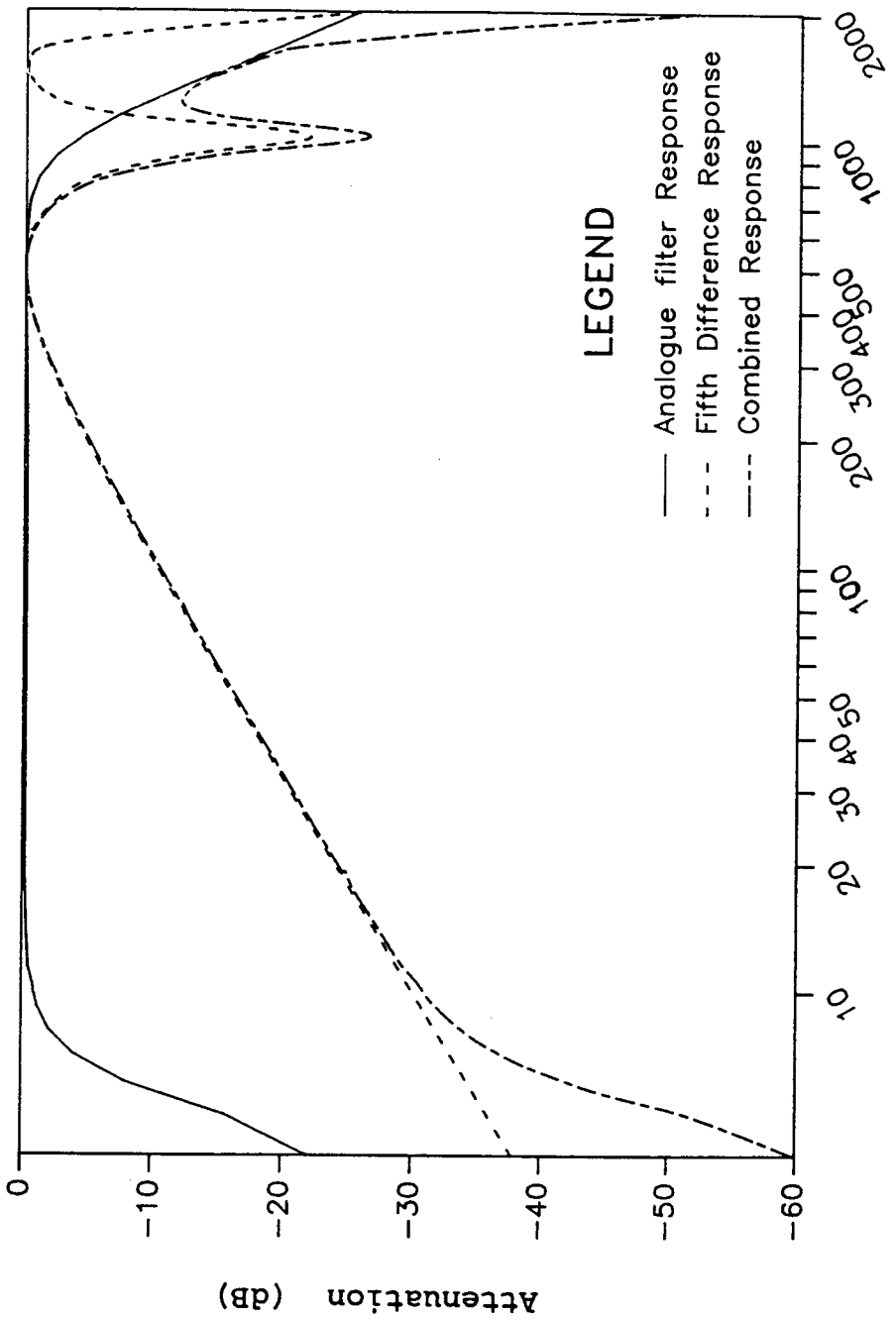


Figure 7 Filter Magnitude Responses

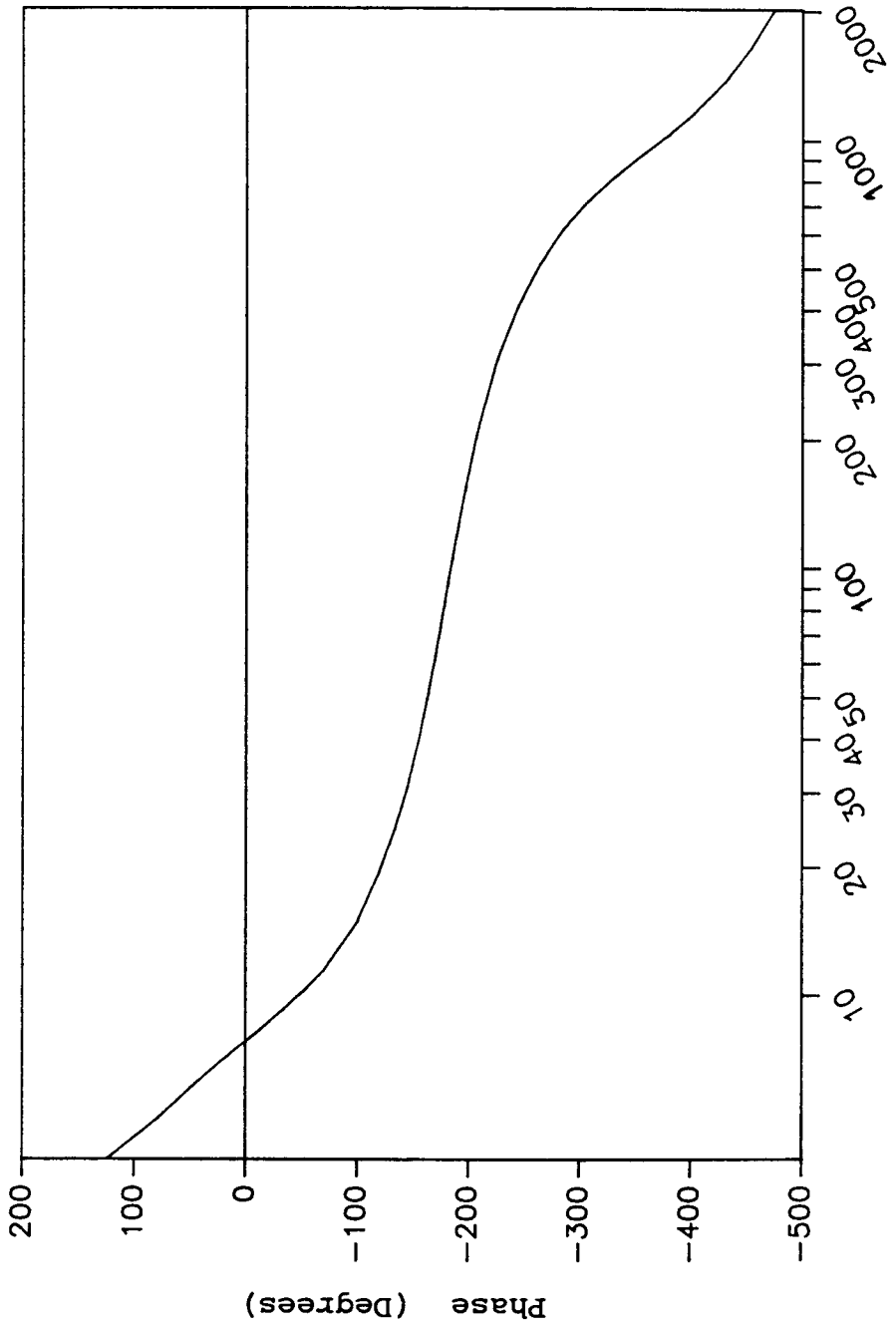
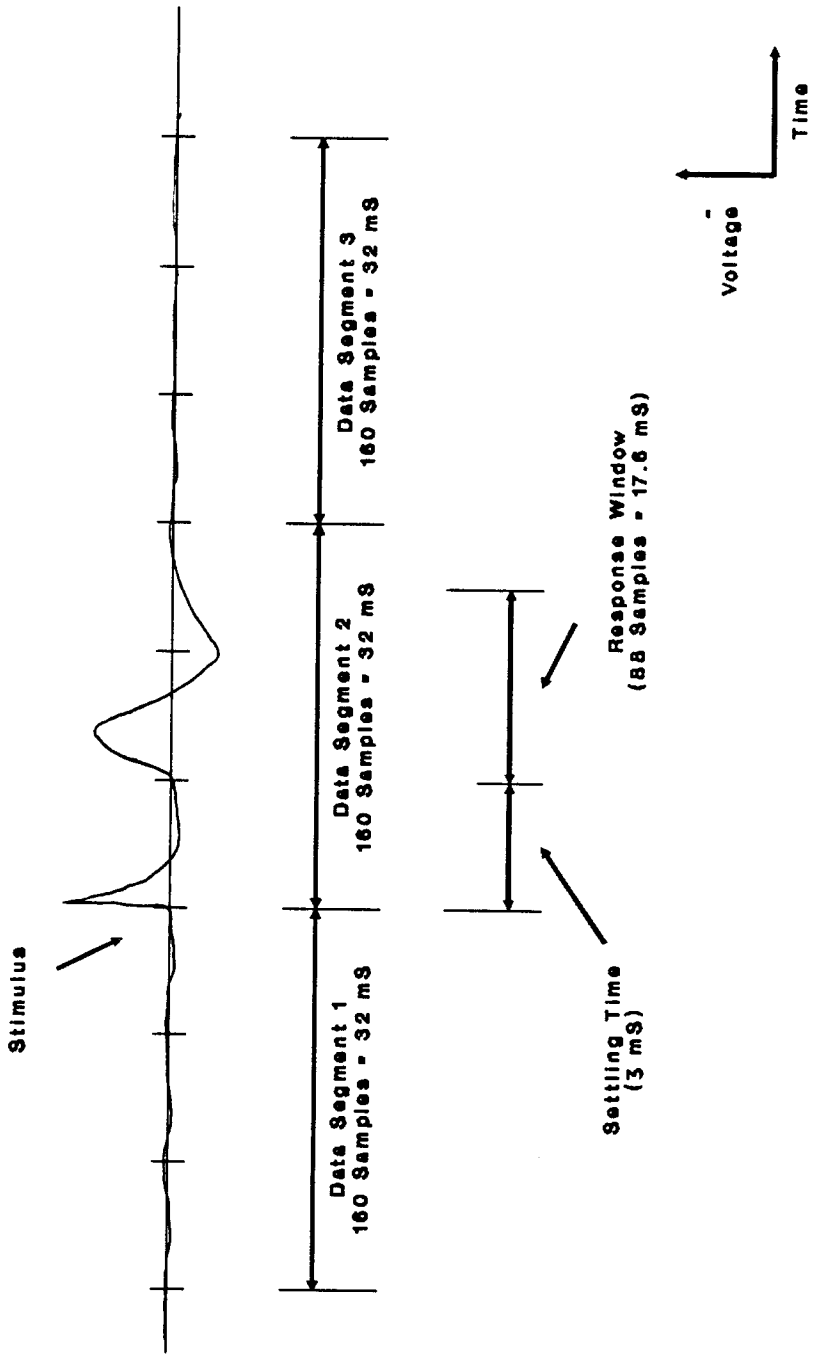


Figure 8 Analogue Filter Phase Response

The parameters passed to AQ by the calling program (MP or AP) determine the stimulation amplitude, the number of samples to be collected in each data segment (L), and the sampling period. AQ returns three data segments each containing L samples along with the mean values for the first and third segments. The first segment is collected before the application of the stimulus, the second immediately following it, and the third after that (Figure 9). The second segment will contain the stimulus artifact and the evoked response while the first and third are used to assess the background noise. If the mean or standard deviation of the samples in these segments exceed empirically determined limits the noise is deemed to be excessive and the signal is discarded by the calling program. The signals are further checked for A/D saturation before being used by the calling program. For the purpose of the studies conducted using MAMUCS I a sampling frequency of 5 kHz was chosen and the data segments were 160 samples (32 mS) in length. The data segment containing the response is further windowed to 88 samples (17.6 mS) following a user selectable settling time (typically 3 mS for the thenar muscle group) which accounts for the variable response latency and removes most of the stimulus artifact.

In addition to sharing the same data acquisition routine, MP and AP use the same data display routine which produces a display on the Tektronics graphics terminal that mimics that of a storage oscilloscope. Provision is made for halting either MP or AP instantaneously by depressing an infrared remote control switch connected to the schmitt trigger input of the LPS-11 which sets the clock control/status register

Figure 9 Signal Epochs



(CSR). Prior to calling AQ (and therefore applying a stimulus pulse) both MP and AP call a routine which polls the CSR to determine whether the remote control button has been pressed and therefore whether program execution is to be suspended.

2.2 Experimental Protocol

Although the protocol used by Jasechko called for acquiring the CR before the MEP in order to give the subject the opportunity of becoming accustomed to the gradually increasing stimulus amplitude, it was subsequently found that acquiring the MEP before the CR offered several advantages:

1) It was often found that if the most uncomfortable part of the test was completed first the subject was more relaxed during the CR acquisition resulting in fewer signal rejections due to excessive noise.

2) A poor recording electrode placement resulting in degraded signals could be quickly recognized by examining the MEP amplitude/area.

3) A poor stimulating electrode placement resulting in an excessively high stimulus threshold for the MEP would be discovered immediately so that the CR acquisition would not have to be repeated following instrumentation adjustment.

Thus the experimental protocol consists of instrumenting the patient, testing the placement with the stimulator under manual control

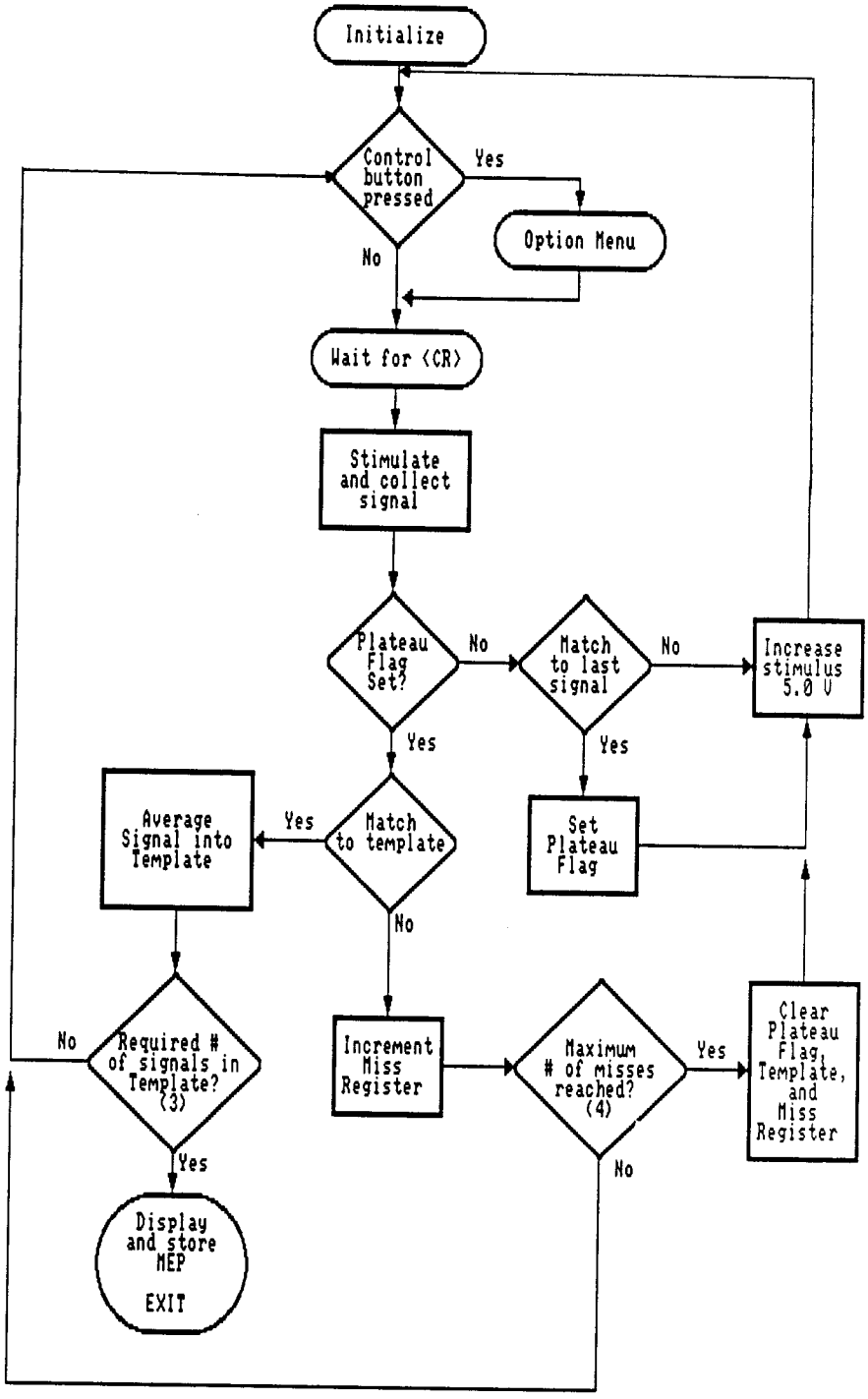
while observing the responses on a storage oscilloscope, making any instrumentation adjustments, and then running MP, AP, and EST.

2.3 MP - The Maximum Evoked Potential Program

The algorithm for MP is summarized in the flowchart in Figure 10. Because of the large stimulus amplitudes used, the program execution is semi-automatic, ie. each response is displayed on the vector graphics terminal and the next stimulation/acquisition/display cycle is executed only after the enter key is pressed. In this way the operator can closely monitor the progress of the collection and the patient is not subjected to a rapid series of intense electric shocks. If the remote control is triggered at any time execution is suspended and an option menu is displayed which allows the operator to alter the stimulus amplitude, gain factor, etc.

The objective of the algorithm is to increase the stimulus amplitude until the response displays no increase in size and therefore contains the summated responses of all the MUs in the muscle. The stimulus increment (2.76 V) is a compromise between being too large which could lead to overshooting the MEP by stimulating adjacent muscles and being too small which results in an excessive number of stimulations and could lead to mistaking a local plateau in the response increments for the MEP. When the area between two successive responses falls below 3% of the total area of the first of these responses, the second response is taken as a sample of the MEP. MP then attempts to collect two more samples of this response at the next voltage level. If four responses which differ

Figure 10 MP Flowchart



by more than 3% are elicited before the three samples are obtained, the response plateau is considered to have been local and the program resumes searching for the MEP. Once three samples of the MEP are collected they are averaged, displayed, and stored on disk. The number of sample points (M), comprising the first 80% of the total MEP area is stored in a file along with the other parameters (noise thresholds, gains, discrimination levels, etc.) used by the succeeding programs.

2.4 AP - The Composite Response Program

Figure 11 shows the normalized amplitude spectra for five responses with greater than average high frequency content. Most of the signal power is concentrated in the low frequencies with all of the spectra at least 20 dB down at 600 Hz.

It was found that the unfiltered area difference and Euclidean distance measures used by Jasechko for response classification did not have sufficient resolution in the mid frequencies where small MUs tended to fall. If the discrimination threshold was set low enough to pick out these units classification errors would result from baseline shifts, changes in stimulus artifact, and high frequency noise.

The response classification protocol used by MAMUCS I performs a temporal comparison of two signals r(j) and s(j), j = 1,M using a filtered Euclidean distance measure (D_T) normalized for the window length M (80% of MEP area). The filtering is in the form of a Kth difference where K is the sampling frequency in kHz:

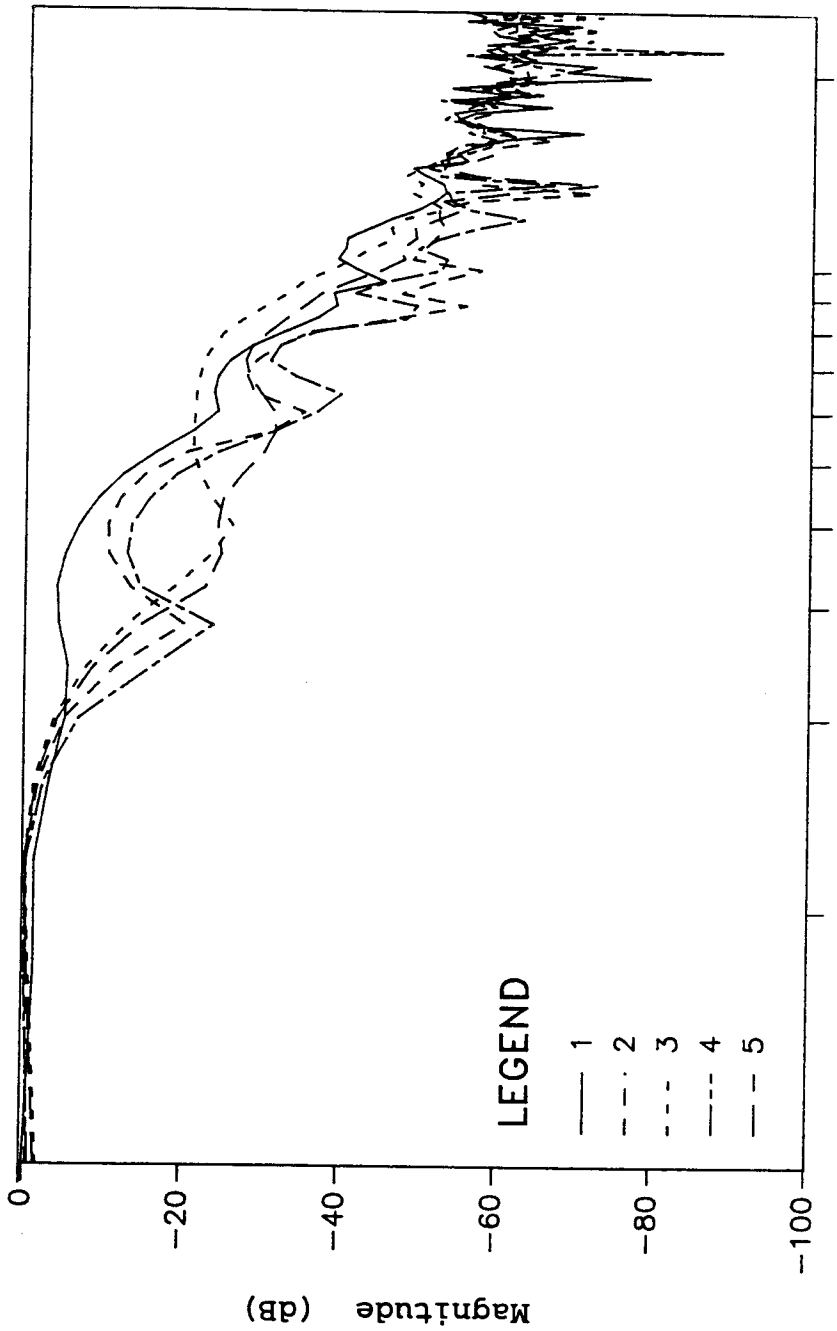


Figure 11 Normalized Template Magnitude Spectra

$$T(j) = r(j) - s(j) \qquad j = 1,M$$

$$D_T = \sqrt{\frac{\sum_{j=K+1}^{M} [T(j) - T(j-K)]^2}{(M - K)}}$$

This computationally efficient linear phase FIR filter generates a cyclic frequency response with nulls at integer multiples of 1 kHz (Principe and Smith, 1986). When this response is cascaded with that of the analogue instrumentation a passband with 3 dB frequencies of approximately 250 and 750 Hz is generated (Figure 7).

The window of length M is used to save computation since the low amplitude tail of the responses is unimportant for classification. Since the value of M will change for each test depending on the MEP shape, the time domain distance measure D_T must be normalized so that a constant discrimination threshold can be set. It was necessary to use this signal processing technique since the computer had insufficient memory for storage of template samples and features separately. A conventional FIR filter would have been too computationally inefficient for this application.

To further reduce unnecessary computation the pattern recognition system pre-screens responses by comparing peak amplitudes and fails any that do not match within 30 μV. The response classification protocol is

summarized in Figure 12.

Responses that match no previously collected responses are stored in temporary save bins while matching responses are averaged into templates. Figure 13 summarizes the overall algorithm for AP. Upon initialization the program attempts to obtain a sample of the baseline as close as possible to the stimulation threshold of the first MU. This is accomplished by commencing the stimulation at a preset level and incrementing the SPA until a greater than baseline response is obtained, ie. the first CR increment. The operator is asked to verify that the preceding response is in fact the baseline at which the collection is to begin. After confirmation the program stimulates, collects, and classifies responses without further operator intervention. The stimulation rate is approximately 2 Hz and the responses are first checked for noise as previously outlined and are then compared to any existing templates. If the distance measure for the closest match falls below the discrimination threshold the response is averaged into that template. If not, the response is compared to the responses that are stored in the save bins by the same criteria. If the response matches a save bin the two signals are assigned to a template. If there are no available templates the two signals are averaged and left in the save bin. If there is no match the response is assigned to a save bin on a first in first out basis.

There are two modes of stimulus control, the execution of which depends upon the current state of the test. Normally, the stimulus tracking mode is implemented which increments the stimulus amplitude by

Figure 12 Response Classification Flowchart

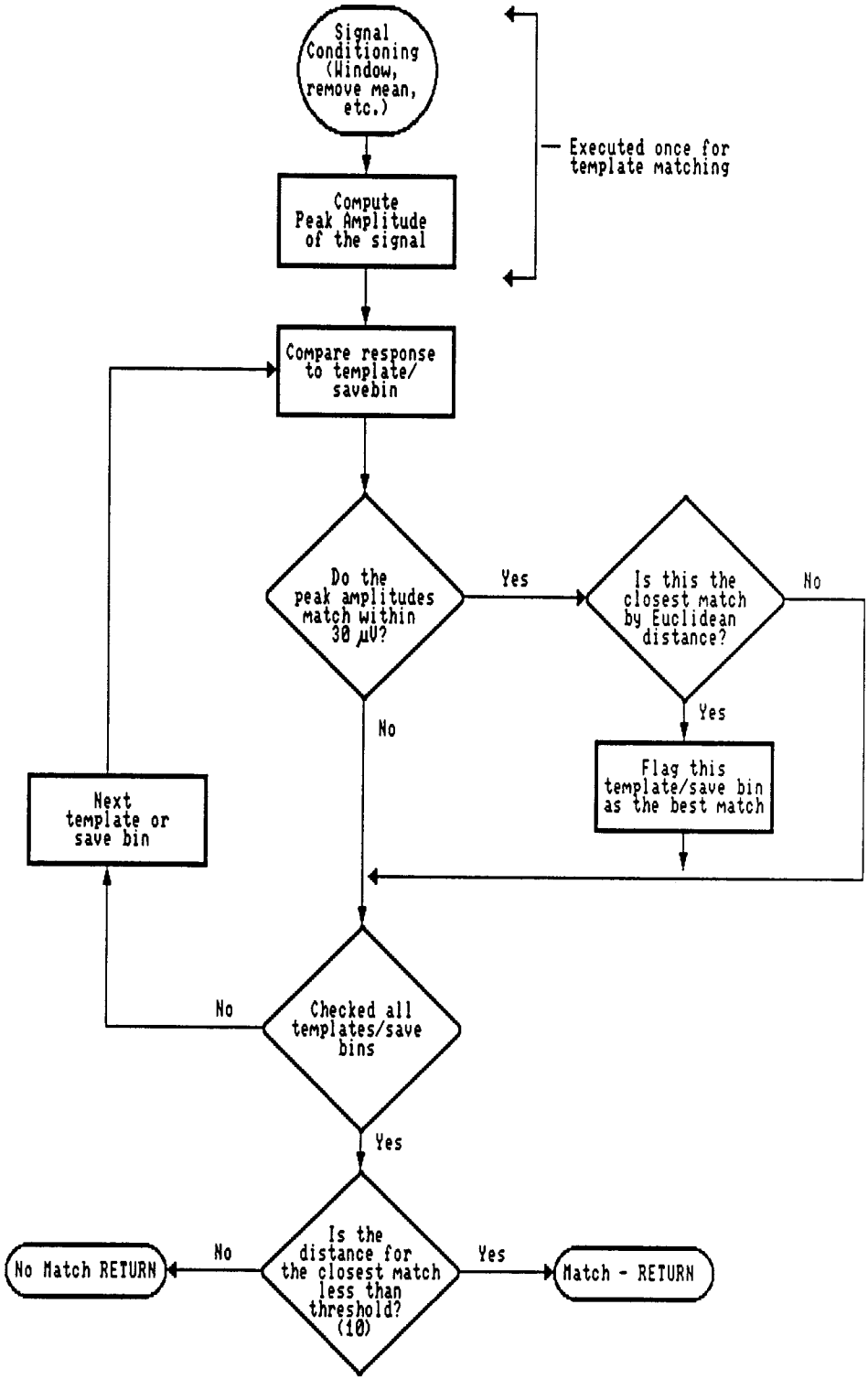
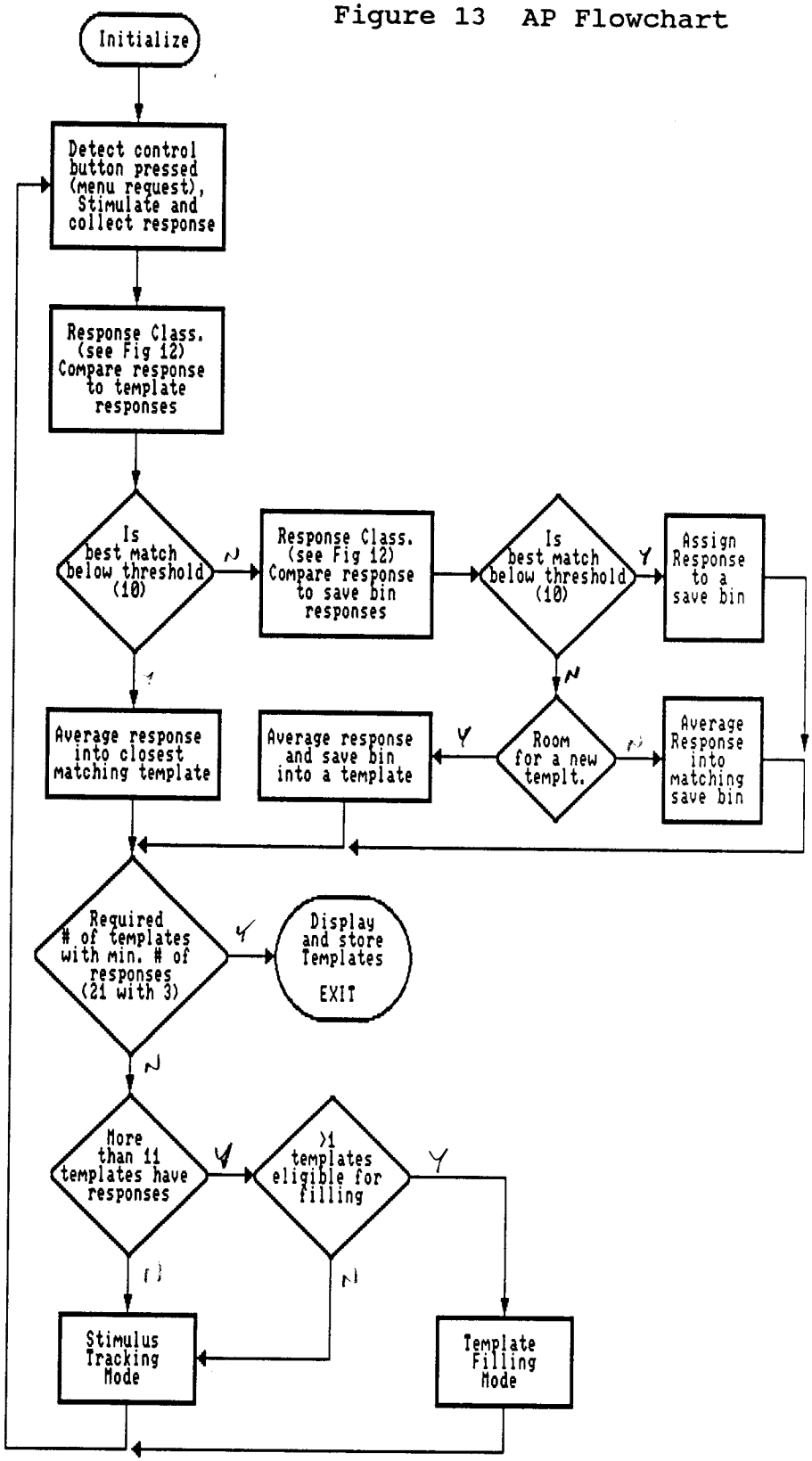


Figure 13 AP Flowchart



one voltage increment (.092 V) if the response matches a template, decrements it by the same amount if it doesn't, and increments it by 10 times this amount if the responses are matching the same template repeatedly. In this way the stimulus is controlled not only to avoid missing intermediate gradations in the CR but also to overshoot local plateaus to speed up the collection. In action this scheme mimics the search pattern used by the manual operator without having to stimulate at every voltage level.

Once half the available templates contain responses the template filling mode is executed. The desired minimum number of responses to be averaged in each template is five while the acceptable minimum is three. The program will attempt to obtain five responses for a template within ten attempted fills. The fill mode is only executed if there are at least two templates eligible for filling. The filling cycle consists of stepping through the existing templates that contain less than five responses and have had less than ten fill attempts, and attempting to obtain another response for that template. A fill attempt consists of stimulating at the mean amplitude for those responses already in the template plus or minus a small random variation. By introducing a random variation in the stimulus amplitude it is hoped that any intermediate responses missed along the way will by elicited. Any new templates created at this time are appended and become part of the filling cycle in their turn.

At each iteration a check is performed to see if the desired number of templates with the acceptable minimum number of responses has

been reached. If the cycle is completed (less than two templates eligible for filling) without this number being reached the stimulus tracking mode resumes. If at any point in the collection there is insufficient memory for a new template that is to be created, a check is made to see if any of the existing templates have had their ten fill attempts and still do not have at least three responses. If so, that template is discarded and the new template is put in its place. Spurious responses that do not repeat are eliminated in this way.

Once the desired number of templates with the minimum number of responses is obtained, collection ceases and the template with the largest peak amplitude is displayed. The operator is then given the option of adjusting the display gain and the templates comprising the CR are displayed (Figure 14), their features are calculated, printed and stored on disk, and the templates are then stored on disk for further processing by EST.

2.5 EST - The MU Count Estimation Program

Because of the search pattern and discarding of spurious templates performed by AP in collecting the CR, the templates will be in no particular order beyond template #1 (baseline). The first task performed by EST must therefore be a ranking of the templates from smallest to largest based on some template feature. A successive subtraction of the templates will then yield the individual MUAPs that have summated to form the CR (Ballantyne and Hansen, 1974). The ranking can be performed based on template area, peak template amplitude, or mean

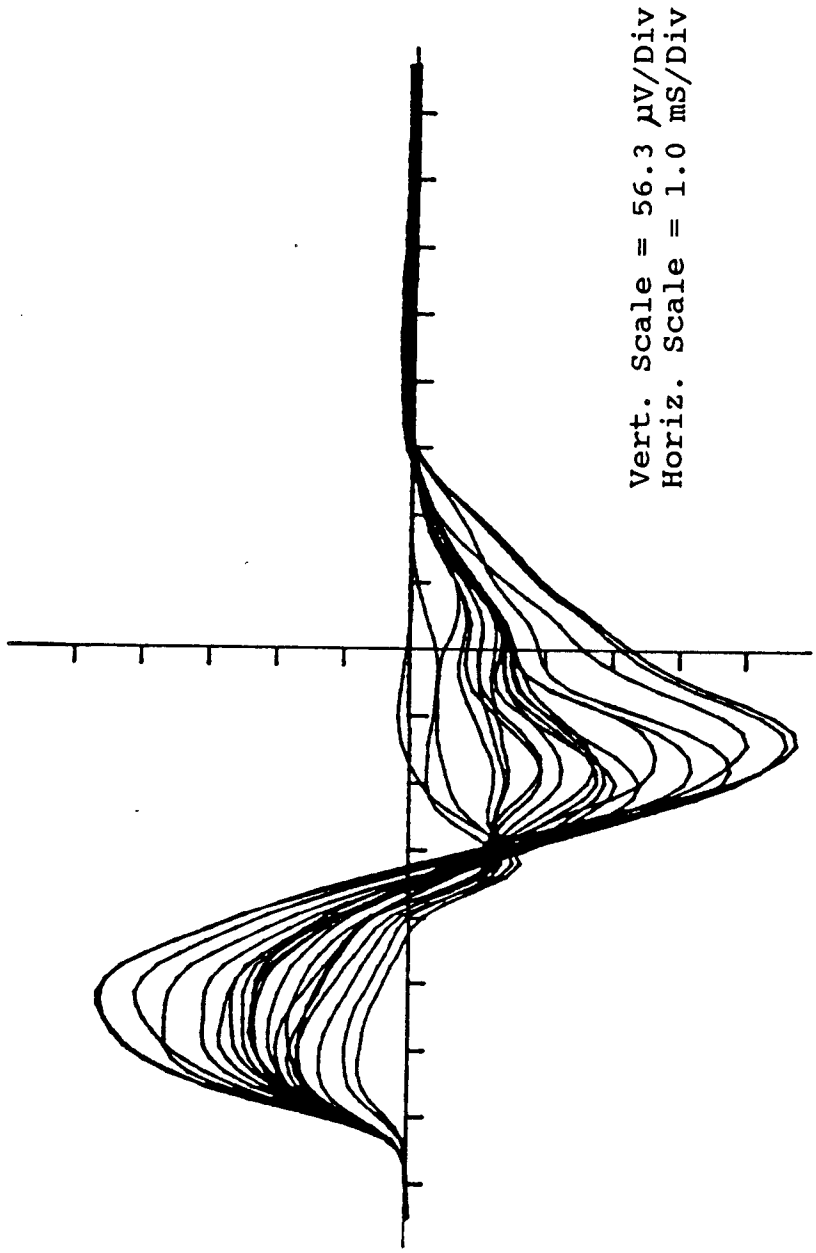


Figure 14 CR obtained for Sample Test 1 (Thenar)

template SPA. Since considerable overlap in stimulus thresholds was common in our studies it was found that the mean SPA was not a suitable feature for template ranking. Figure 15 illustrates the MUAPs extracted from the CR shown in Figure 14 when the templates are ranked in order of increasing area. Since there will be errors in the ranking regardless of the feature selected, the putative MUAPs extracted by the successive subtraction will not always correspond to the true MUAPs contributing to the CR. For this reason they will be referred to as 'extracted' MUAPs throughout this thesis.

The three extrapolation techniques used by Jasechko were each performed based on two features (area and peak amplitude) to yield six estimates as mentioned in Chapter 1. The third technique, which consists of averaging the extracted MUAP features to obtain the AMUAP feature, assumes that the MUAP features sum linearly to form the MEP feature. This assumption is almost always violated and the estimates were typically on the order of 50% lower than those yielded by the other two methods which are based on a piecewise non-linear model. Because of this obvious inaccuracy the third extrapolation technique was abandoned early in the development of MAMUCS. In summary we were left with two methods for performing the extrapolation:

1) Linear regression of the response feature against the number of MUs thought to contribute to it.
2) End point extrapolation - the method used in the manual implementation of the McComas technique. (Figure 5)

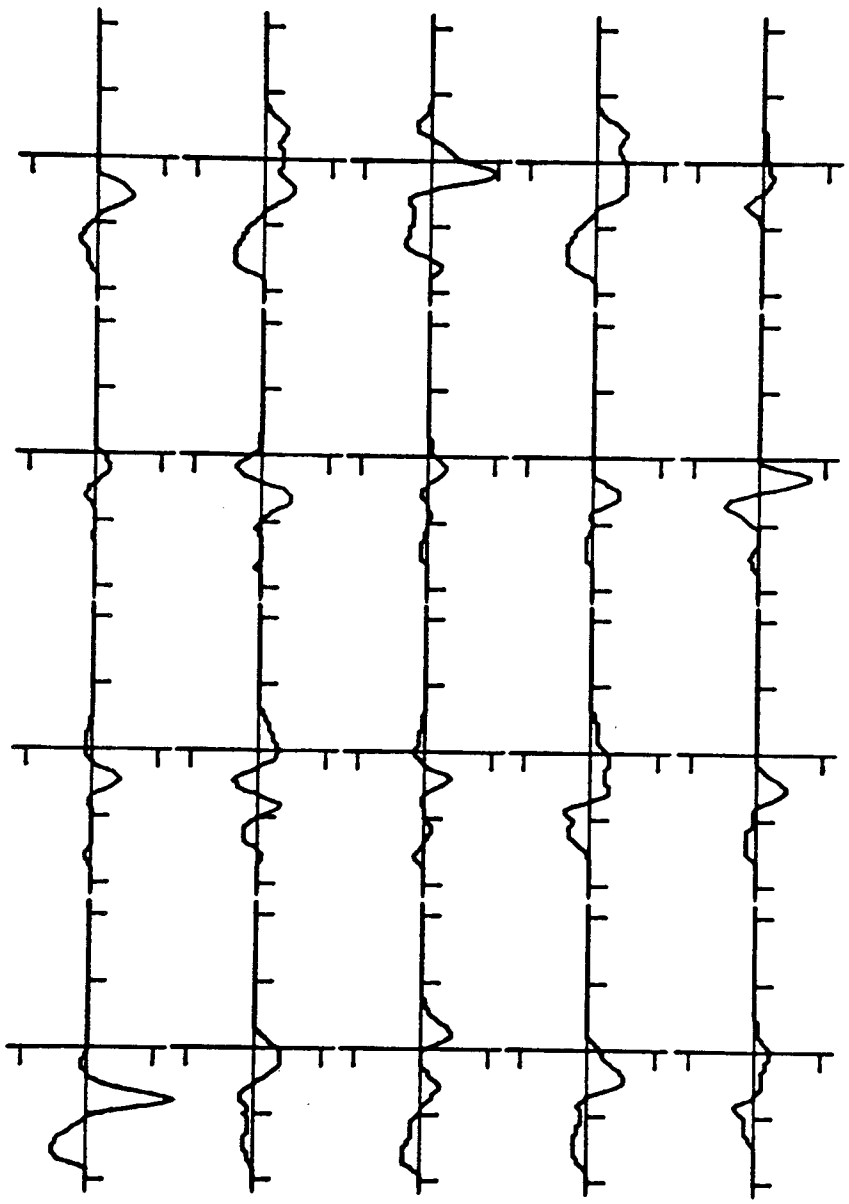


Figure 15 MUAPs Extracted for Sample Test 1

Vert. Scale = 72.7 μV/Div Horiz. Scale = 4.0 mS/Div

Each of these methods can be performed based on the two response features: peak amplitude as per McComas et al., and area under the response curve as per Ballantyne and Hansen, to yield a total of four estimates.

In an attempt to determine whether the small number of MUAPs sampled in the CR are representative of the total population contributing to the MEP with regard to shape, the largest template in the CR (ie. the sum of all the MUAPs sampled in the CR) is divided by the number of MUs contributing to it. This average MUAP is then multiplied by the estimated count and the resulting signal is compared to the MEP. Because of the large difference between the SPA used to acquire the MEP and that used to acquire the CR, latency differences can be introduced and a crude latency correction (shifting an integer number of samples) is therefore performed to yield a minimum area difference between the two signals. This area difference as a percentage of the MEP area is called the extrapolation fit indicator (EFI) and can be used as a figure of merit to indicate how well the shape of the CR matches that of the MEP for a particular estimated count. Figure 16 shows the MEP and the scaled version of the largest template for the test shown in Figures 14 and 15. Since the regression estimates are based on the features of each of the templates in the CR, such a calculation would be inappropriate for them. The only figure of merit available for the regression estimates is the coefficient of determination (R^2) which indicates the linearity of the CR feature incrementation.

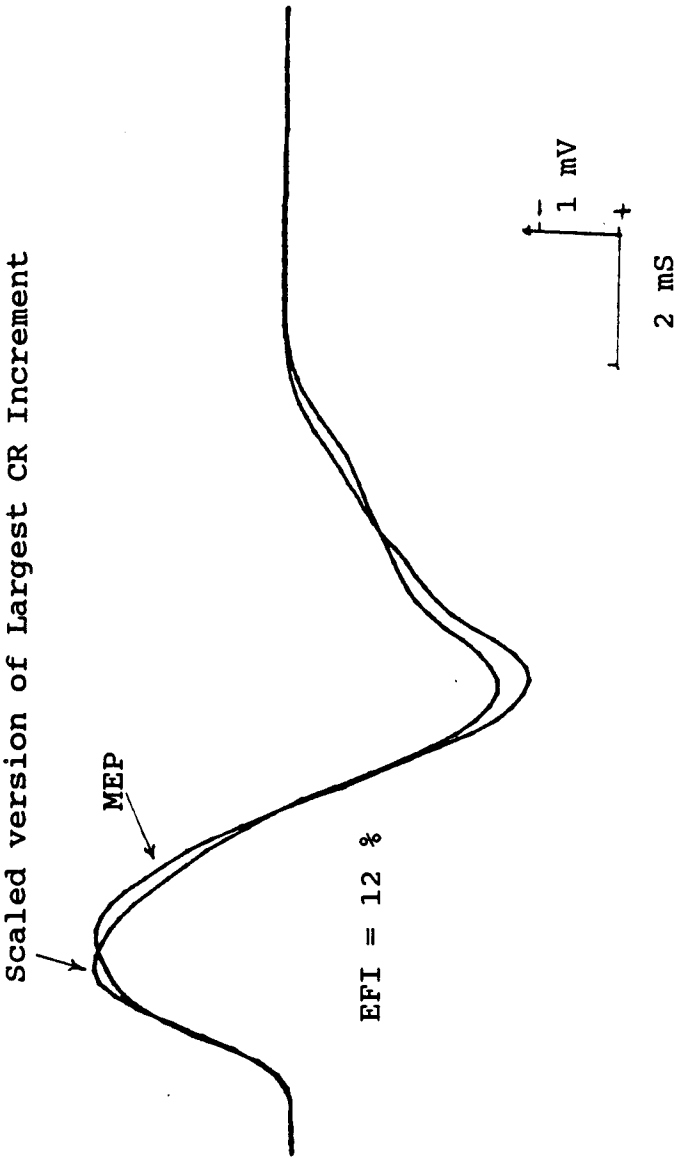


Figure 16 MEP and Extrapolation Fit for Sample Test 1

A logical extension of the EFI calculation was to develop an algorithm that finds the estimate which yields the minimum EFI. The algorithm consists of calculating the minimum area difference for integer multiples of 100 units between 0 and 3000. The estimate G with the smallest difference (ie. the best fit) now becomes the centre point for the search. The same calculation is performed for integer multiples of 10 units between G $\pm$ 100 units. The estimate G' with the best fit now becomes the centre point for the search at one unit increments between G' $\pm$ 10 units. The estimate G'' yielded by this search should have the best fit in the global sense. This estimate can be thought of as being based on response shape as opposed to area or peak amplitude. Thus the EST protocol consists of ranking the templates, extracting and displaying the MUAPs for operator examination, and performing a total of 5 MU count extrapolations by the following methods:

Method #1 - End point Extrapolation based on response area.

#2 - End point Extrapolation based on peak amplitude.

#3 - Minimum EFI.

#4 - Linear regression based on response area.

#5 - Linear regression based on peak amplitude.

All of these techniques assume that each increment in the CR corresponds to the contribution of one additional MU that has been recruited. Because of the large number of stimulations used and the active search for intermediate gradations performed by AP, the probability

of a gradation being missed, and therefore the contribution of two or more MUs being mistaken for one, is low. It is much more likely however that the number of MUs sampled by the CR is smaller than the number of gradations. The phenomenon responsible for this potential discrepancy is referred to as alternation (McComas et al., 1971) and is discussed in detail in the next chapter.

CHAPTER 3

ALTERNATION AND PRELIMINARY TEST RESULTS

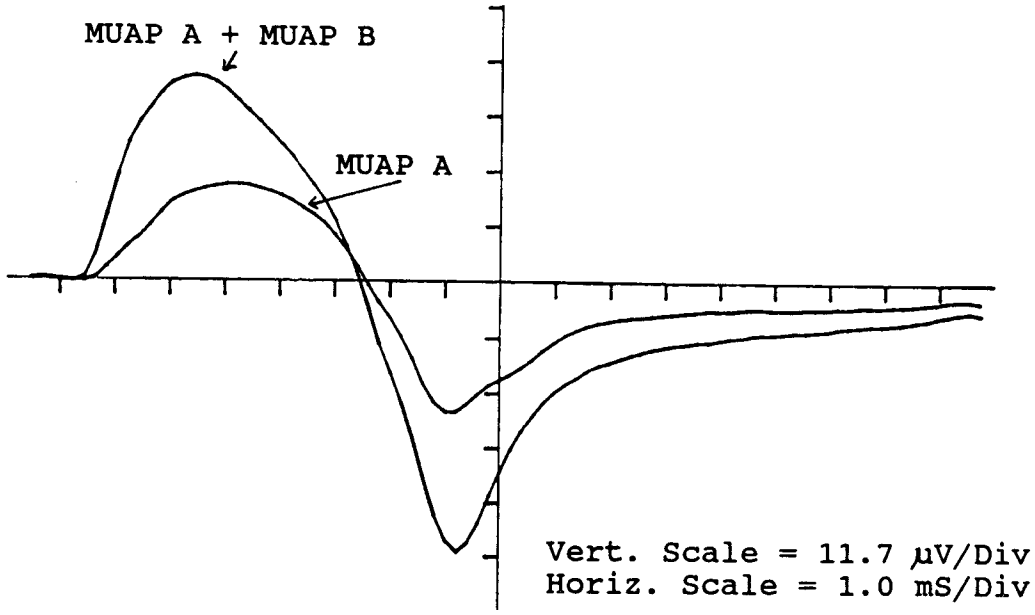
3.0 Introduction

As mentioned in the preceding chapter, it is unlikely that the responses of two MUs firing in unison will be mistaken for a single MUAP. Consequently it is reasonably certain that the first response increment in the CR above the baseline will represent the response of a single MU. It is however, uncertain as to how many motor units have contributed to any of the other increments. As illustrated in Figures 17a and 17b, two MUs, A and B, can produce up to 3 distinct responses (17b) instead of the two assumed by the McComas technique (17a). A group of MUs firing in diverse combinations to produce more CR increments than there are MUs is called alternation (McComas et. al.,1971).

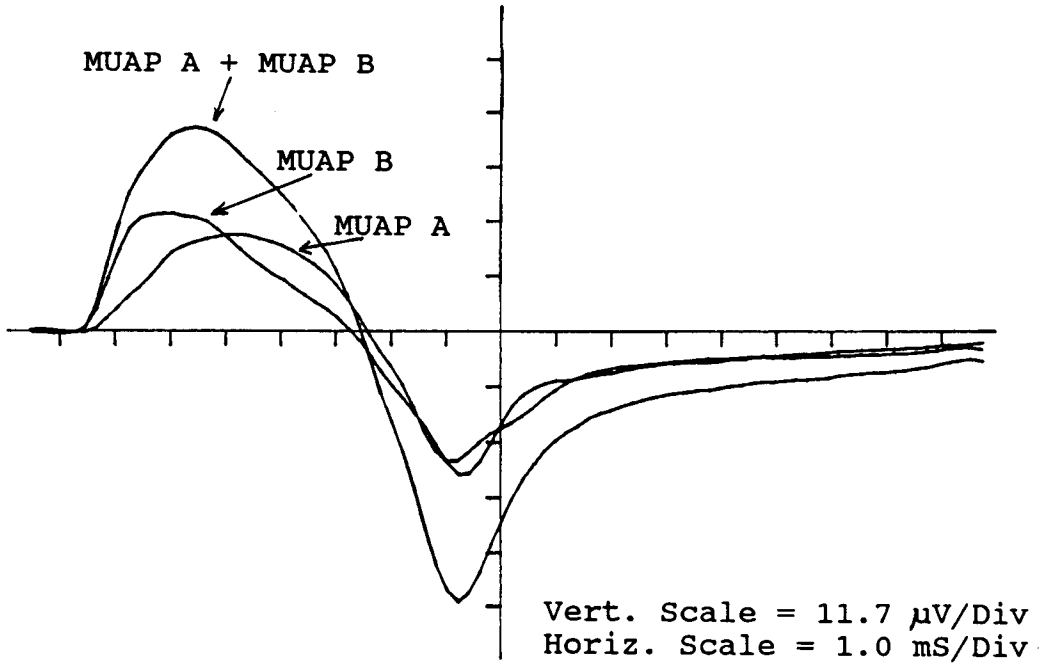
Unfortunately, excitation thresholds for MUs vary over time and one can therefore only speak of the probability that a MU will fire at any given SPA. Over a small stimulus voltage range the probability that a MU will fire can vary from 0% to 100%. Although the precise shape of the probability curve is of limited importance in this discussion, the degree of overlap of the curves for different MUs sampled in the CR will determine the amount of alternation encountered. In the worst case, if the firing probability curves for K motor units overlap completely,

Figure 17 Possible CR Increments Generated by Two MUs

a) Without Alternation



b) With Alternation



2^K-1 CR gradations are possible if all the MUs fire in every possible combination (Brown and Milner-Brown, 1976). While this extreme case is unlikely to occur, a modest degree of overlap producing a few alternations can significantly reduce the estimated AMUAP extrapolation feature and thus lead to an over-estimation of the MU count. In other words, alternation leads to over-counting the number of MUs contributing to the CR and therefore under-estimating the slope of the line used to extrapolate the count.

3.1 The Alternation Detection Algorithm

An examination of the example of alternation in Figure 17b shows that if the alternated responses are ranked and a successive subtraction performed, the extracted signals will be:

1) MUAP A

2) MUAP B - MUAP A

3) MUAP A

If these signals are displayed as the extracted MUAPs, MUAP A will appear twice.

In the course of the development of MAMUCS many examples were found where several MUAPs extracted through the successive subtraction of CR increments were identical in shape. Sample test 2, whose extracted MUAPs are shown in Figure 18, illustrates such an example. Note the similarity of MUAPs A and B which are compared in Figure 19a. Since it

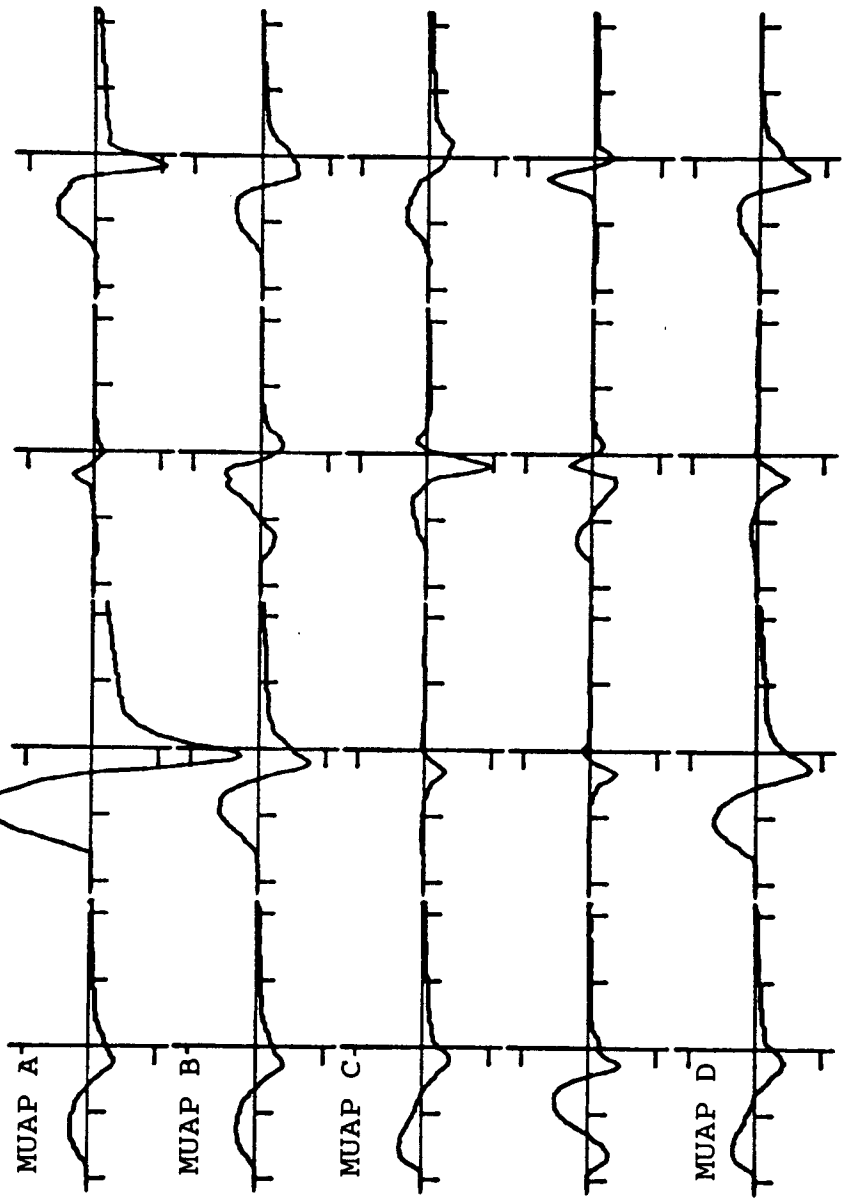
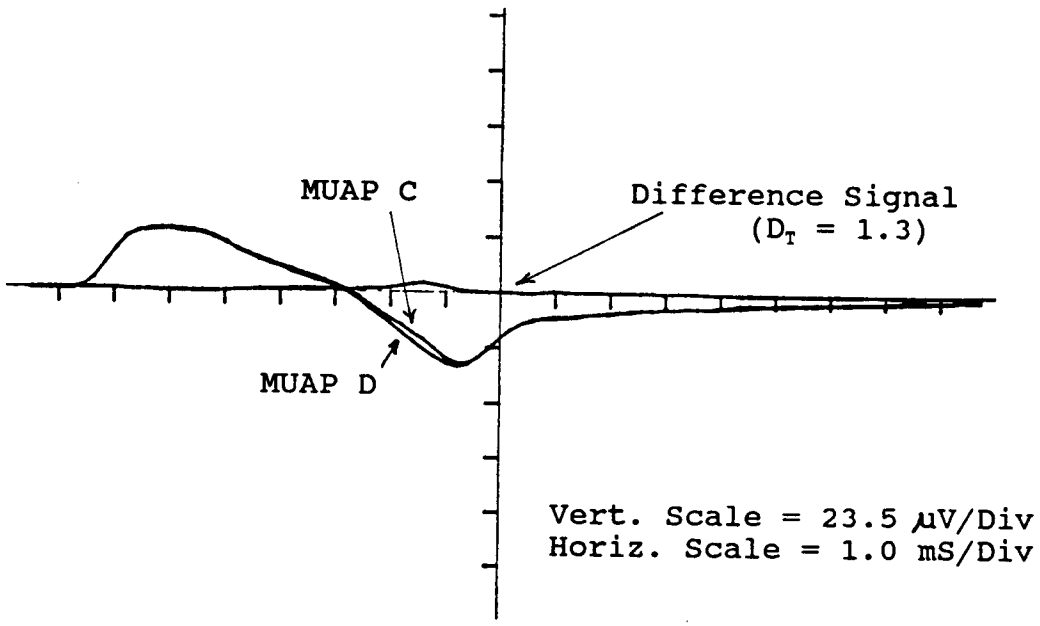


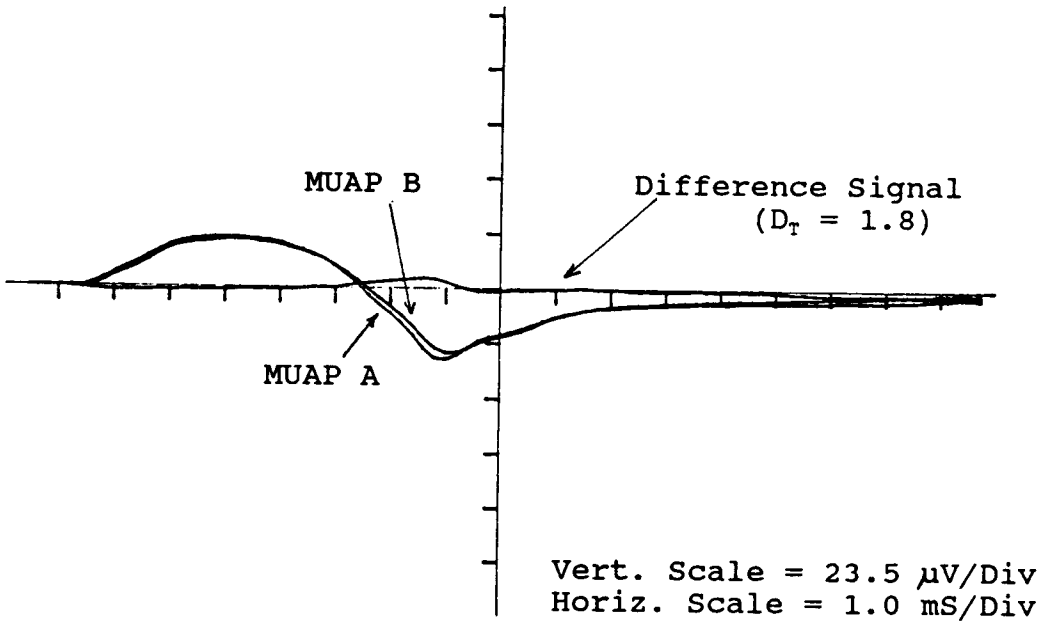
Figure 18 MUAPs Extracted for Sample Test 2

Figure 19 Comparison of Extracted MUAPs (Sample Test 2)

a) Example of Duplicate MUAPs (Alternation)



b) Example of Duplicate MUAPs (Not Alternation)



is safe to assume that almost all MUAPs will be unique in shape this observation should indicate the presence of alternation.

Not all cases of alternation will be of the form constructed for Figure 17 and a straightforward serial subtraction of the ranked CR increments will not reveal them as duplicated MUAPs. For example, if 3 MUAPs A, B, and C are recruited in an alternating fashion to form the following ranked increments:

Increment #1 = Baseline (No units)
#2 = A
#3 = B
#4 = A + C
#5 = A + B
#6 = A + B + C

The MUAPs extracted by serial subtraction will be:

MUAP #1 = A
#2 = B - A
#3 = A + C - B
#4 = B - C
#5 = C

Although alternation has occurred, serial subtraction of the ranked CR increments has not revealed it in the form of duplicate MUAPs. A more sophisticated algorithm that subtracts each response from all the successive responses is required. Such an algorithm is summarized in Figure 20. The ranked response templates $T(i)$, $i = 1,N$ are analysed and if alternation is detected the appropriate templates causing the reduncancy are deleted to yield a revised set of extracted MUAPs $M(j)$, $j = 1,L$. Obviously, there is a limit to how complicated a case of alternation this algorithm will decipher. In the worst case where every

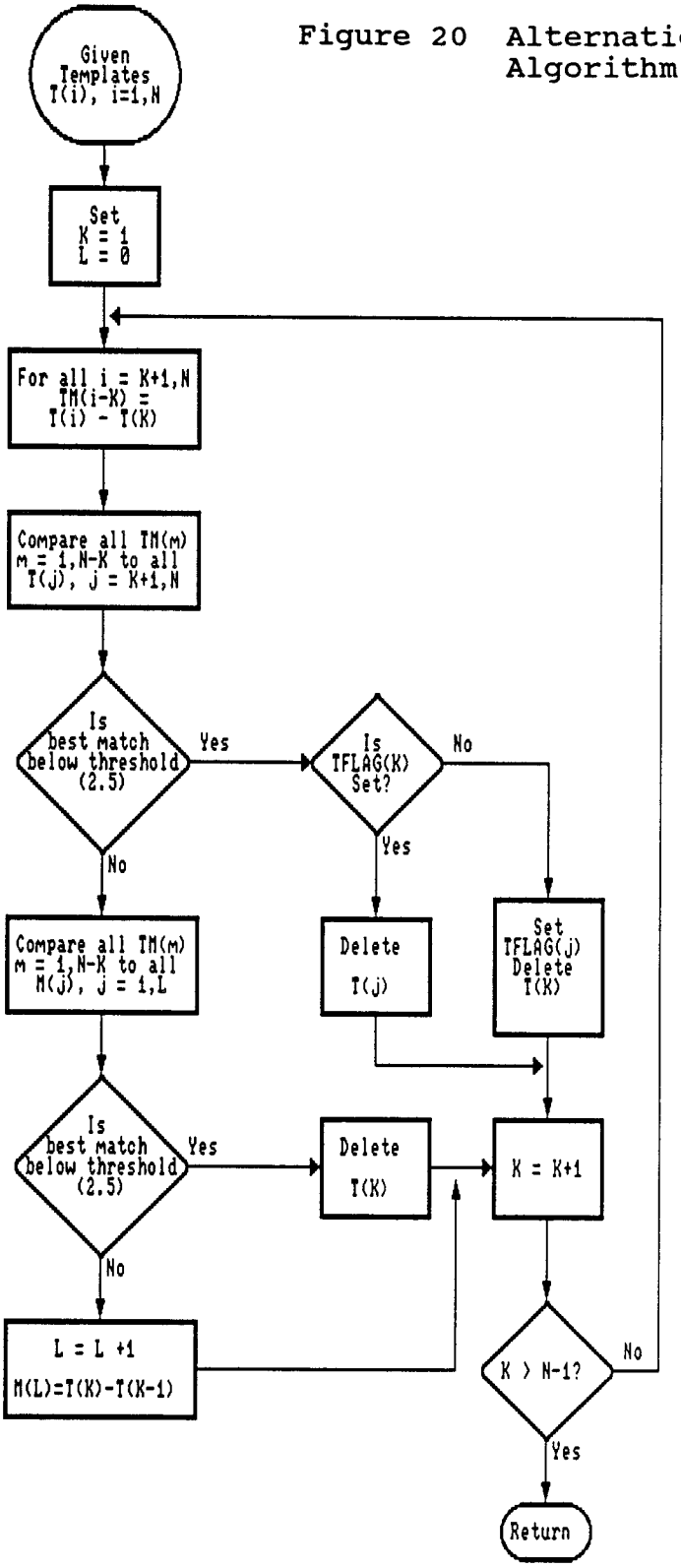


Figure 20 Alternation Detection Algorithm Flowchart

response in the CR is a single MU firing in isolation, there is no redundancy to detect (no sequence of subtractions will generate duplicate MUAPs) and the problem is insoluble by any means.

By creating increasingly complex examples of alternation such as the one illustrated above, it is simple to verify that the algorithm will detect any case of simple alternation. This algorithm is implemented in the program EST after the template ranking in order to correct the number of MUs contributing to the CR before the MU count extrapolation is performed. To verify that the program was faithfully implementing the algorithm a test suite was created to simulate the various cases of alternation which were expected. A typical MUAP extracted from an earlier test was scaled in duration and amplitude and shifted in time to create a known set of unique signal waveforms that could be visually identified for verification. These simulated MUAPs were then summated in various combinations to form CRs. These CRs were then decomposed using the alternation detection algorithm. Although the extracted MUAPs were not always of the correct shape due to errors in the template ranking (non-linear summation of the ranking feature), as long as the degree of alternation was confined to what was mathematically soluble the algorithm succeeded in detecting the correct number of alternations introduced in the simulation.

The alternation detection scheme compares extracted signals using the same Euclidean distance measure as was used to classify responses in AP (the first pass of comparing peak amplitudes was omitted). Obviously, two successively extracted MUAPs that match in shape cannot be a case of

alternation and are not flagged as such by the algorithm. The virtual absence of such cases observed in the course of testing this system indicates a relative uniqueness of MUAP shapes for this recording electrode configuration. One of the rare cases of this phenomenon that was observed is illustrated in Figure 18. Note the similarity between MUAPs C and D which are compared in Figure 19b. This example was used in conjunction with numerous other examples of visually identified alternation to set the discrimination threshold. Thus, if two signals compared during the execution of the alternation detection scheme have a difference signal whose distance measure is less than 2.5, they are considered to represent a case of alternation. For reference, the mean distance measure for twenty baseline responses in a typical test was measured to be 1.2.

With the implementation of this algorithm the first version of the automated system, MAMUCS I, was complete. Although hundreds of tests had been performed on a variety of subjects during development, the values of the various test parameters were now held fixed for controlled serial testing.

3.2 Test Results - Study 1

In order to assess the reliability of MAMUCS I a serial study was conducted on a subject's right thenar muscle group. The study consisted of 20 tests performed in 10 sessions over a span of two months. The number of tests per session varied between 1 and 4. The stigmatic recording electrode was placed over the thenar eminence perpendicular to

the first metacarpal bone, crossing the latter at the junction of its proximal and middle thirds. The reference electrode was placed about 1 cm distally, parallel to the stigmatic electrode. The ground electrode was positioned over the dorsum of the wrist. The stimulating electrodes were placed over the median nerve at the wrist (see section 2.0 and Figure 6).

The results for each session were averaged and are summarized in Table 1a (alternation detection disabled) and 1b (alternation detection enabled). The number of alternations per test varied from 0 to 5 with a mean of 1.8 and a standard deviation of 1.5. Obviously the MEP statistics and EFIs will not be affected whether or not alternations are detected.

To quantify the variability of the estimates within a study we normalize the standard deviation to obtain the coefficient of variation or CV:

$$CV = \frac{\text{Standard deviation of estimates}}{\text{Mean of estimates}} \times 100\%$$

The extrapolation technique which yielded the estimates with the lowest CV was method 1 with alternation detection enabled. The mean estimated MU count was 197 with a CV of 8.4%. Without alternation detection these figures would have been 219 and 12% respectively. It is interesting to note that the MEP areas used in the generation of these estimates were almost twice as variable as the estimates.

The mean EFI for method 1 estimates was much larger than those for the estimates obtained using methods 2 and 3. Since matching peak

Table 1a Summary of Results of Study 1 (Alternation detection disabled)

Session Number	Extrapolation Feature: MEP Area (mVmS)	MEP Amplitude (μV)	AMUAP Area (mVmS)	AMUAP Amplitude (μV)	Estimated count by method #: 1	2	3	4	5
1	63.5	10500	0.339	64.5	187	163	167	144	125
2	65.9	10400	0.343	57.0	192	182	181	187	178
3	66.9	10600	0.259	52.0	258	203	208	225	177
4	41.8	7150	0.196	44.7	212	159	153	210	160
5	45.8	8580	0.201	41.2	229	208	204	228	205
6	44.4	8500	0.171	36.8	259	230	228	246	221
7	52.5	8810	0.261	53.3	203	167	160	189	157
8	56.5	9010	0.268	52.4	211	171	167	183	147
9	54.7	8660	0.282	54.6	202	165	164	201	164
10	47.2	7620	0.203	37.6	233	202	188	231	200
Mean	53.9	8990	0.252	49.4	219	185	182	204	173
St.Dev.	8.74	1120	0.0595	9.00	25.4	24.2	24.5	30.0	29.0
CV	16%	13%	24%	18%	12%	13%	14%	15%	17%
Mean EFI					.28	.22	.22	n/a	n/a
Mean R^2					n/a	n/a	n/a	.92	.91

Table 1b Summary of Results of Study 1 (Alternation detection enabled)

Session Number	Extrapolation Feature: MEP Area (mVmS)	MEP Amplitude (μV)	AMUAP Area (mVmS)	AMUAP Amplitude (μV)	Estimated count by method #: 1	2	3	4	5
1	63.5	10500	0.339	64.5	187	163	167	144	125
2	65.9	10400	0.343	57.0	192	182	181	187	178
3	66.9	10600	0.324	65.0	206	162	166	186	147
4	41.8	7150	0.231	52.6	180	135	130	173	132
5	45.8	8580	0.206	42.2	223	203	198	218	191
6	44.4	8500	0.196	42.1	227	202	199	213	193
7	52.5	8810	0.278	56.9	194	159	151	181	150
8	56.5	9010	0.283	55.3	200	163	157	176	142
9	54.7	8660	0.319	61.7	178	145	144	176	142
10	47.2	7620	0.238	44.3	198	172	160	193	166
Mean	53.9	8990	0.276	54.2	197	167	164	185	157
St.Dev.	8.74	1120	.0553	8.73	16.5	21.4	21.8	20.9	24.0
CV	16%	13%	20%	16%	8.4%	13%	13%	11%	15%
Mean EFI					.28	.22	.22	n/a	n/a
Mean R^2					n/a	n/a	n/a	.92	.92

amplitudes of the signals will also match shapes to a certain extent, it is to be expected that method 2 will give estimates with lower EFIs than method 1, while method 3, by definition, gives the estimate with the absolute lowest EFI. Unfortunately, method 3 also gave the estimates with the largest mean CV of the first three extrapolation techniques. The reason for the lower repeatability of the linear regression estimates (methods 4 and 5) is unclear. Since they are based on each increment of the CR as opposed to the largest one, even if the same MUs were recruited in each test, changes in their order of recruitment between tests would alter the regression line fitted to the increments and therefore the estimated MU count obtained.

Figures 21 and 22 depict the areas and peak amplitudes of the CR increments for each of the twenty CRs in this study. Because alternation detection alters the number of MUAPs making up a particular CR, the curves are normalized along both axis. The vertical axis represents the CR increment feature as a fraction of the largest CR increment feature. This value is plotted against the number of MUAPs summing to form the CR increment as a percentage of the number of MUAPs in the largest CR increment. There is no consistent trend in the shape of the curves despite the fact that the ranking function ensures that each additional MUAP causes an increase in the response feature. The best guess possible is a first order fit which will vary considerably depending on the order in which the MUAPs sum. Although it was suggested by Jasechko (1987) that a higher order fit be used, the extrapolation's dependence on the order of MUAP recruitment would probably lead to even higher variabilities.

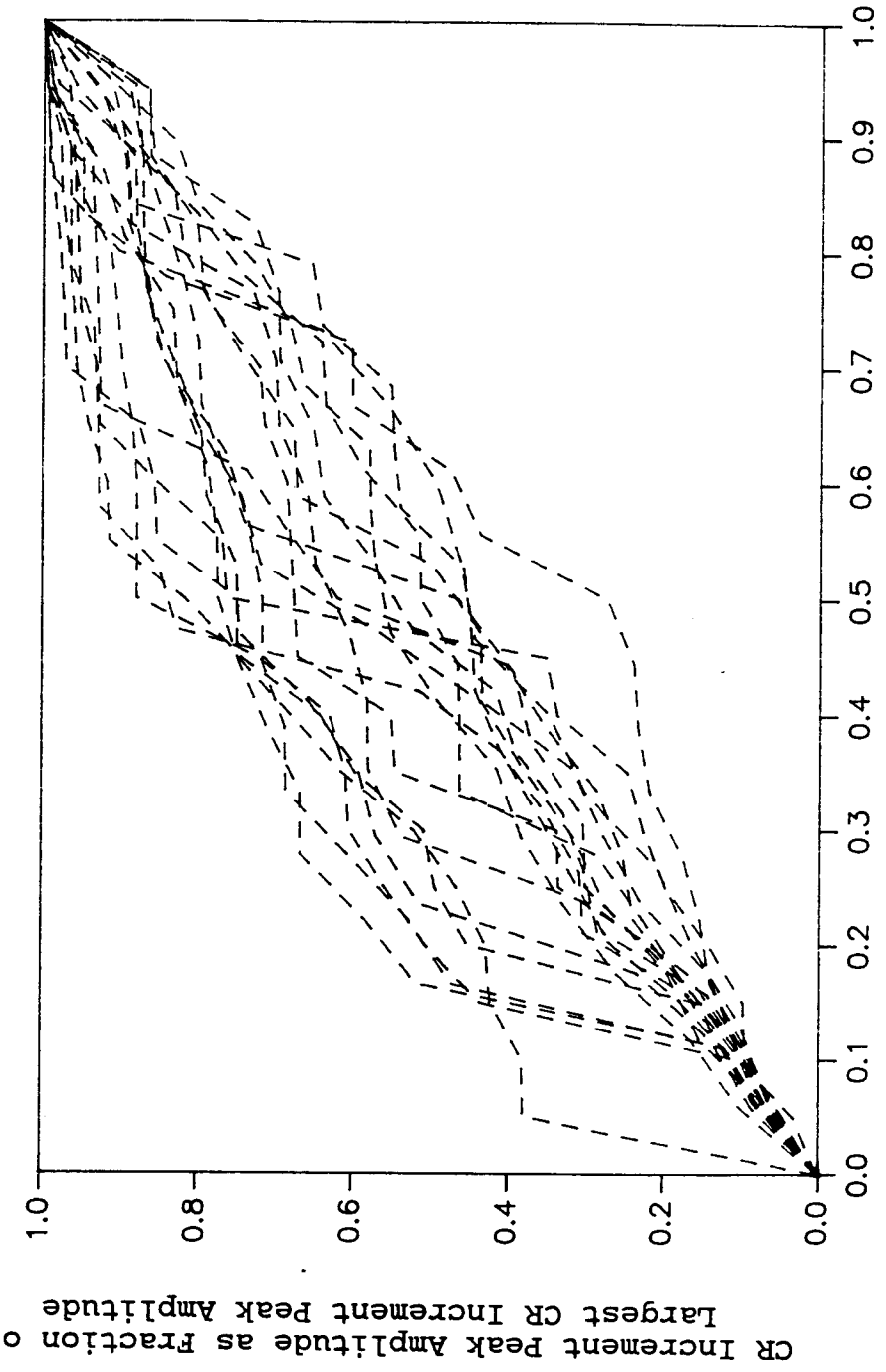


Figure 21 CR Increment Areas (Study 1)

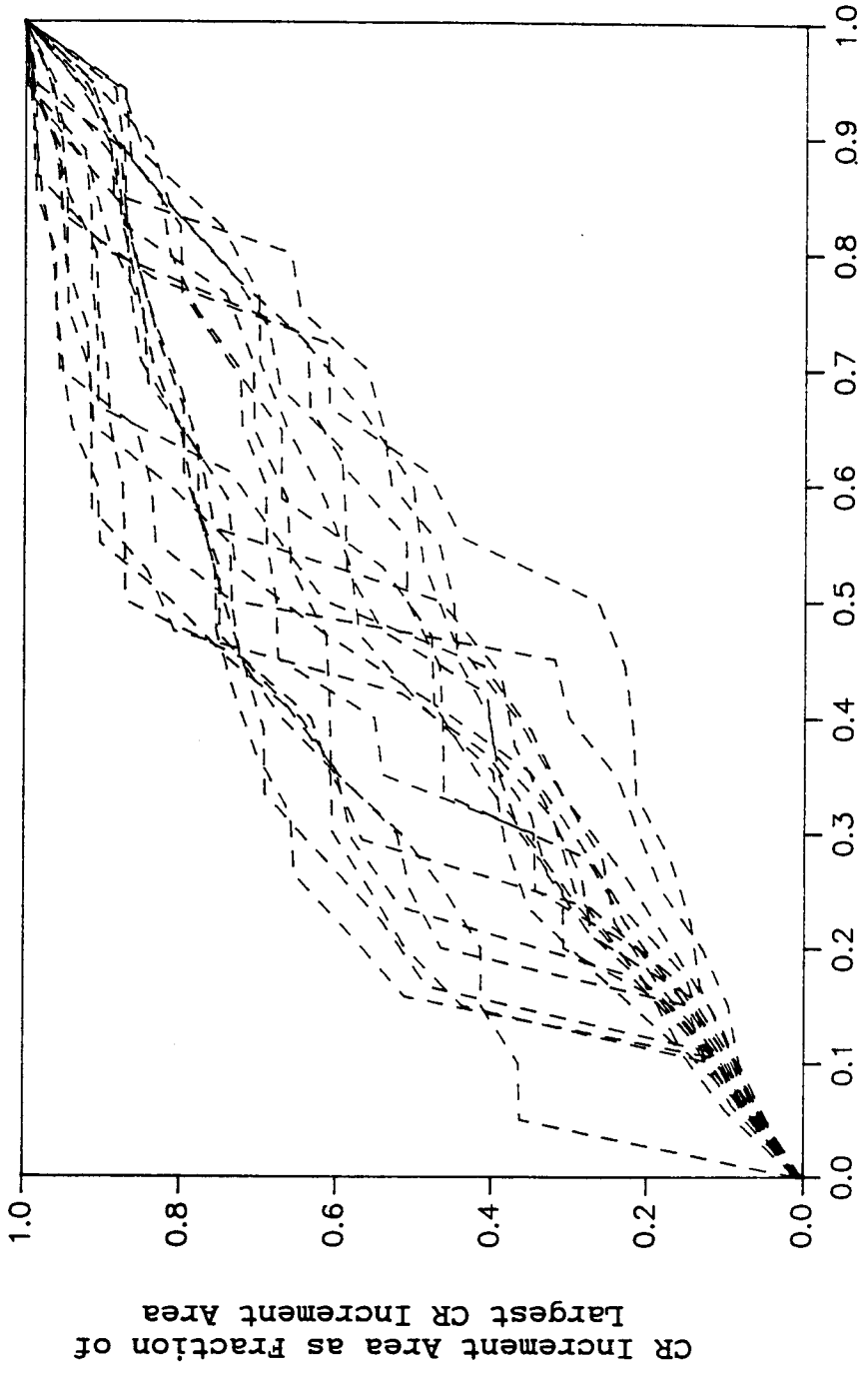
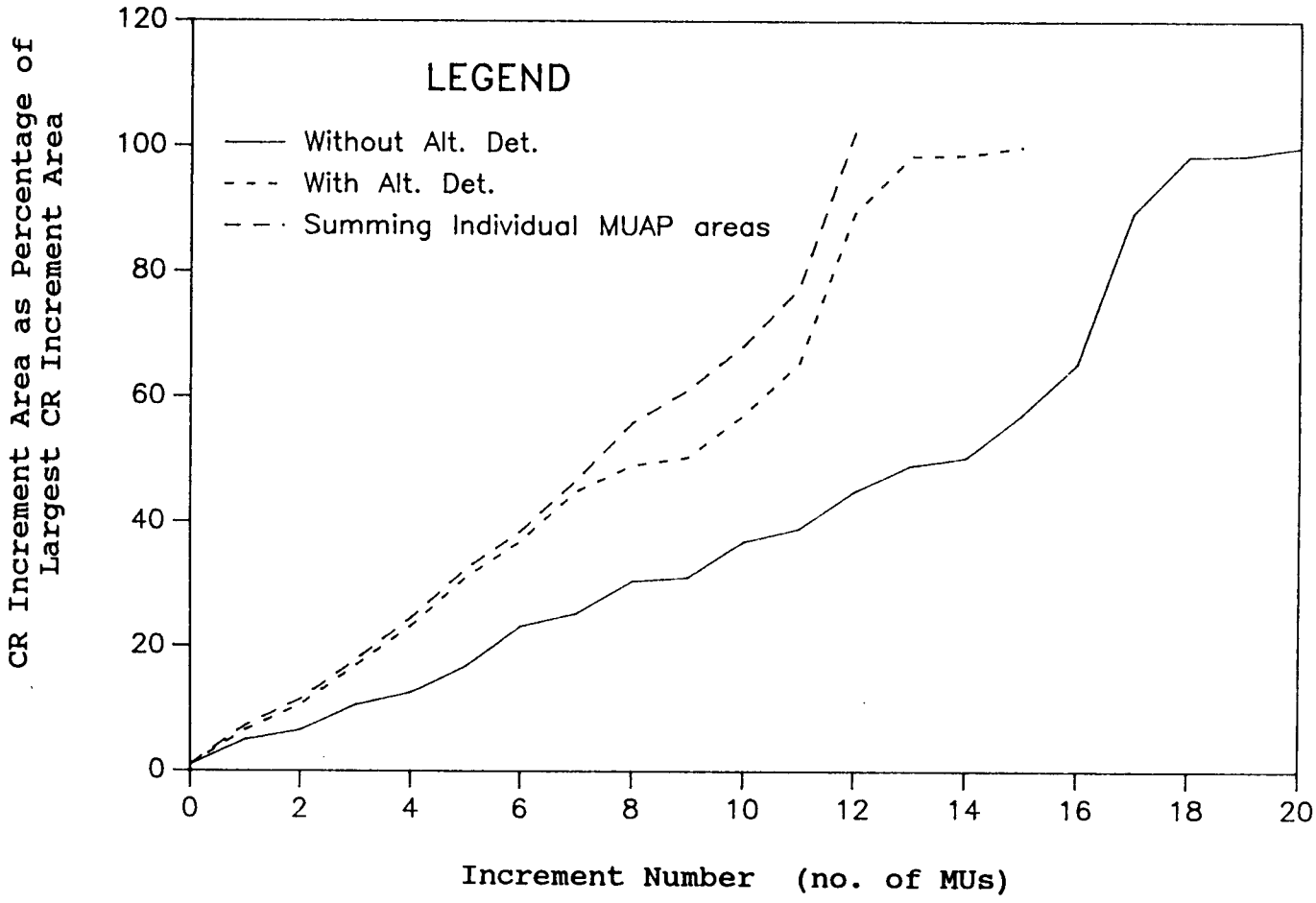


Figure 22 CR Increment Peak Amplitudes (Study 1)

To examine the effect of the alternation detection algorithm, Test No. 15 is considered. This test had the largest number of alternations in the study, 5 out of 20 MUAPs extracted being redundant. Figures 23 and 24 present the areas and peak amplitudes of the CR increments with and without alternation detection. The third curve in each figure illustrates the way the feature of each CR increment would increase if the features of each of the extracted MUAPs summed linearly (as Jasechko's third extrapolation technique assumed). The difference between this curve and the curve for alternation detection illustrates the non-linearity of MUAP feature summation. The smaller difference between the curves for Figure 23 compared to Figure 24 illustrates that MUAP area sums more linearly than peak amplitude (as suggested by Ballantyne and Hansen, 1974). In this test, alternation detection decreased the estimated count by 25%. The marked improvement in estimate repeatability achieved by using the alternation detection algorithm indicates the efficacy of the technique. Henceforth, all estimated MU counts quoted in this thesis (for MAMUCS I and II) will be with the alternation detection algorithm enabled.

The area, peak amplitude, and filtered Euclidean distance measure (from a null vector) for each of the 365 MUAPs extracted in this study were calculated, tabulated, and those falling outside $\pm$ 3 standard deviations of the mean were discarded. The remaining data were plotted in the histograms shown in Appendix A.1. The mean of the distance measure histogram distribution was 28.0, the standard deviation was 14.6, and the skewness was 1.06 (no. of MUAPs considered = 344). Only 3.8% of the extracted MUAPs had distance measures that fell below the template

Figure 23 CR Increment Areas (Study 1 : Test #15)



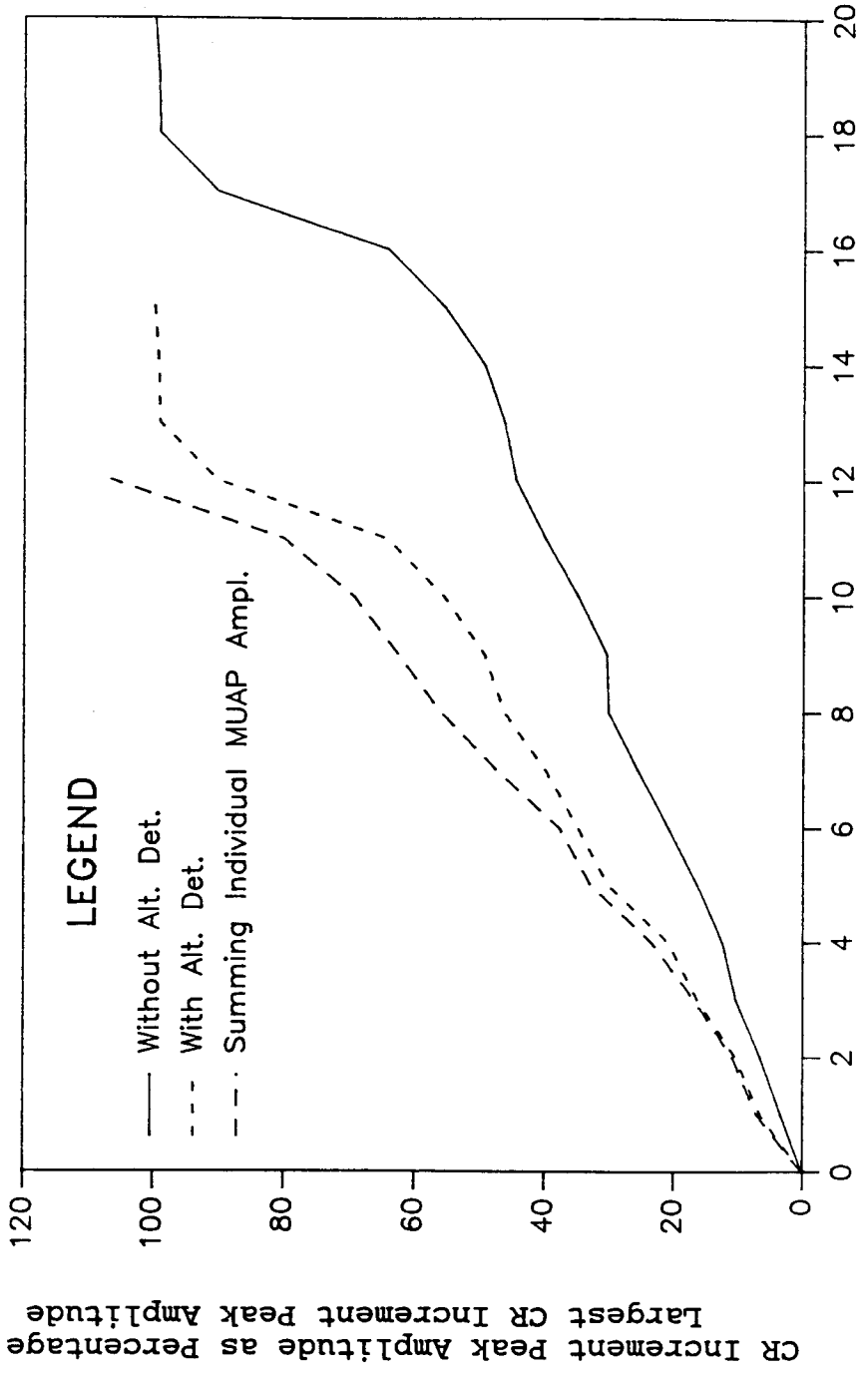


Figure 24 CR Increment Peak Amplitudes (Study 1 : Test #15)

discrimination threshold of 10. If a large number of actual MUAPs had distance measures below the threshold (ie. the threshold was set too high) we would expect the distribution to be more clustered around the threshold. It therefore appears that, at least for the muscle under investigation, the threshold value of 10 was a good compromise. Although the CRs in this study were collected using SPAs ranging from 30.1 to 73.8 volts, the CR for a particular test was often acquired within a SPA range of less than 2 volts. The mean voltage used in collecting the MEPs was 120.7 volts.

3.3 Test Results - Study 2

The muscle used in Study 1 was tested extensively during the development of MAMUCS I and was therefore somewhat archetypal. Our next study consisted of testing the left and right thenar groups of 5 nominally normal male subjects (age range 25 to 54 years) ten times each. The ten tests were divided into 5 sessions, the two tests in each session being performed serially without disturbing the instrumentation or significantly moving the subject's hand. The experimental protocol for each test was identical to that used in Study 1. By organizing the tests in this fashion it was hoped that the impact of re-instrumentation could be assessed. Two separate coefficients of variation were calculated for each experimental parameter in an effort to quantify the difference between intersession and intrasession variability. The intersession coefficient of variation (CV1) was calculated as in Study 1 by averaging the results for each session and calculating the CV of the five averages. If $X_1(j)$ and

$X_2(j)$ are the parameter values for tests 1 and 2 of the jth session respectively and X(j) is their average:

$$X(j) = \frac{X_1(j) + X_2(j)}{2} \qquad j = 1,5$$

$$\text{then} \qquad CV1 = \frac{\sigma_{\bar{X}}}{\mu_X}$$

where $\sigma_{\bar{X}}$ and μ_X are respectively the standard deviation and mean of X(j) over the five sessions. The intra-session coefficient of variation (CV2) is obtained by calculating the CV of the parameter for each session and averaging the five CVs. If CV(j) is the coefficient of variation of the experimental parameter for the jth session:

$$CV(j) = \sqrt{2}\,\frac{\left|X_1(j) - X_2(j)\right|}{X_1(j) + X_2(j)} \qquad j = 1,5$$

$$\text{then} \qquad CV2 = \frac{\sum_{j=1}^{5} CV(j)}{5}$$

The results for the 10 muscles are summarized in Tables 2, 3a, and 3b. Table 2 lists the mean MEP and AMUAP features and their respective CVs. Table 3a lists the average number of alternations detected per test and the mean extrapolated MU counts by the 5 methods and their respective figures of merit (EFIs and R^2s). Table 3b lists the CVs for these

Table 2 Summary of Results of Study 2 - Extrapolation Features

Subject Code	MEP Feature						AMUAP Feature					
	Area			Peak Amplitude			Area			Peak Amplitude		
	Mean (mVmS)	CV1 (%)	CV2 (%)	Mean (μV)	CV1 (%)	CV2 (%)	Mean (mVmS)	CV1 (%)	CV2 (%)	Mean (μV)	CV1 (%)	CV2 (%)
1R	29.4	13	3.4	5560	16	2.2	0.0809	25	4.1	16.6	26	4.0
1L	18.7	24	3.4	3080	17	2.3	0.0795	32	4.8	12.9	31	6.2
2R	33.7	14	1.8	5290	14	2.2	0.0461	23	9.5	7.64	15	10
2L	23.7	15	3.2	4030	9.5	3.3	0.0458	18	8.5	8.14	15	7.7
3R	31.6	23	3.8	5140	15	4.3	0.0643	32	23	10.5	35	27
3L	25.9	36	8.9	3580	24	8.9	0.272	58	26	38.1	62	26
4R	51.2	10	2.0	8550	6.4	1.7	0.249	14	8.1	49.4	12	7.0
4L	31.1	31	8.1	5200	25	5.7	0.0346	27	12	6.63	16	14
5R	29.1	17	3.7	5940	14	3.5	0.144	25	6.3	27.2	24	6.2
5L	32.5	26	1.7	5970	11	1.4	0.0565	24	11	11.4	32	13
Mean	30.7	21	4.0	5230	15	3.5	0.107	28	11	18.9	27	12
St.Dev.	8.52	8.4	2.5	1530	5.7	2.3	0.0865	12	7.3	14.6	15	8.2

Table 3a Summary of Results of Study 2 - Estimated Counts

Subject Code	Mean # of Altns	Extrapolation Technique: Method 1 Mean	Method 1 EFI	Method 2 Mean	Method 2 EFI	Method 3 Mean	Method 3 EFI	Method 4 Mean	Method 4 R^2	Method 5 Mean	Method 5 R^2
1R	0.2	378	.23	348	.20	334	.20	446	.93	396	.93
1L	0.7	242	.15	247	.15	232	.13	275	.94	282	.92
2R	0.0	751	.43	708	.41	646	.38	1000	.92	912	.92
2L	0.1	528	.33	506	.32	478	.31	675	.94	626	.95
3R	0.4	527	.33	546	.35	422	.28	630	.95	668	.92
3L	0.5	122	.16	129	.17	119	.15	132	.90	131	.89
4R	1.9	207	.31	175	.24	169	.23	204	.93	172	.93
4L	0.0	907	.38	794	.35	790	.35	1170	.91	996	.92
5R	0.4	207	.30	224	.30	214	.29	193	.84	206	.84
5L	0.2	599	.71	566	.67	354	.60	764	.76	726	.76
Mean	0.4	447	.33	424	.32	376	.29	549	.90	512	.90
St.Dev.	0.6	260	.16	232	.15	215	.14	359	.057	316	.057

Table 3b Summary of Results of Study 2 - Coefficients of Variation

Subject Code	Extrapolation Technique: Method 1 CV1	Method 1 CV2	Method 2 CV1	Method 2 CV2	Method 3 CV1	Method 3 CV2	Method 4 CV1	Method 4 CV2	Method 5 CV1	Method 5 CV2
1R	22	4.7	22	4.6	23	5.7	23	4.3	27	10
1L	15	2.4	15	6.2	16	3.4	15	6.6	14	6.9
2R	14	8.4	19	9.8	14	8.3	14	13	25	16
2L	16	9.8	18	9.9	17	8.1	17	14	17	14
3R	16	25	23	26	19	19	12	25	27	27
3L	52	20	65	22	54	19	55	11	61	11
4R	5.6	8.7	8.8	8.4	10	8.1	9.6	9.7	11	11
4L	21	13	22	14	23	13	15	12	17	11
5R	10	6.5	11	7.0	12	7.8	3.5	6.5	3.4	9.5
5L	28	12	29	14	9.4	12	36	8.4	36	12
Mean	20	11	23	12	20	10	21	11	24	13
St.Dev.	13	6.9	16	7.0	13	5.2	15	5.7	16	5.4

estimates.

While CV1 and CV2 are not equivalent measures and care should be taken in comparing them, the larger CV1s indicate that much of the variability in the tests is introduced by re-instrumenting the subject. The different geometry of the recording electrodes will change the way the responses are recorded and the different stimulating electrode placement will recruit a different sample of the MU population.

Changes in the MEP feature within a session, though small, were not insignificant. Some factors contributing to these changes may include:

a) Changes in the stimulating/recording electrode geometry caused by small shifts in the hand position.

b) Changes in the MUAPs due to repetitive stimulation and circulation restriction (the electrodes are tightly bound with surgical tape).

c) Changes in skin and tissue impedance characteristics over time due to perspiration and absorbtion of the electrode paste.

These changes, combined with different MUs being excited in different orders account for the larger than expected CV2s for the AMUAP feature and MU count. Overall, extrapolation method 3 (end-point extrapolation based on minimum EFI) yielded the estimates with the lowest variability, with method 1 (end-point based on area) a close second. While the EFI is

only a crude figure of merit with regard to response shape and does not necessarily reflect the accuracy of a particular count, the validity of estimates with very large EFIs (eg. subject #5 right thenar) should be viewed with scepticism. A high EFI indicates that the MUAPs forming the CR have shapes or sum in ways which are not representative of the population at large.

Once again, we note that the regression techniques generally produced less repeatable estimates than the end-point extrapolation techniques. If we compare end-point extrapolation based on area (method 1) with linear regression based on area (method 4) we note that it is between sessions that differences arise. Within a session, the regression technique's estimates are just as repeatable. This discrepancy is to be expected because of the regression estimation's dependence on order of MU recruitment which will tend to change more between sessions than within sessions. In any case, the differences are negligible and this study indicates that from a reliability point of view (as measured by the variability of serial estimates performed on the same subject), extrapolation methods 1,3 and 4 are roughly equivalent. Method 1 however, is by far the simplest to implement.

As was done in Study 1, the features of the extracted MUAPs were tabulated, those beyond ± 3 standard deviations of the mean were discarded, and those remaining were plotted in histograms (Appendix A.2). The distribution of MUAP distance measures has a mean of 19.8, a standard deviation of 9.51, and a skewness of 1.16 (1898 MUAPs considered). Only 8% of the extracted MUAPs had distance measures lower than the template

discrimination threshold of 10. Although the distribution's proximity to this threshold indicates that there may be small MUAPs which are not being detected, or that the smallest MUAPs extracted do not represent valid MU responses, experimentation with different thresholds indicated that the value used was a good compromise.

The estimates themselves tended to be somewhat higher than the expected range of 340 $\pm$ 87 for normal thenars (Sica, McComas, Upton, and Longmire, 1974). The low count of 122 (Method #1) seems to indicate some abnormality. Discussions with the subject revealed that he had in fact suffered a neck injury in the past which affected the left side of his body. When his extensor digitorum brevis (EDB) muscles were tested, similarly lowered counts on the left side were observed . The high count of 907 (method #1) is not so easily explained. Over the course of the study it was found to be difficult to stimulate this subject's left thenar without also activating the 1st and 2nd lumbrical muscles. These distant MUs may have contributed small increments to the CR which caused corresponding increases in the counts. In addition, it appeared that there may have been alternation beyond the deciphering capabilities of the system. Sica et. al. (1974) noted that they were unable to obtain satisfactory results from about 5% of the normal population due to excessive alternation.

Since the manual operator concentrates on peak amplitudes he will not identify as many increments in the CR as MAMUCS which scrutinizes the entire signal. Although some of these additional increments identified by the automated system will undoubtedly correspond to small MUAPs

normally missed by the manual operator because of their nonlinear contribution to the CR amplitude, some increments will also be spurious and represent the contributions of noise, extraneous MUAPs from adjacent muscles, and latency shifts in the responses. This last factor was a surprising discovery made during Study 2 which prompted a re-evaluation of the requirements for the response classification system and is the subject of the next chapter.

CHAPTER 4

MAMUCS II

4.0 Latency Shifting

The propagation delay or response latency illustrated in Figure 2 will be the sum of the following individual delays:

a) Initiation of the AP in the motor neuron

b) Propagation of AP down the motor axon to the terminal branches

c) Propagation of AP across the synaptic gap

d) Propagation of the AP down the muscle fibres

The lengths of these delays are subject to small random fluctuations over time due to numerous factors. Since the largest component of the delay is b), the propagation of the AP down the axon, changes in this component will have the greatest impact on the total response latency.

Electrical stimulation of an AP in the motor axon is most likely to occur at the nodes of Ranvier. Depending on the current distribution under the stimulating electrodes, initiation of the AP will occur simultaneously at several nodes around the cathodic electrode. Because

of the all or nothing nature of the AP and the refractory nature of the excitable membranes, this will effectively be a stimulation at the most distal of these nodes. If this most distal node is just on the threshold of activation, on repeated stimulation we would expect the site of stimulation to alternate between this node and the next most proximal node. Such a shift in the stimulation site will cause a discrete shift in the response latency corresponding to the internodal distance divided by the AP propagation velocity along the motor axon. The mean internodal conduction time for normal ventral root nerve fibres of internodal lengths between 0.75 and 1.45 mm has been measured as 19.7 μS with a standard deviation of 4.6 (Rasminski and Sears, 1972). Small displacements of the stimulating electrodes during a test will cause similar changes in the stimulation site.

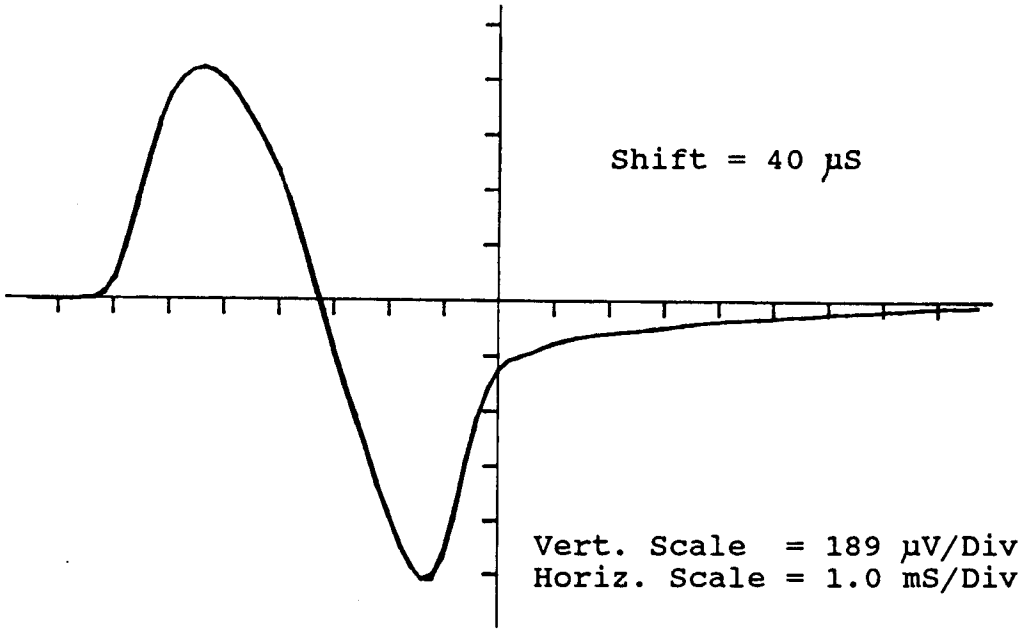
During the development and testing of MAMUCS I numerous responses were observed that appeared to be identical except for small time shifts. Several muscles tested had a single low threshold MU that could be excited in isolation over a fairly wide voltage range. As the SPA was slowly ramped up from threshold the MUAP was observed repeatedly on the oscilloscope. This MUAP would suddenly appear shifted slightly in time (different latency) and then return to its previous position while the SPA was still far below the threshold of the next unit. While the small discrete latency shift between these two signals would go unnoticed by the manual operator because his mental pattern recognition system is keyed to shape and size, MAMUCS recognizes the responses as distinct because the misalignment causes a distance measure between them greater than the

template discrimination threshold. This shifting is to be expected on an individual MU basis and if it occurs for the dominant MUAP in a CR we will also observe a shift in the entire response. Subtracting a time shifted version of a typical MU response from itself (Figure 25a) produces a characteristic difference signal with a significant distance measure (Figure 25b). Since a response template and its time shifted 'twin' will have virtually identical areas (and peak amplitudes) they will be ranked adjacently by EST. Thus, if latency shifting were corrupting our tests, we would expect to occasionally see extracted MUAPs which resemble the signal in Figure 25b. Figures 26a and 26b illustrate a thenar test which shows signs of latency shifting (note MUAP A). Figure 27a shows the templates which were subtracted to extract MUAP A. Figure 27b illustrates how this difference signal can be virtually reduced to zero by shifting one of the template signals 32 μS before subtraction. The difference signal cannot be totally reduced to baseline since each of the template signals is the average of several responses and the sum of several MUAPs (only some of which may have shifted). These would each require individual latency compensation.

A more drastic example of latency shifting from an EDB test is illustrated in Figures 28a and 28b. In this case shifting the signals 0.2 mS prior to subtraction eliminates the difference signal.

Figure 25 Simulated Latency Shift

a) Template and Time-shifted Twin



b) Difference Signal generated by Latency Shift

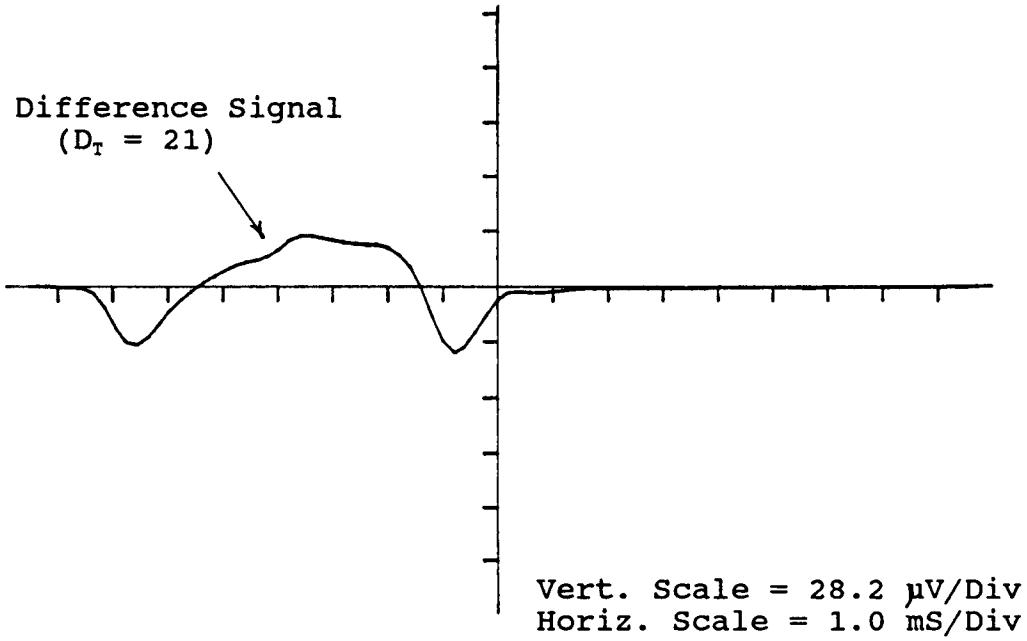
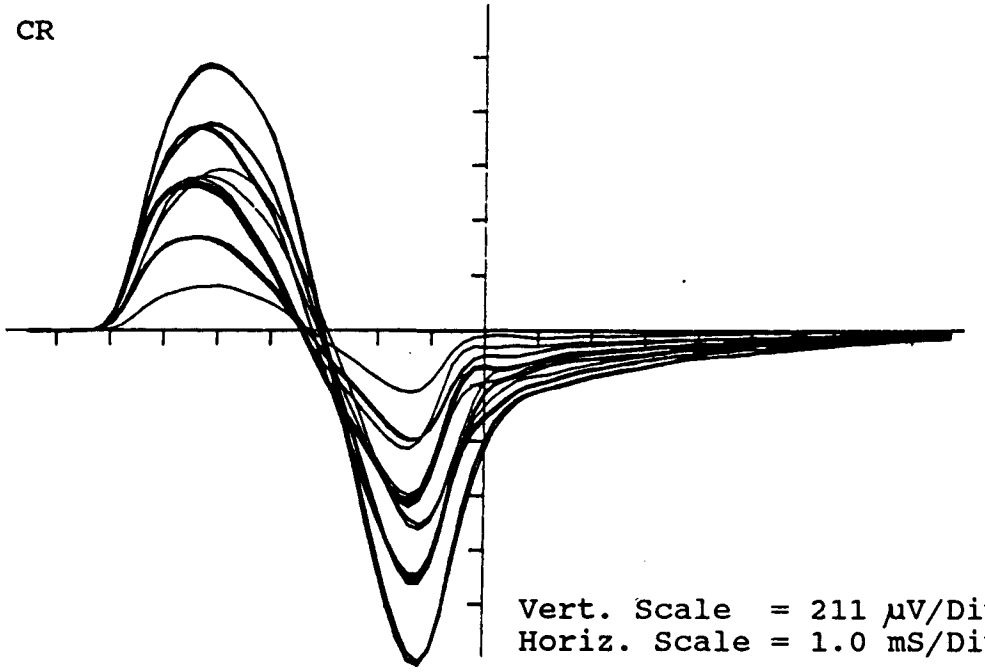
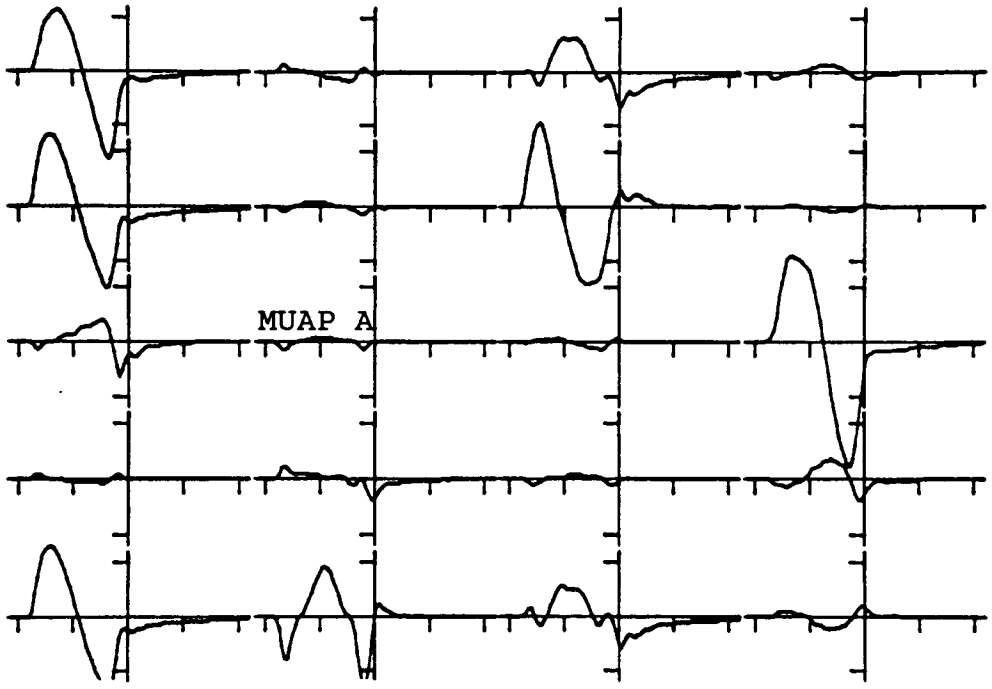


Figure 26 Sample Test 3 - Example of Latency Shifting

a) CR



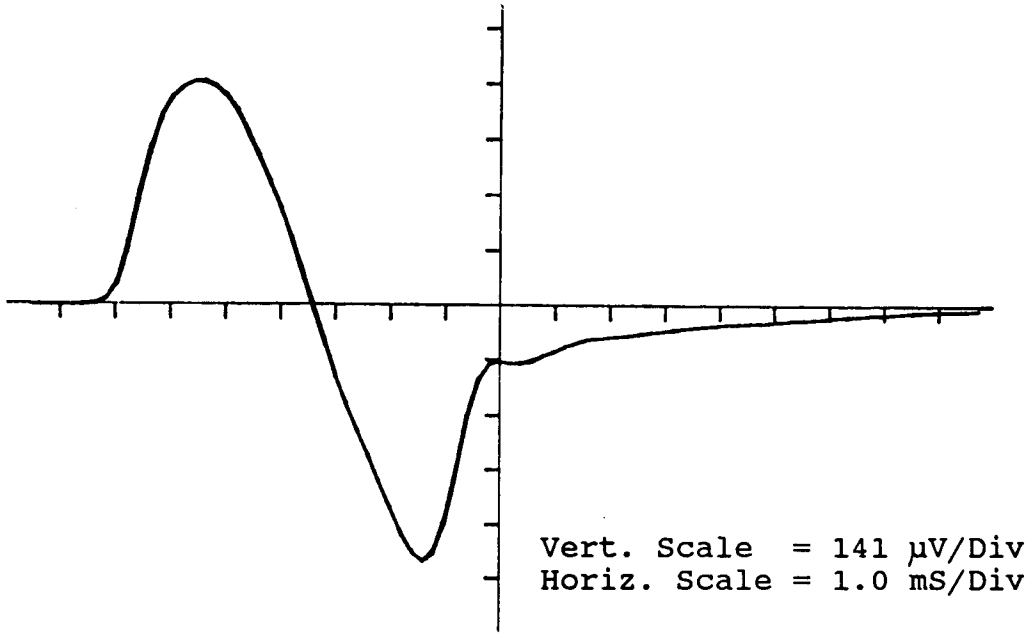
b) Extracted MUAPs



Vert. Scale = 145 µV/Div Horiz. Scale = 4.0 mS/Div

Figure 27 Observed Latency Shift from Figure 26

a) Template and Time-shifted Twin



b) Difference Signal (MUAP A) and Effect of Latency Correction

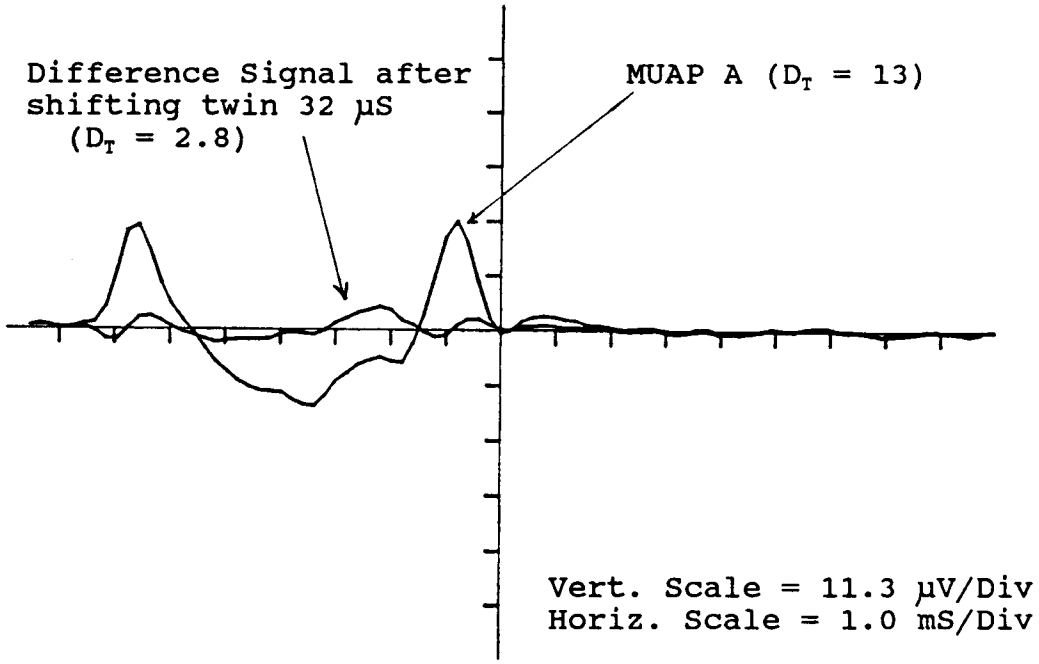
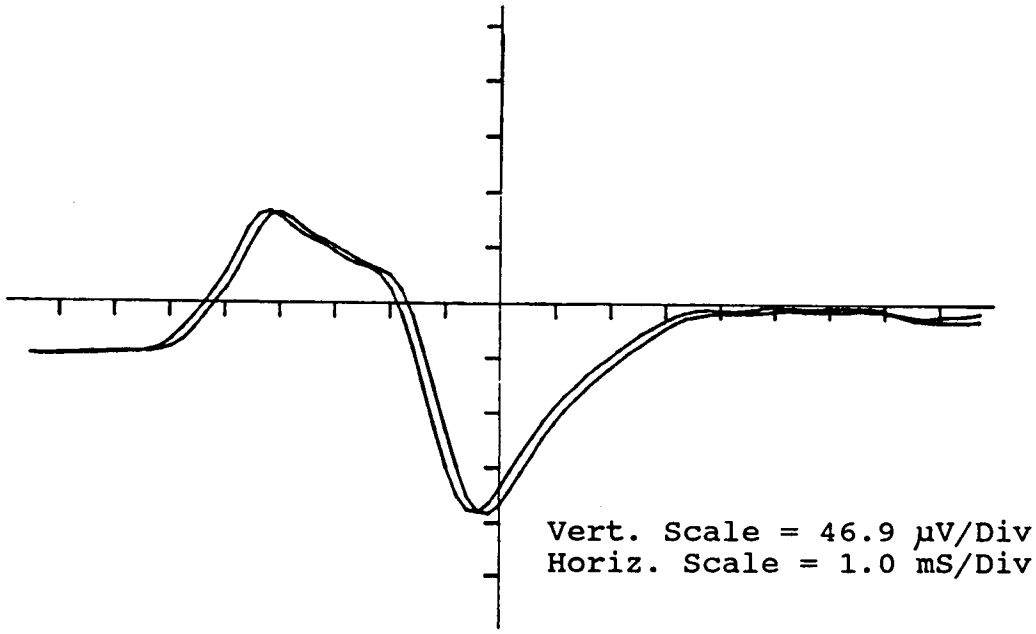
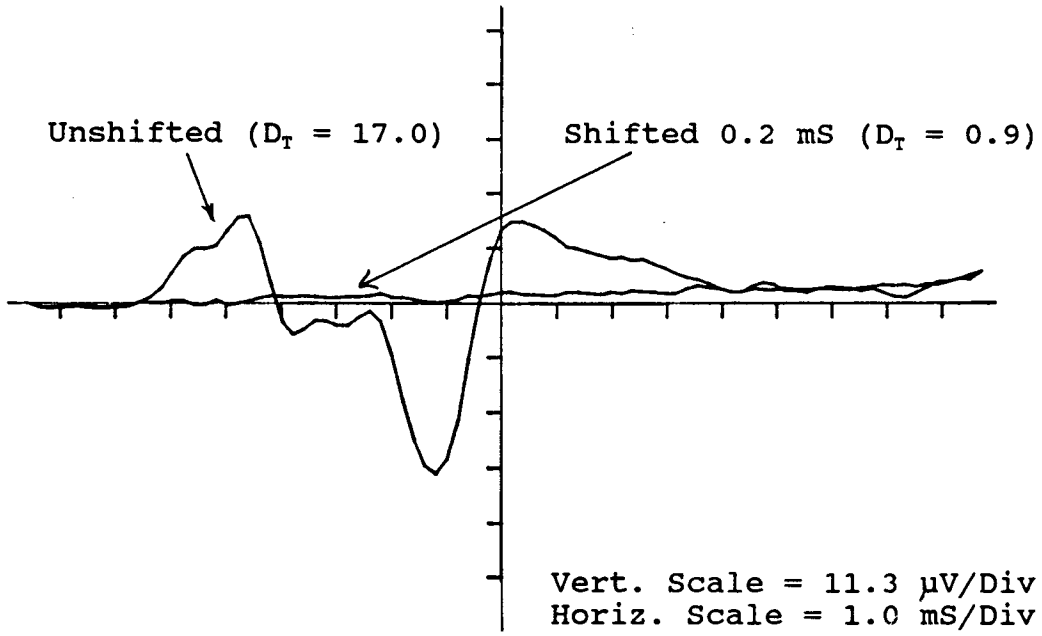


Figure 28 Observed Latency Shift in EDB Muscle

a) Template and Time-shifted Twin



b) Difference Signal and Effect of Latency Correction



4.1 The Frequency Domain Response Classification System

It was realized from the outset that the pattern recognition system used in MAMUCS I was far from ideal. Because of limited computer memory it was not possible to store the template pattern classification features (digitally filtered time samples) separately and they had to be generated each time a template matching was performed. This necessitated the use of a fairly crude, though effective, digital filter (Kth difference) to ensure reasonably fast response classification. Although it was recognized at an early stage that a more compact representation of the signals would alleviate some of these problems, the parallel development of a system operating in the frequency domain was not considered necessary until the identification of latency shifting during Study 2 demonstrated the need for a more powerful pattern recognition system.

Because of the band limited nature of the template signals, once the signal has been converted to a frequency domain representation only the significant Fourier coefficients need be retained. As well, a lower sampling frequency can be used since temporal comparisons are no longer being performed. With a 3 kHz sampling frequency a 64 point (21.3 mS) response window can be used. Of the 64 complex Fourier coefficients generated by an FFT, one half need not be kept as they are the complex conjugates of the other and can be regenerated as needed. For the thenar signals recorded in studies 1 and 2, fewer than the first 16 coefficients were found to be significant. Although the sampling frequency has been chosen such that some high frequency noise signal propagated through the

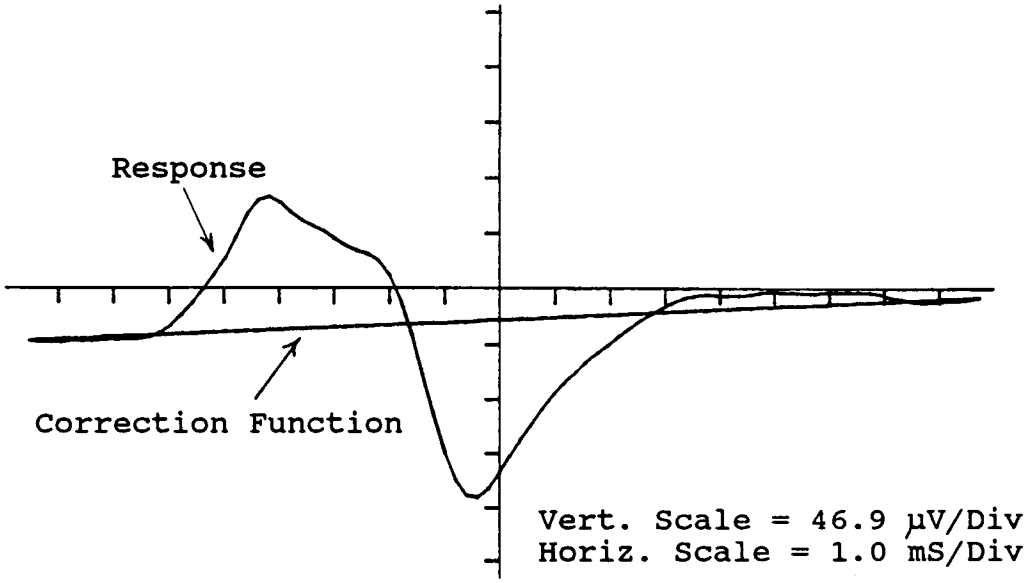
analogue stages could conceivably lead to aliasing, discarding the upper half of the 32 Fourier coefficients will eliminate any resulting higher frequency distortion. By only storing the 16 complex Fourier coefficients as opposed to 88 real data points for each response template (or save bin), the new AP program uses over 50% less memory for signal storage. In this way memory has been freed for storage of the response classification features. These features were chosen as the magnitudes of the 2nd to the 9th Fourier coefficients (47 -375 Hz, the 1st is the D.C. component while those beyond the 9th are rarely significant for template matching). Using the magnitudes effectively accomodates the latency shifts described in section 4.0. Thus, for each template (or save bin) there are 16 complex Fourier coefficients, 8 spectral response classification features, and 3 time domain features (area, peak amplitude, and peak latency) used for pre-screening.

When a response is collected it must be preconditioned before the FFT is applied. To prevent leakage due to the endpoints of the signal not being equal to zero, a line interpolated from the first point to the last point in the response window is subtracted (Figure 29). Since the responses are typically superimposed on the exponentially decaying stimulus artifact, it was felt that this baseline correction technique effectively removed most of the artifact and introduced less distortion than windowing.

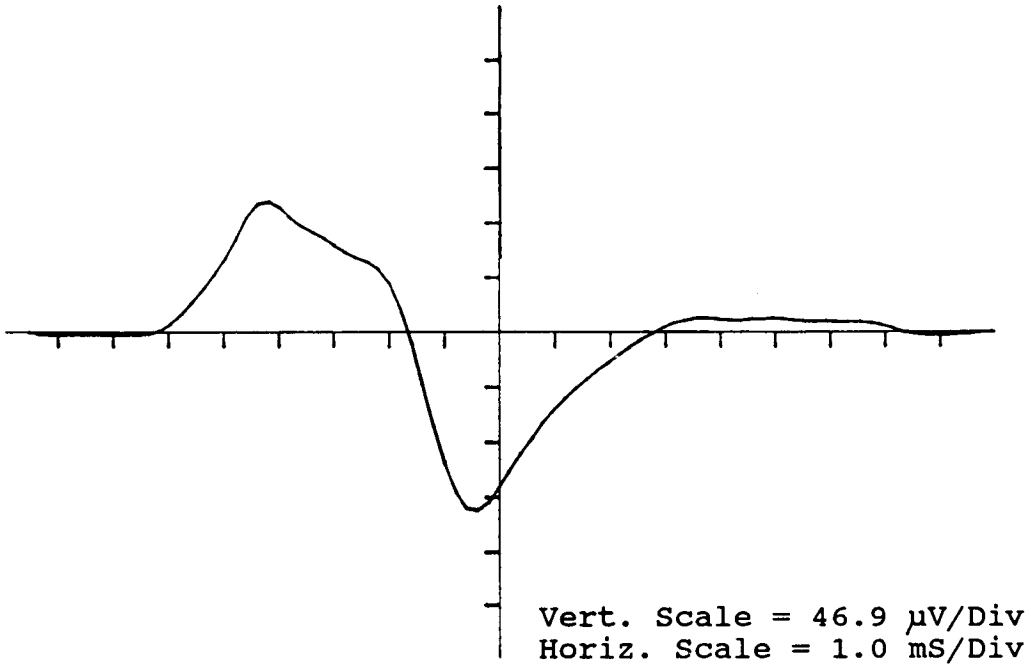
After the baseline correction, the time domain features are calculated and the FFT is performed using a standard decimation in time algorithm. The 8 spectral features are calculated and the response is

Figure 29 Correction for Baseline Artifact

a) Example of Response with Correction Function



b) Corrected Response



classified. The response is compared to existing template/save bins in 2 stages. The pre-screening stage consists of ensuring that the peak amplitudes agree within 30 μV as in MAMUCS I (the mean extracted MUAP amplitude from Study 2 was about 32 μV). In addition, the latencies of these peaks must agree within 1 mS. This additional pre-screening criterion is necessary to ensure that small signals with different shapes but similar amplitude spectra are not classified together.

If the pre-screening is passed the spectral features of the two signals are compared using a spectral magnitude distance measure analagous to the distance measure used for MAMUCS I:

$$D_S = \sqrt{\frac{\sum_{j=1}^{8} [C_R(j) - C_T(j)]^2}{8}}$$

$C_R(j)$ = spectral features of the response

$C_T(j)$ = spectral features of the template/save bin

After some experimentation a template discrimination threshold of 75 was adopted for this distance measure. When a match is found the Fourier coefficients of the response are averaged with those of the matching template and the template's features are updated. Not having to re-compute all the template/save bin features for each classification combined with the smaller number of features involved in the comparisons compensates for the computation time expended in calculating the FFT.

Aside from these differences in the response classification protocol, AP remains unchanged for the new system which is designated MAMUCS II. The only change in MP is the length of the response window and sampling frequency since all calculations for acquiring the MEP remain in the time domain. In EST, the pattern recognition system used for alternation detection is an enhanced version of the previously outlined spectral system used in AP.

While the responses that form the CR are large and tend to increase in size in a stepwise fashion, the MUAPs extracted by EST will tend to be smaller and more uniform in size. The chance of two distinct MUAPs having similar magnitude spectra is much greater than that for two templates. Therefore, although latency shifting can still cause problems, the phase components of the spectra can no longer be ignored. When two signals are compared for alternation detection their Fourier coefficients are subtracted and this difference signal is examined in order to detect a match. The Euclidean norm of the phase delays (in seconds) of the spectral components with significant magnitudes is computed and used for pre-screening signals before the magnitudes of the spectral components are considered. This pattern recognition system uses Fourier coefficients 2 to 12 (47 - 517 Hz) because of the greater resolution needed at this level. If the norm of the phase delays is less than 1.5×10^{-4} and the norm of the magnitudes is less than 20, the signals are considered to be identical and therefore a case of alternation.

Aside from these changes to the signal representation and pattern recognition system all other aspects of MAMUCS II are identical to MAMUCS

I. For this reason, comparing test results obtained using the two systems should provide an indication of the relative merits of each response classification technique. The next chapter describes studies in which both MAMUCS I and II were pitted against an experienced manual operator and their performance assessed.

CHAPTER 5

COMPARATIVE STUDIES

5.0 The Thenar Muscle Group

One observation that was made during Study 2 that caused considerable concern was the large difference between CV1 and CV2 for the MEP extrapolation features. Although changes in the stimulating electrode placement between sessions could alter the relative latencies of the MUAPs slightly and therefore the way in which they sum to form the MEP, these changes would be small. Experimentation revealed that small changes in the angular orientation of the recording electrodes with respect to the axis of the muscle belly produced large (on the order of 25%) changes in the MEP area and peak amplitude. It was found that although a monopolar electrode configuration (reference electrode is remote from the stigmatic recording electrode and over inactive tissue) is somewhat less selective, the recorded response is less sensitive to electrode placement. The high sensitivity of the bipolar configuration acts as a variable gain that makes the choice of fixed discrimination thresholds for signal comparisons difficult to justify. For subsequent tests the reference electrode was shortened to 3.0 cm and placed along the dorsal aspect of the proximal phalanx of the thumb.

The objective of the next set of studies was to compare the performance of the 5 extrapolation techniques and the 2 response classification schemes with that of an experienced manual operator. The experimental protocol for each session consisted of instrumenting the subject and then performing 2 motor unit count estimates by each of 3 methods:

1) MAMUCS I (Study 3)

2) MAMUCS II (Study 4)

3) Manually (Study 5)

Every effort was made to avoid disturbing the electrodes while performing the 6 tests. As in Study 2 each muscle was tested over 5 sessions for a total of 10 estimates. In this case subject No. 5's left thenar could not be tested due to some recent surgery so a 6th subject's right thenar was substituted to complete the complement of 10 muscles to be tested. It should be noted that although some of the subjects from Study 2 participated in these studies, they were not assigned the same numbers in all cases. Tables 4a and 4b summarize the overall CVs for Studies 3 and 4.

As expected, the variability of the MEP extrapolation features dropped considerably compared to Study 2. The estimates obtained using linear regression show the largest variability by far and for the sake of

Table 4a Summary of Coefficients of Variation
(Extrapolation Features - Studies 3 and 4)

	MEP Feature				AMUAP Feature			
	Area		Peak Amp		Area		Peak Amp	
	CV1	CV2	CV1	CV2	CV1	CV2	CV1	CV2
Study 3	12	2.6	26	2.5	27	14	27	13
Study 4	12	2.3	15	2.2	20	11	23	11

Table 4b Summary of Coefficients of Variation
(Estimated MU Counts - Studies 3 and 4)

	Extrapolation Technique									
	Method 1		Method 2		Method 3		Method 4		Method 5	
	CV1	CV2	CV1	CV2	CV1	CV2	CV1	CV2	CV1	CV2
Study 3	27	13	28	13	27	12	33	16	33	14
Study 4	21	10	24	11	41	13	25	11	27	10

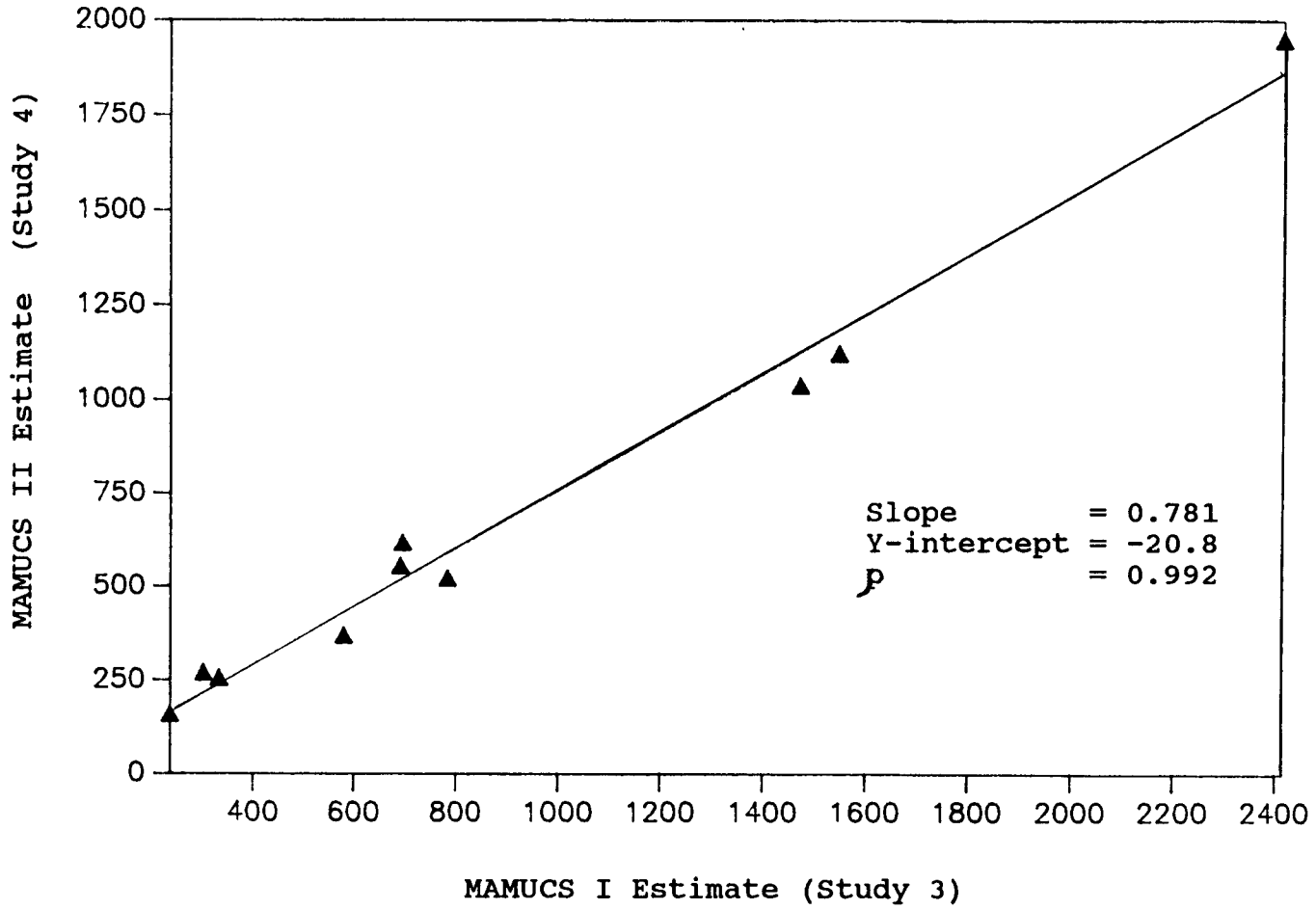
brevity will not be discussed further. The end-point extrapolation techniques all show comparable intrasession variability but Method 1 shows the lowest intersession variability. Method 3 failed to live up to its performance in Study 2 because subject #2's right thenar gave triphasic CR responses which often could not be matched to the normal biphasic MEP that was recorded. As a result, the estimates for this muscle by Method 3 varied considerably (MAMUCS II CV1 = 220%). While a poor fit indicates that the MUAPs forming the CR are not a representative sample of those forming the MEP with regard to shape, they may be perfectly acceptable in terms of size. In the case of dubious estimates, it is best left to the clinician to judge their validity. For the above reason it was felt that Method 1 is the preferred extrapolation technique, and henceforth all estimates quoted will be those obtained using this method.

Appendices B.1, B.2, and B.3 contain the tabulated results for Studies 3, 4, and 5 respectively. Table 5 summarizes the mean estimates and their mean CV's for the 10 muscles across the 3 studies. Even a cursory examination of the estimates reveals a trend towards lower counts from one study to the next. Because MAMUCS II should theoretically produce fewer spurious CR increments than MAMUCS I, this reduction in the estimates is expected. The mean estimates obtained by the two automated systems for each subject are plotted against each other in Figure 30. The regression line has a slope of 0.781, a y-intercept of -20.8 and a coefficient of correlation of 0.992. Although it is difficult to quantify how altering the response classification system affects the estimates, it appears to have done so in an extremely linear fashion.

Table 5 Summary of Results of Comparative Thenar Studies

Subject Code	Mean Estimate			Mean CV1			Mean CV2		
	Study			Study			Study		
	#3	#4	#5	#3	#4	#5	#3	#4	#5
1R	580	369	219	52	24	20	9.7	7.4	16
1L	333	255	193	20	16	22	13	6.9	11
2R	691	555	241	17	8.2	13	19	11	10
2L	695	618	256	41	39	15	13	11	4.8
3R	237	157	91	13	6.2	17	9.8	3.8	10
3L	2410	1950	685	29	20	3.8	17	16	13
4R	1470	1040	486	29	32	20	13	16	6.6
4L	783	522	296	38	28	11	12	5.6	6.5
5R	303	269	173	20	20	24	9.8	13	15
6R	1550	1130	349	8.1	19	23	15	14	6.1
Mean	906	686	299	27	21	17	13	10	10
St.Dev.	696	548	173	14	10	6.3	3.1	4.4	3.8

Figure 30 Comparison of Mean Estimates: (Study 4 vs Study 3)



Histograms of the features of the extracted MUAPs for Studies 3 and 4 are plotted in Appendices A.3 and A.4. The areas and peak amplitudes of the extracted MUAPs have roughly equivalent distributions for the two studies (the slightly longer response window of MAMUCS II will incorporate more of the decaying tail of the responses and therefore slightly larger MUAP areas are expected). While the distributions of MUAP distance measures are not directly comparable, we note that the difference between the distribution mean and the discrimination threshold as a percentage of the distribution mean is larger for Study 4 than for Study 3 (63.9% vs 51.1%), indicating better resolution. In addition, the distance distribution for Study 4 has a greater skewness than that for Study 3, again indicating that the distribution is further removed from the threshold. It would appear that MAMUCS II can extract MUAPs with roughly equivalent sizes to those extracted by MAMUCS I but their distance measures are on average further from the template discrimination threshold. Lowering the threshold for MAMUCS I to compensate would cause the creation of even more spurious templates and proportionally higher counts. Of the 1968 MUAPs extracted in Study 3, 8.95% had distance measures that fell below the discrimination threshold of 10. Only 4.65% of the 1893 extracted by MAMUCS II in Study 4 fell below its threshold of 75. Further evidence of the efficacy of the spectral response classification system used in MAMUCS II is the larger number of alternations detected in Study 4; 107 as opposed to 32 in Study 3.

5.1 Comparison with Manual Results

By creating fewer spurious templates and detecting more alternations MAMUCS II gives lower estimates than MAMUCS I. However, these estimates are still consistently higher than those obtained manually (Table 5). The exact number of MUs in a muscle cannot be determined with a known degree of accuracy by any method, and anatomical studies are somewhat vague in their confirmation of the accepted normal range for thenar counts obtained by the McComas technique. Nevertheless, the highest counts obtained with MAMUCS II should be viewed with a certain degree of skepticism.

Figure 31 plots the mean estimates for each muscle from Study 4 against the corresponding figure from Study 5. Again we see a remarkably linear relationship with good correlation ($\rho = 0.96$). The additional CR increments responsible for the higher counts obtained using the automated system are the products of several mechanisms:

1) Small thenar motor units whose responses normally go unnoticed by the operator.

   The operator concentrates on peak amplitude changes in the first phase of the response, while the computer scrutinizes the entire waveform to a high degree of resolution. Small, long latency MUAPs whose peak amplitudes do not contribute linearly to the CR amplitude tend to be ignored by the operator.

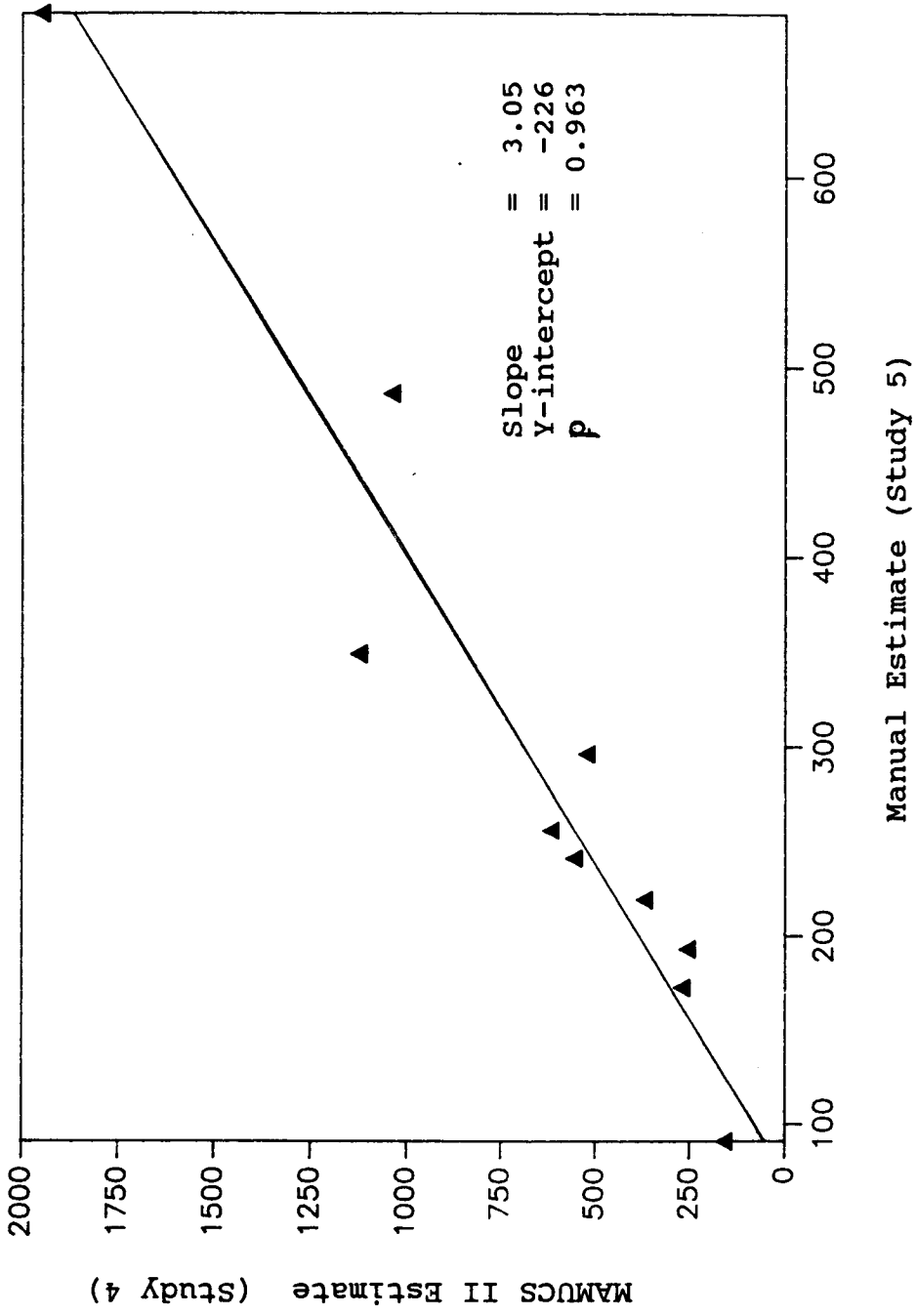


Figure 31 Comparison of Mean Estimates: (Study 4 vs Study 5)

While this may account for some of the differences between manual and automated counts it does not explain the extreme high counts.

2) CR increments that do not correspond to MUAPs but are due to:
   a) Alternation beyond the deciphering capabilities of the system. The larger number of stimulations used in an automated test and the fine degree of control over the SPA makes it more likely for alternation to occur.
   b) Axonal branching proximal to the stimulation site will cause CR increments which correspond to subsections of motor units.
3) Small MUAPs from adjacent muscles that are inadvertently stimulated. This can have the effect of not only decreasing the average CR increment (AMUAP) but also of increasing the size of the MEP. In some of the thenar muscles tested the 1st and 2nd lumbrical muscles proved troublesome in this respect.
4) Spurious templates created by response classification errors due to noise, latency shifting, etc.

It is difficult to estimate the relative contributions of these potential sources of error. In the absence of any rigid criterion for judging what constitutes a valid MUAP and what can safely by ignored,

every effort was made to maintain a high degree of resolution in the response classification systems. If after consultation with medical authorities better criteria can be established, a template rejection algorithm can be implemented to discard spurious CR increments. This approach is preferable over simply raising the template discrimination threshold since it does not compromise the performance of the alternation detection algorithm which depends on precision in the CR response classification. In addition, by performing the processing on stored data, different approaches can be tested without the need to recollect the data.

5.2 Biased Sampling of the MU Population

If, for the purpose of discussion, all the CR increments identified in Study 4 are assumed to be the valid contributions of thenar motor units, it would seem to lend support to the criticism that the MUAPs sampled by this technique are not representative of the population at large. Advocators of this point of view claim that there is a correlation between MU size and order of recruitment by electrical stimulation. There is however, considerable controversy in the literature over whether this proportionality is direct or inverse (Feasy and Brown, 1974; Leifer, 1981;). One of the problems with this argument is the assumption that large MUs will have large recorded MUAPs and vice versa. While this will be true to a certain extent, the size of the recorded MUAP will also be a function of:

1) Temporal dispersion of the fibre action potentials summing to form the MUAP.

2) The spatial relationship between the MU fibres and the recording electrodes.

Although only 5 - 10% of the MUs in a muscle are sampled in forming the CR, repeating the test with a new stimulating electrode placement tends to excite a different sample of the MU population. Thus, the MUs sampled are also a function of the spatial relationship of the motor axons with respect to the stimulating electrodes. If there is a preferential stimulation of small MUs at lower voltages, one would expect to see some evidence of an upward trend when plotting MUAP size vs order of recruitment. Figure 31 is such a plot for the areas of the 1842 extracted MUAPs from Study 4 whose areas fell within ± 3 standard deviations of the mean area for the 1893 MUAPs extracted. As can be seen the slope is virtually zero as is the coefficient of correlation.

While it seems that preferential stimulation of small MUs within a muscle is unlikely, what can occur is a preferential stimulation of one muscle within the thenar group. The median nerve innervates 3 muscles; the abductor pollicis brevis, the opponens pollicis, and part of the flexor pollicis brevis. Since these muscles are unequal in size and distance from the recording electrodes, responses of unequal size and shape are to be expected from them. If, while collecting the CR, motor units from a more distant muscle or one with smaller units are

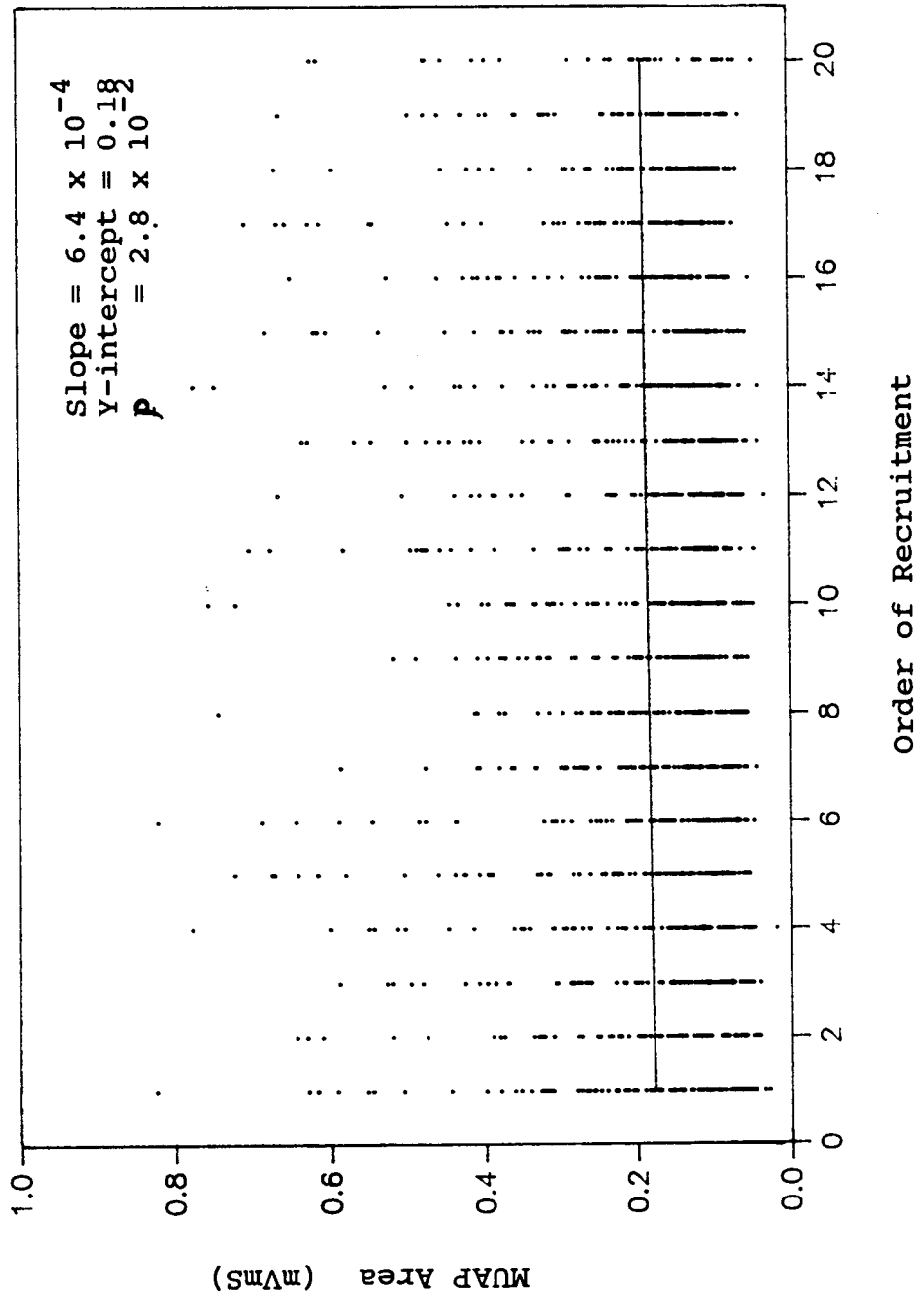


Figure 32 MUAP Area vs Order of Recruitment (Study 4)

preferentially stimulated, the resulting small CR increments will not be representative of the MU population at large. The MU count estimates obtained under these circumstances will therefore be disproportionately high. Although this phenomenon would affect both manual and automated estimates, the manual operator misses some of the very small increments and the error will be lower. If this problem is in part responsible for the very high thenar counts obtained for subjects 3L, 4R, and 6R, it would account for the fact that the proportionality between manual and automated estimates is maintained. In muscles that are not divided as the thenar group is, we might expect to see a much smaller range in the estimates for different subjects.

In any case, it must be remembered that the absolute value of the estimate is of limited importance for diagnostic purposes. It is the relationship between the estimate and the accepted normal range which is of importance to the clinician. A fortuitous illustration of this principle may be found in these studies. The extreme average estimates from Study 4 (157 and 1949) came from opposite hands of the same subject (No.3). This seems odd in view of the fact that the subject was an otherwise clinically normal, active male (age 25), with good muscle bulk in both thenars. Indeed, the mean MEP areas for these muscles were both equal to about 64 mVmS, the highest value for any muscles tested in the study. This subject was tested extensively during the development of both MAMUCS I and II and the discrepancy between his thenars was consistent, leading one to conclude that the cause is physiological. In fact, the subject had suffered a deep laceration to the volar aspect of his right

wrist during childhood. This injury could conceivably have damaged the median nerve and therefore reduce the number of motor units in his right thenar group. Collateral reinnervation would lead to larger motor units and no decrease in muscle size.

5.3 The Extensor Digitorum Brevis

Of the muscles typically tested using the McComas technique, the thenar was chosen for the preliminary testing of MAMUCS because it is conveniently accessed and easily instrumented. During the development and testing of MAMUCS the hypothenar and extensor digitorum brevis (EDB) were also tested. Upon completion of the thenar studies it was decided to conduct similar studies on the EDB to demonstrate the system's flexibility. Studies 6 and 7 were conducted using the 10 EDB muscles of 5 subjects with an experimental protocol that was identical to the thenar studies except that in this case only MAMUCS II was used with end point extrapolation based on area (Method 1). The stigmatic recording electrode was applied obliquely across the proximal section of the EDB belly as in McComas' original study (1971). The reference electrode was placed over the medial aspect of the foot while the ground was placed distal to the stigmatic electrode. The stimulating electrodes were placed over the deep peroneal (anterior tibial) nerve above the ankle.

In preliminary tests on several subjects it was noted that the EDB responses tended to have higher frequency content than the thenar muscles tested. For this reason the number of coefficients used in the frequency domain representation of the signals was raised to 20 while the

number of features used in the spectral response classification algorithms for both AP and EST was raised to 12. Also, the settling time was extended to accomodate the increased response latency for this muscle.

The estimated motor unit counts obtained manually and using the automated system are summarized in Table 6. The most notable feature of the results is the decrease in the range of values for both the manual and automated estimates compared with the thenar studies. Although the overall mean estimate for Study 6 (automated) exceeds that for Study 7 (manual), both fall within the range of 199 $\pm$ 60 given by McComas et al. (1971). This observation lends support to the argument that some of the high thenar counts obtained in the previous studies result from the preferential stimulation of a particular muscle within the thenar group whose MUs generate recorded MUAPs that are not a representative sample of the entire population composing the MEP. Since the EDB is a single muscle, it is not expected that such a phenomenon would be observed. It is also notable that although the overall mean (intrasession) CV2s for studies 6 and 7 are comparable to those for thenar Studies 4 and 5, the mean (intersession) CV1s are considerably higher. It would appear that eventhough the MUAPs sampled in the EDB studies may be more representative of the population at large than those sampled in the thenar studies, the sample is less consistent between sessions. While the overall mean MEP area for Study 4 was 44.4 mVmS with a mean CV1 of 12% and CV2 of 2.3%, Study 6 gave values of 21.5 mVmS, 23%, and 4.1% respectively for these figures. While the approximate halving of the extrapolation feature is expected for the smaller EDB muscle (with correspondingly fewer MUs), the

Table 6 Summary of Results of Comparative EDB Studies

Subject Code	Study 6 (MAMUCS II)			Study 7 (Manual)		
	Mean Estimate	CV1 (%)	CV2 (%)	Mean Estimate	CV1 (%)	CV2 (%)
1R	207	21	14	165	30	9.7
1L	268	32	6.3	195	33	3.9
2R	192	15	15	145	11	8.3
2L	288	12	6.6	217	18	17
3R	227	14	4.7	122	20	7.4
* 3L	313	41	20	159	29	7.0
4R	283	51	11	178	15	8.3
4L	155	46	13	88	38	14
5R	184	34	7.6	114	22	13
5L	291	38	17	116	27	8.1
Mean	241	30	11	150	24	9.5
St.Dev.	54.6	14	5.0	40.4	8.5	3.6

* - Only 4 test sessions conducted on this muscle

fact that the variability of the MEP feature between sessions has almost doubled is less easily explained. The source of this variability may be physiological (changes in tissue fluid content, etc.), or a variable gain factor may have been introduced by the instrumentation. If this is the case, the fact that the template discrimination threshold is fixed means that some of the variability in the estimates could be introduced by response misclassification. An indepth analysis of the extracted MUAPs similar to that performed for the thenar studies will be performed for the EDB studies for future publication.

As was the case with the thenar studies, the manual operator obtained more repeatable estimates than the automated system from session to session. However, it must be remembered that the automated system executes each test independently and can in no way benefit from a priori knowledge about a particular subject. While the experimental protocol was designed such that it was unlikely that the operator would recall numerical data associated with previous sessions, the possibility exists that he might recall information about the pattern of increments in the CR. This could have an impact on the estimated counts. In any case, from the viewpoint of standardizing the test, the automated system performed quite well compared to what might be expected if a different operator were used for each manual estimate. In addition, repeatability of results does not imply accuracy.

If we assume that each independent test (including reinstrumentation) gives an unbiased estimate of the true motor unit count, then averaging N estimates should reduce the standard error by a

factor of $1/\sqrt{N}$ (Snedecor and Cochran, 1980). While a manual estimate requires that slow and painstaking measurements be made by a well trained operator, the speed of the automated system permits the performance of repeated tests without the need for concern over operator fatigue. During these studies it was found that a complete test including instrumentation took approximately the same time using the current development version of the automated system (MAMUCS II) as it did when performed manually. A more streamlined clinical version will omit some of the hardcopy and display functions to speed up the test.

5.4 Other Muscles

Encouraging results have been obtained for preliminary tests on several other muscles including the biceps brachii and vastus medialis. Delegating the tedious task of conducting the tests to the computer frees the clinical researcher to devote his energy and concentration to designing experiments to test the suitability of various muscles as well as different instrumentation configurations.

While all the studies described thus far have involved clinically normal subjects, it is interesting to note that several anomalies were observed nevertheless. Unfortunately, a study involving post polio syndrome patients had to be postponed. A preliminary test on one patient however gave an EDB count of 16. In effect, no extrapolation was performed since the CR included the MEP. In fact, it was difficult to eliminate voluntary backround EMG and several of these increments were visually judged to be spurious. In cases of chronic deinnervation with

collateral reinnervation, the resulting enlarged MUAPs should pose few problems for any estimation technique, automated or otherwise. In myopathies, where MUAPs of decreased size are observed, the enhanced resolution of the automated system should allow the identification of CR increments typically overlooked by the manual operator. In pathologies where increased temporal dispersion of the MUAPs is observed, the use of response area as the extrapolation feature should produce more accurate estimates (Ballantyne and Hansen, 1974).

The response classification algorithms have been designed to have good discrimination power with a variety of signal waveforms as it is dangerous to make assumptions about the shape of responses that can be expected from any particular muscle. When a full database of normal and abnormal test results has been compiled, analysis may point out ways in which the system can be improved without compromising its robustness.

CHAPTER 6

CONCLUSION

While the human brain performs pattern classification as a matter of course it must be remembered that the computer is essentially a device for performing arithmetic computation. The computer is well suited to data aquisition, computation, and data storage. However, even rudimentary forms of pattern recognition such as the template matching described in this thesis pose serious problems when speed and memory space are constraints. While improved performance can be obtained by making assumptions about what types of signals will have to be classified, this a priori knowledge will actually degrade the performance of the system when abnormal waveforms are encountered.

The automation of the McComas incremental motor unit counting technique has progressed in an evolutionary manner. Each successive version of the automated system revealed new insights and new problems. The computer provides facilities for signal processing and analysis unavailable to the operator who is constrained to making visual measurements from an oscilloscope display. As is typically the case, this enhanced analytical capability has raised more questions than it has answered.

By reducing the manual operator's heuristic approach to implementing the McComas technique to a structured algorithm with quantified decision criteria, a significant step has been made in the standardization of motor unit counting for clinical use. More importantly, establishing more definite decision criteria for the test procedure allows a systematic investigation of the effects of varying the test parameters. The speed and relative ease with which a test can be performed using this system makes it practical to repeat clinical tests for increased accuracy while the automatic storage of collected data on magnetic media permits simple and accurate archiving for research purposes.

While several ways of improving the system have been evident for some time, it was desirable to conclude the studies being conducted before undertaking any modification. Suggested hardware changes include the use of a constant current stimulator with a biphasic stimulation waveform which is anticipated to provide better correlation between stimulus amplitude and response size, lower stimulus artifact, and less discomfort for the subject. It has also been noted that several preamplifiers, especially isolated ones, have proved to be less prone to stimulus artifact. Furthermore, it is recommended that a thorough study of various stimulating and recording electrode types and placements be conducted so that optimum configurations can be established for each muscle to be tested.

The software itself can be improved as it migrates from the PDP-11/34 to a 80386 based micro-computer. The increased speed and memory

capacity will remove several constraints on the software while the use of an accessible processor will facilitate the efficient clinical deployment of the system.

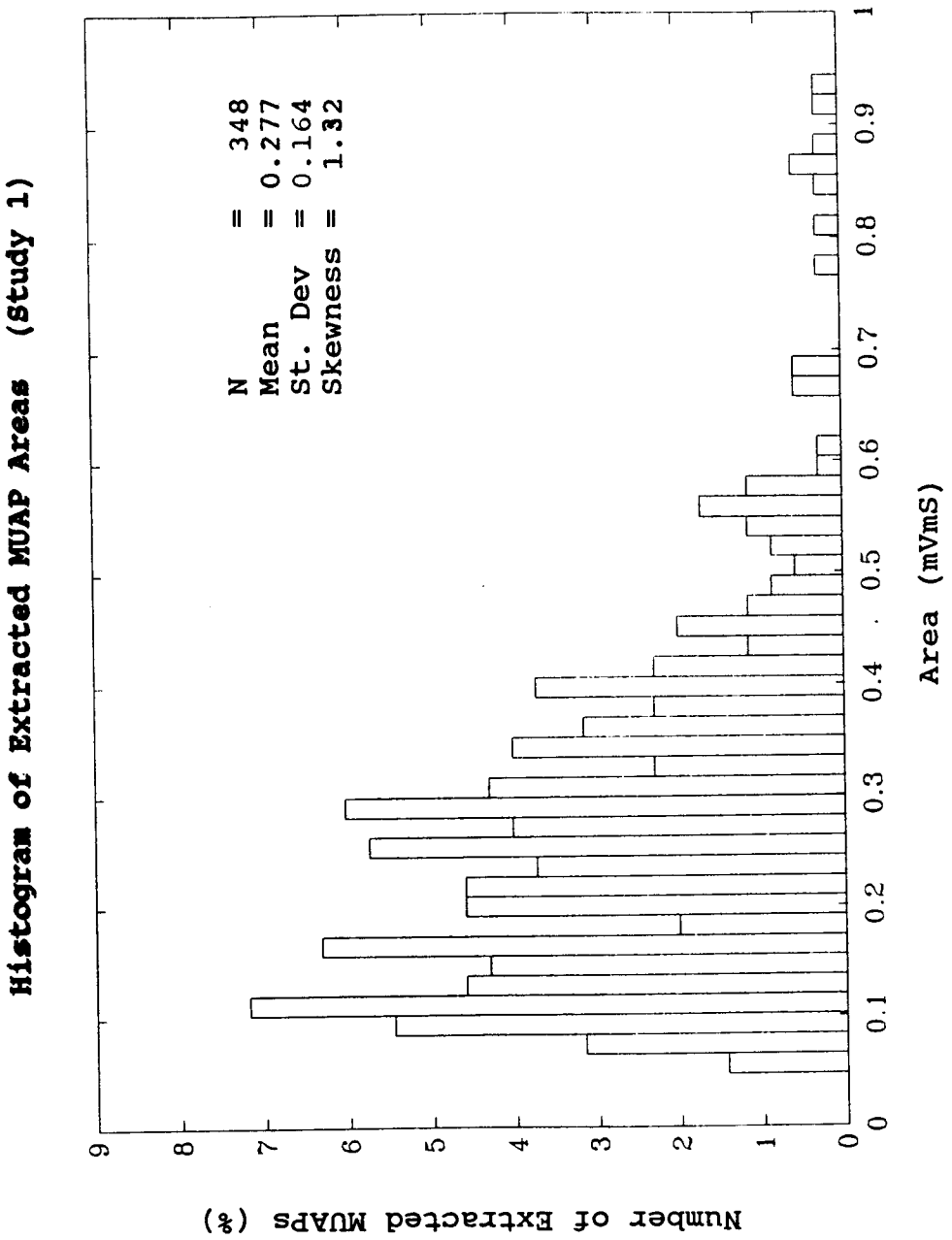
Test data obtained from future studies on post polio syndrome and ALS patients combined with the existing database for normals will be used to assess the current response classification system with a view towards improving both performance and robustness. Although most of the algorithms will remain virtually unchanged, the next phase of development will involve streamlining the code to make it more user friendly and hardware independent.

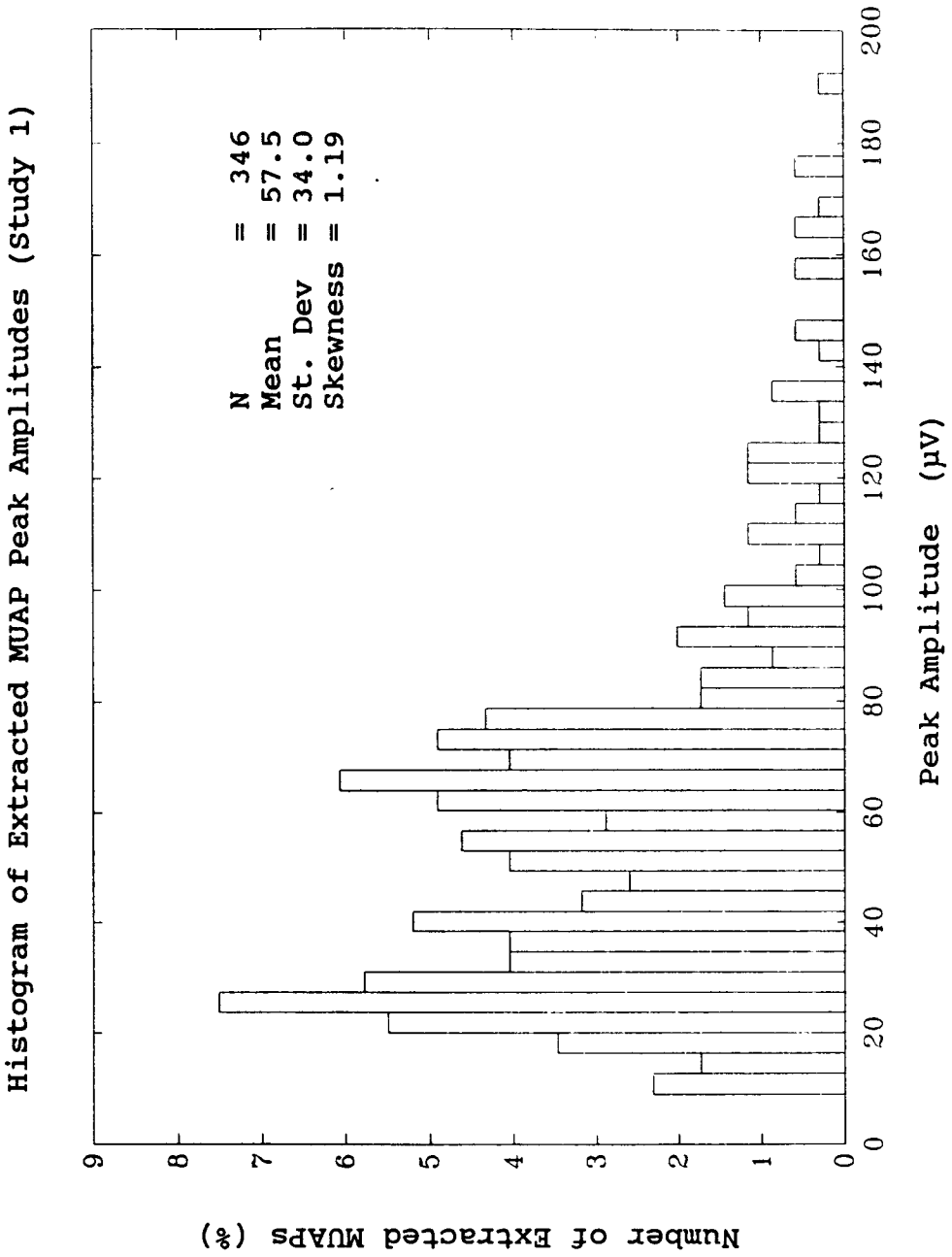
The current system was designed for research and displays a great deal of information which, while useful to the developer, is of little interest to the clinician. The comparative studies and use of the system by people other than the developer has provided invaluable insights into how user selectable test parameters, display functions, and data archiving should be organized for clinical use.

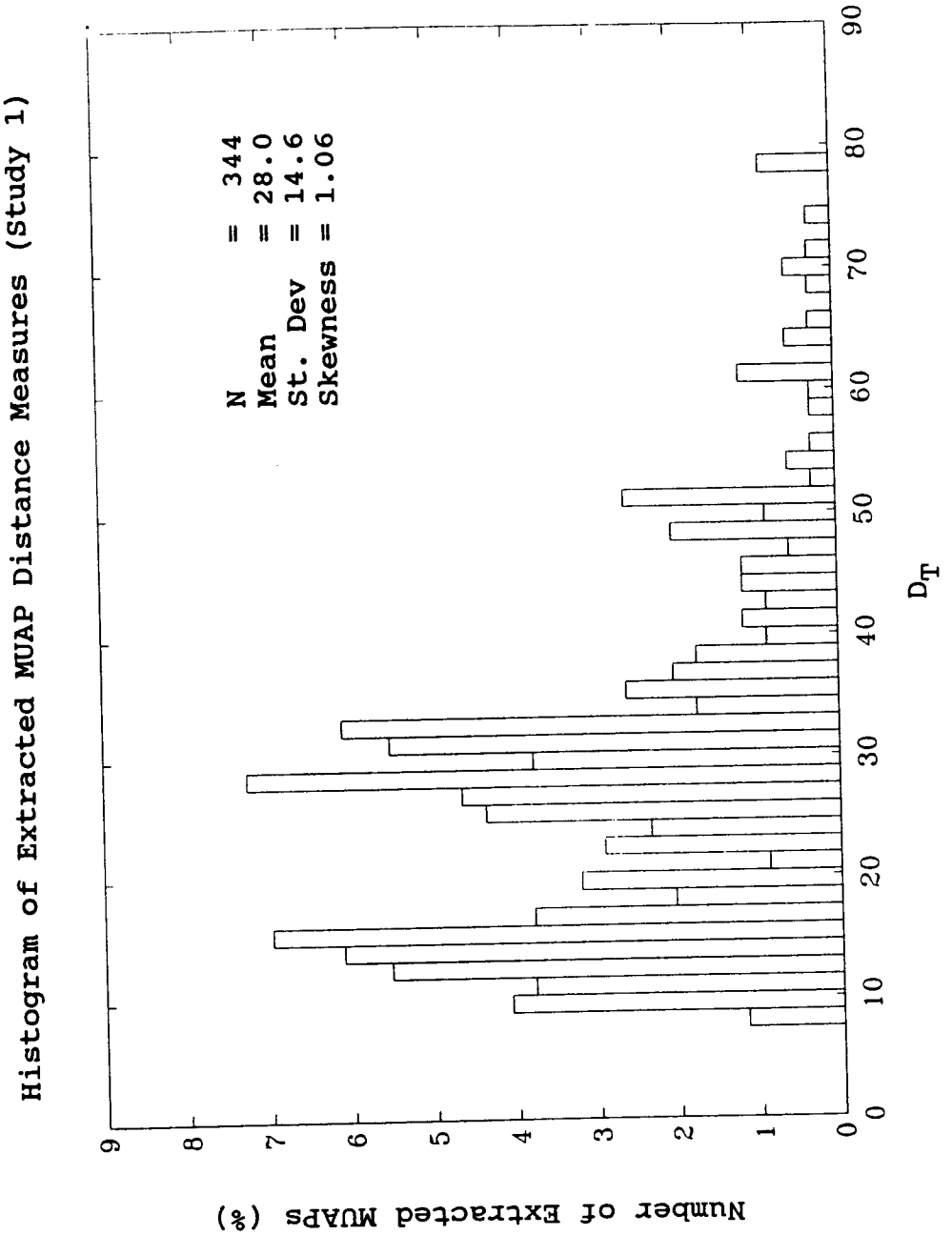
While there may still be problems associated with the fundamental assumptions upon which the McComas technique is based, it was never the objective of this project to validate the technique itself. The goal was rather to provide a useful tool for the researcher and clinician. In addition, the research was aimed at establishing a structured, standardized framework within which these problems might be rigorously investigated and hopefully resolved. The results of the preliminary testing described in this thesis as well as the direction that future research is taking demonstrate that this goal has been achieved.

APPENDIX A HISTOGRAM PLOTS OF EXTRACTED MUAP FEATURES

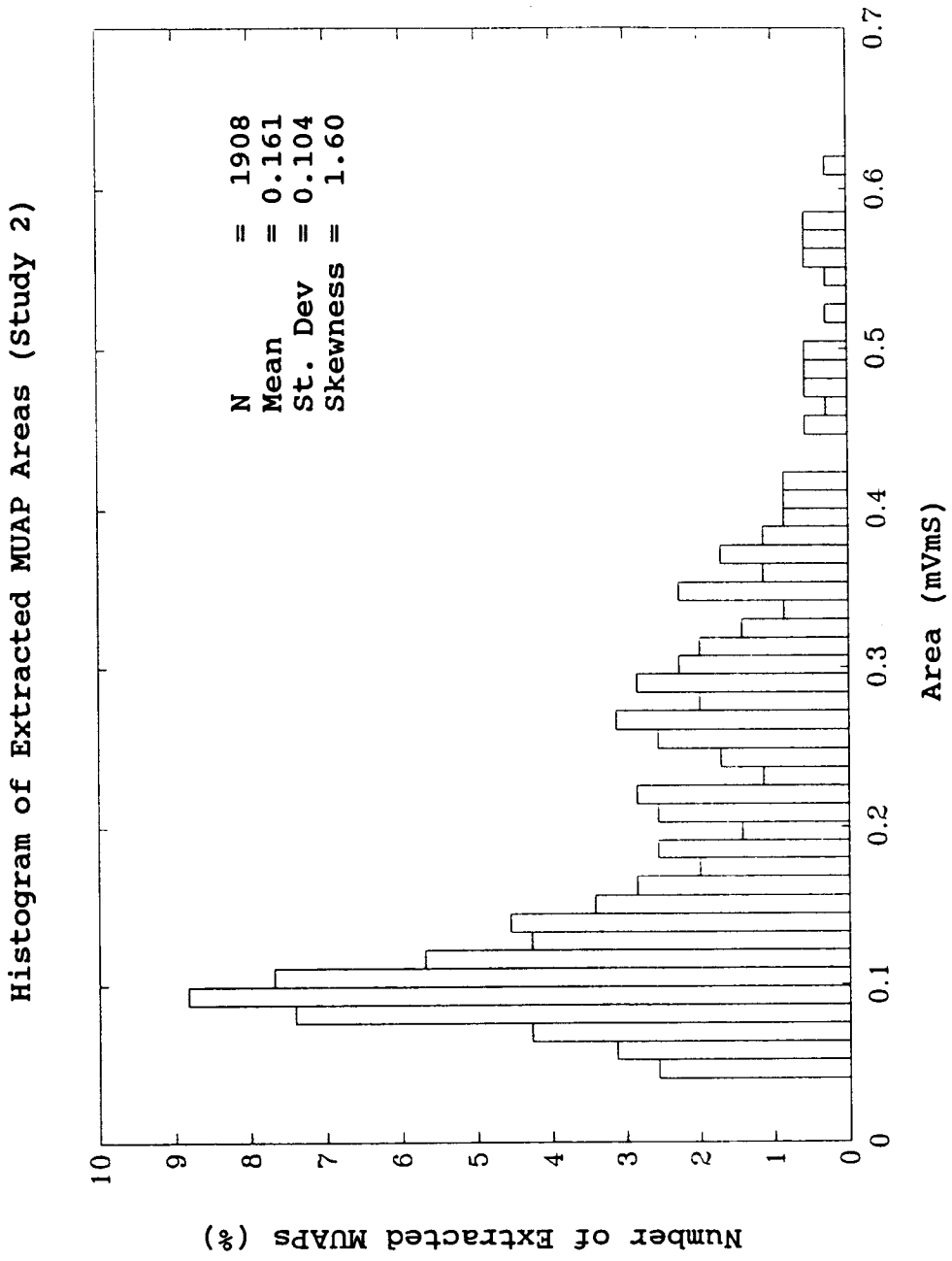
A.1 Histograms for Study 1

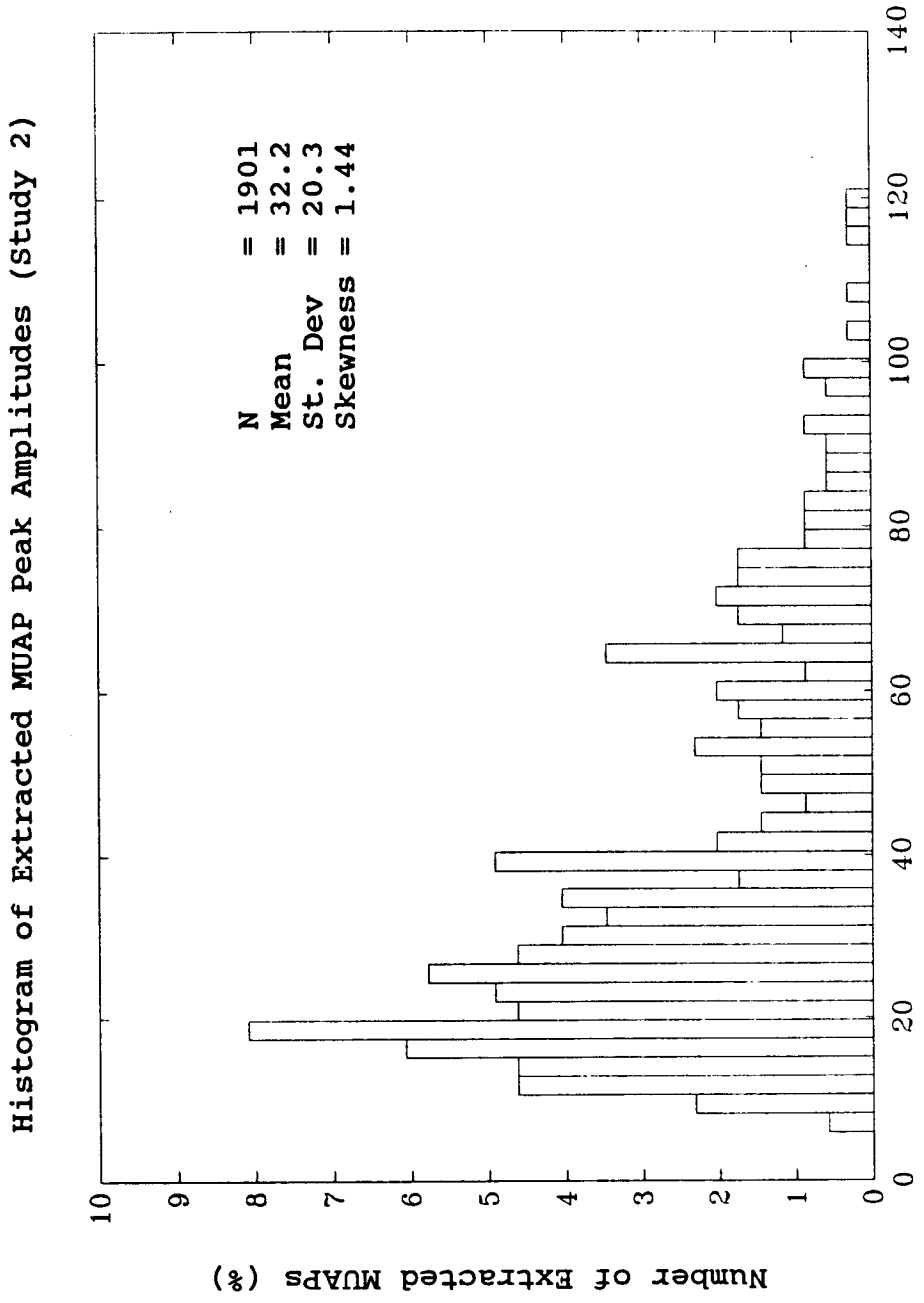

Histogram of Extracted MUAP Areas (Study 1)
N = 348
Mean = 0.277
St. Dev = 0.164
Skewness = 1.32
Number of Extracted MUAPs (%)
Area (mVmS)
0
1
2
3
4
5
6
7
8
9
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1

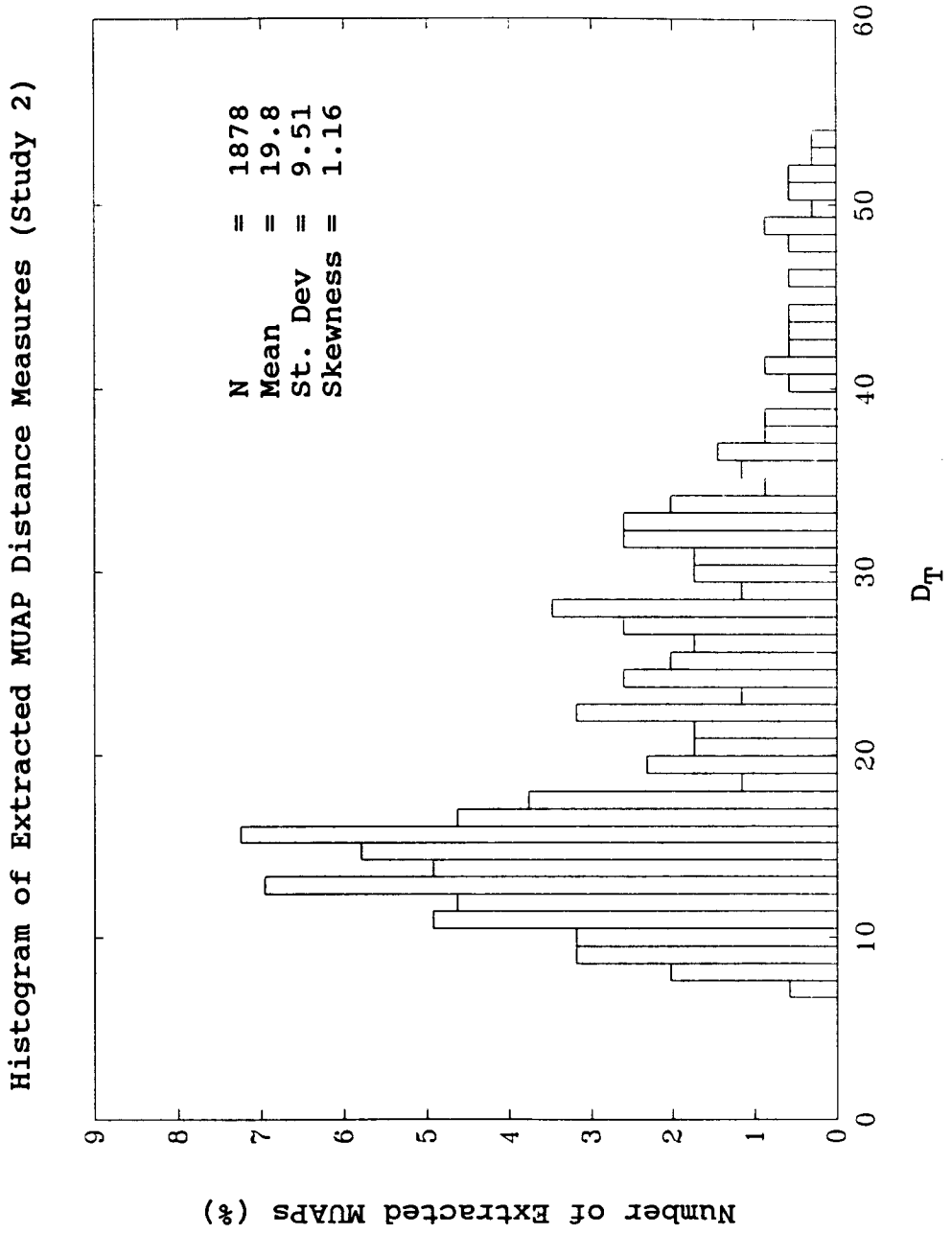

Histogram of Extracted MUAP Peak Amplitudes (Study 1)
N = 346
Mean = 57.5
St. Dev = 34.0
Skewness = 1.19
Number of Extracted MUAPs (%)
Peak Amplitude (μV)
0
1
2
3
4
5
6
7
8
9
0
20
40
60
80
100
120
140
160
180
200


Histogram of Extracted MUAP Distance Measures (Study 1)
N = 344
Mean = 28.0
St. Dev = 14.6
Skewness = 1.06
Number of Extracted MUAPs (%)
D_T
0
1
2
3
4
5
6
7
8
9
10
20
30
40
50
60
70
80
90

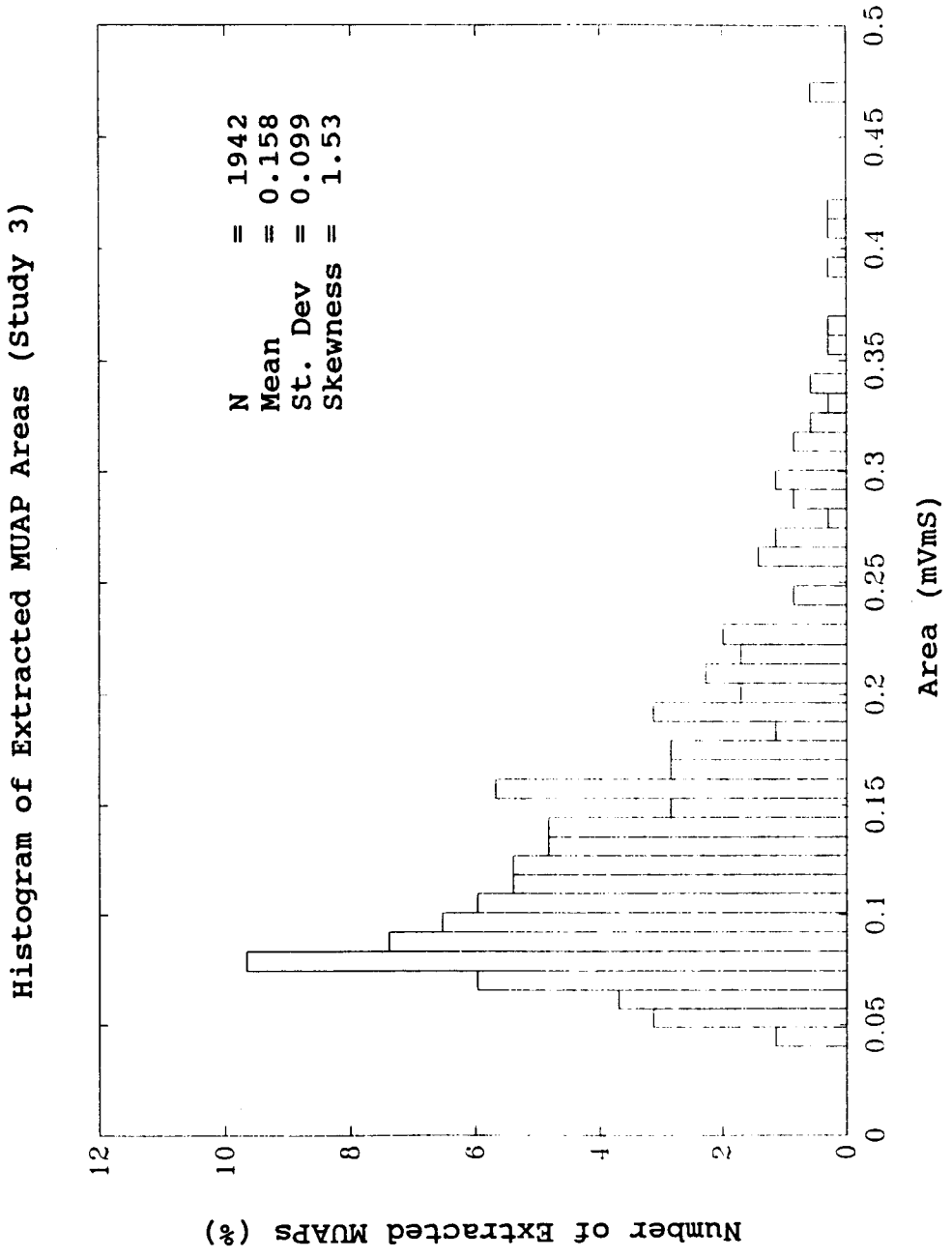
A.2 Histograms for Study 2

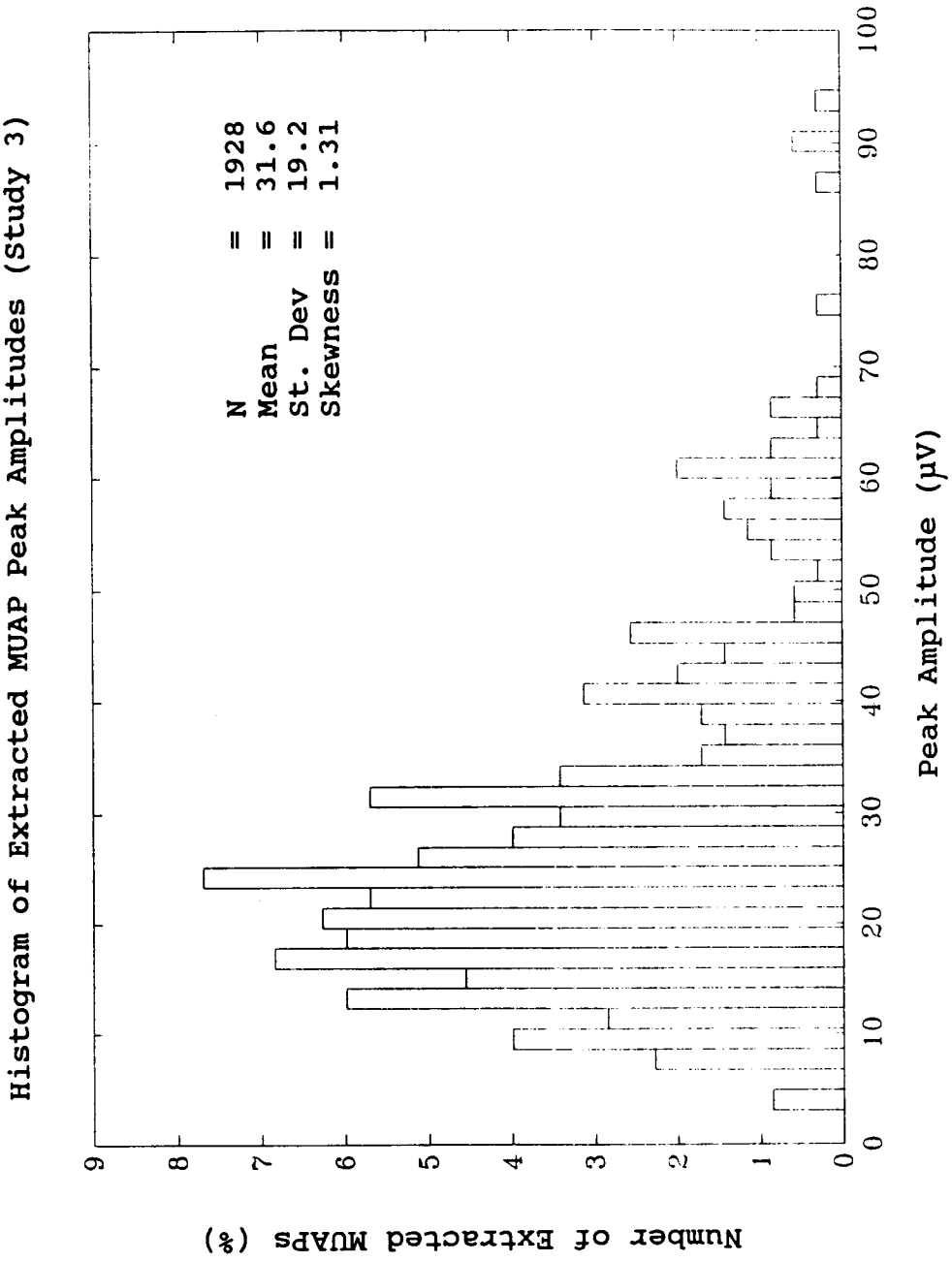

Histogram of Extracted MUAP Areas (Study 2)
N = 1908
Mean = 0.161
St. Dev = 0.104
Skewness = 1.60
Number of Extracted MUAPs (%)
Area (mVmS)
0
1
2
3
4
5
6
7
8
9
10
0.1
0.2
0.3
0.4
0.5
0.6
0.7

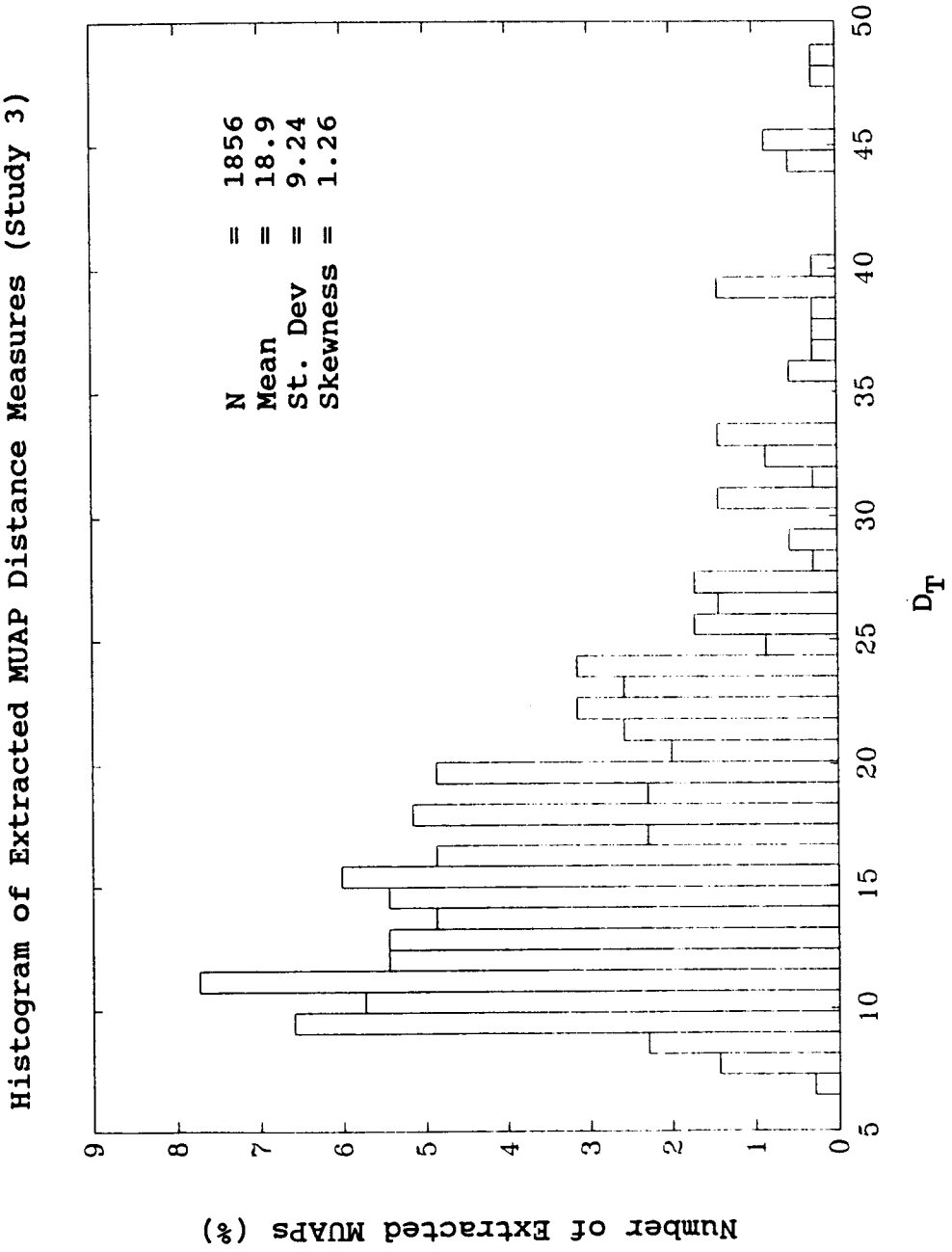

Histogram of Extracted MUAP Peak Amplitudes (Study 2)
N = 1901
Mean = 32.2
St. Dev = 20.3
Skewness = 1.44
Number of Extracted MUAPs (%)
Peak Amplitude (μV)
0
1
2
3
4
5
6
7
8
9
10
0
20
40
60
80
100
120
140


Histogram of Extracted MUAP Distance Measures (Study 2)
N = 1878
Mean = 19.8
St. Dev = 9.51
Skewness = 1.16
Number of Extracted MUAPs (%)
D_T
0
1
2
3
4
5
6
7
8
9
10
20
30
40
50
60

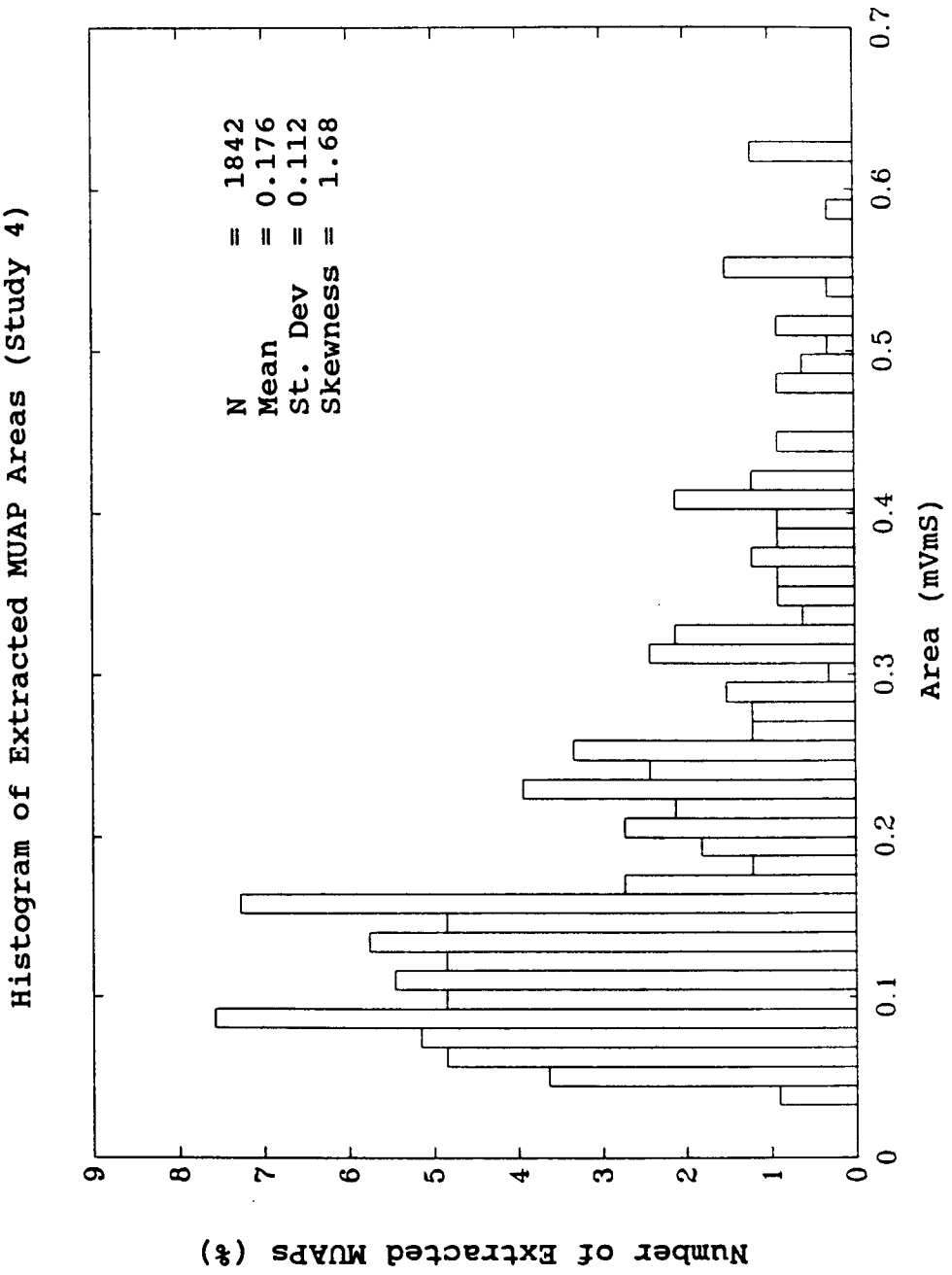
A.3 Histograms for Study 3

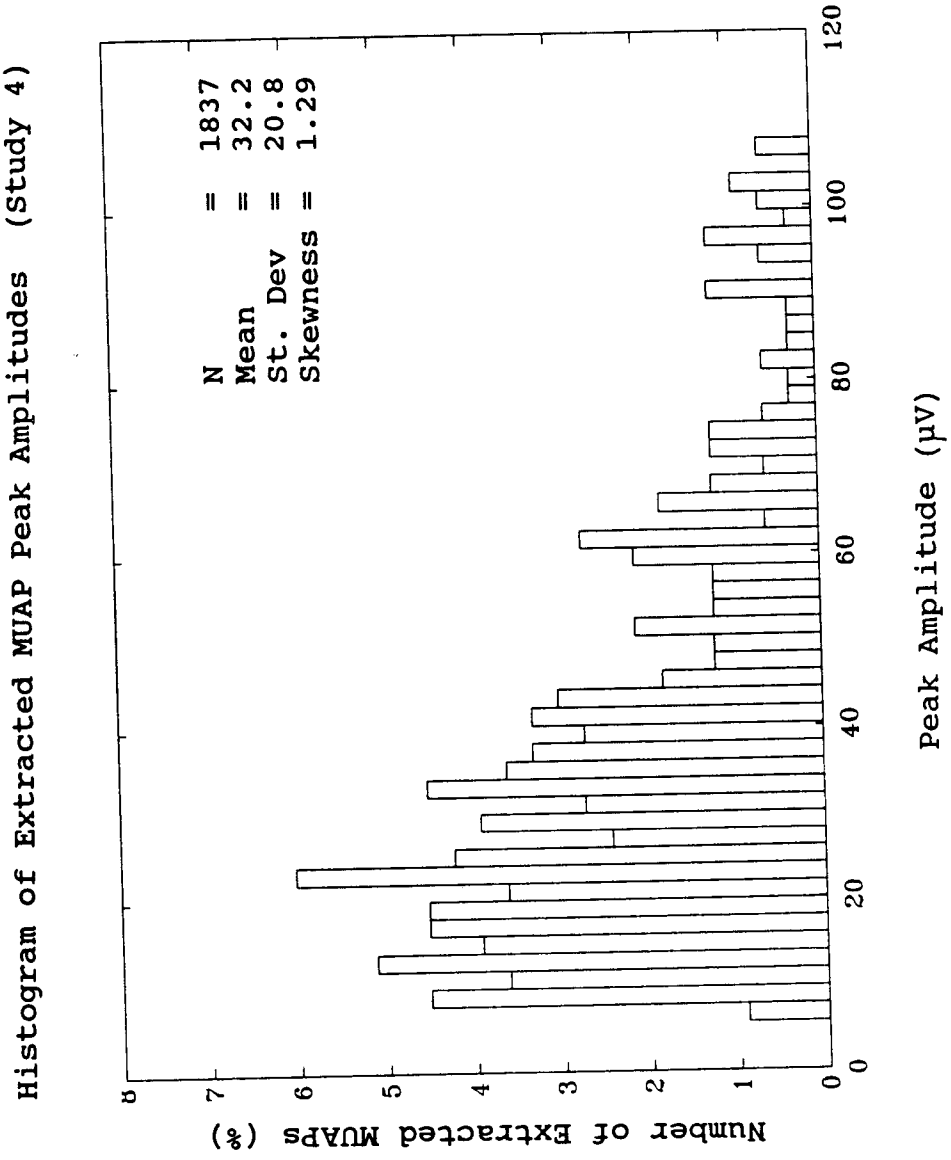

Histogram of Extracted MUAP Areas (Study 3)
N = 1942
Mean = 0.158
St. Dev = 0.099
Skewness = 1.53
Number of Extracted MUAPs (%)
Area (mVmS)
0
2
4
6
8
10
12
0
0.05
0.1
0.15
0.2
0.25
0.3
0.35
0.4
0.45
0.5

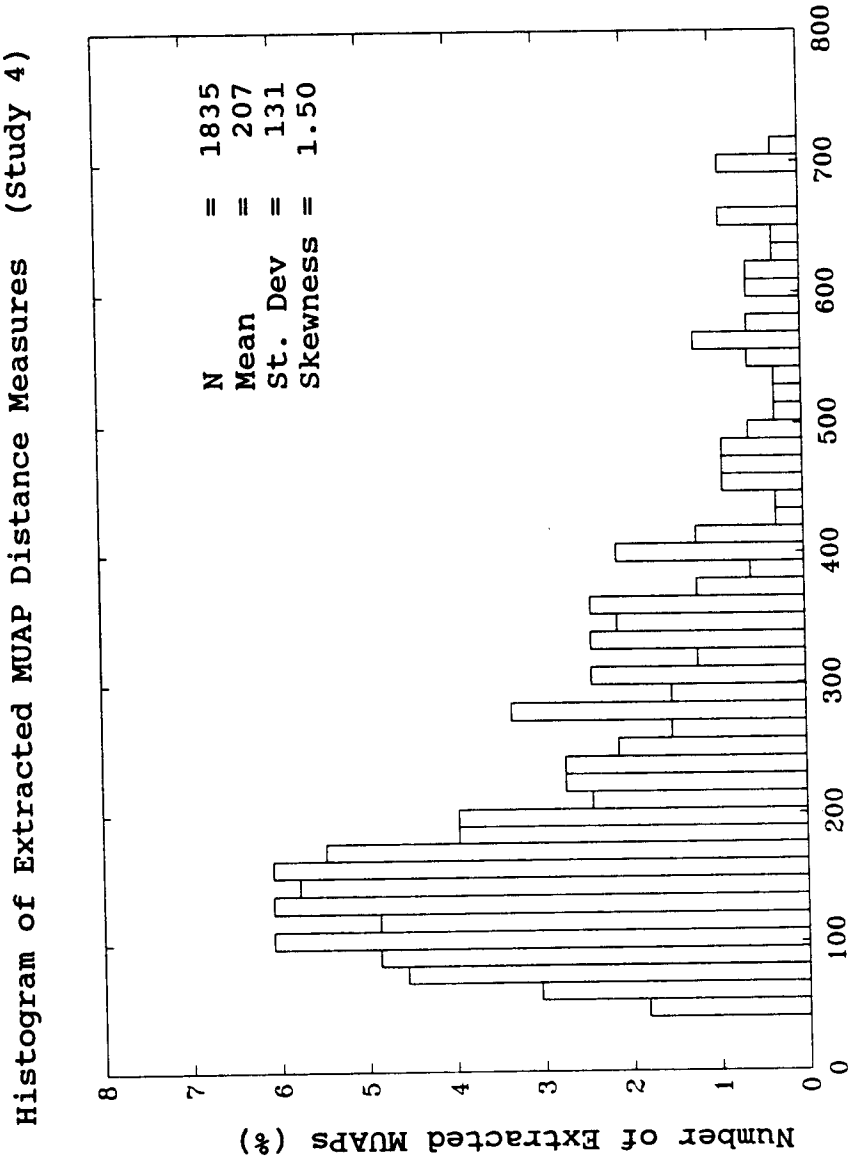

Histogram of Extracted MUAP Peak Amplitudes (Study 3)
N = 1928
Mean = 31.6
St. Dev = 19.2
Skewness = 1.31
Number of Extracted MUAPs (%)
Peak Amplitude (μV)
0
1
2
3
4
5
6
7
8
9
0
10
20
30
40
50
60
70
80
90
100


Histogram of Extracted MUAP Distance Measures (Study 3)
N = 1856
Mean = 18.9
St. Dev = 9.24
Skewness = 1.26
Number of Extracted MUAPs (%)
D_T
0
1
2
3
4
5
6
7
8
9
5
10
15
20
25
30
35
40
45
50

A.4 Histograms for Study 4


Histogram of Extracted MUAP Areas (Study 4)
N = 1842
Mean = 0.176
St. Dev = 0.112
Skewness = 1.68
Number of Extracted MUAPs (%)
Area (mVmS)
0
1
2
3
4
5
6
7
8
9
0.1
0.2
0.3
0.4
0.5
0.6
0.7


Histogram of Extracted MUAP Peak Amplitudes (Study 4)
N = 1837
Mean = 32.2
St. Dev = 20.8
Skewness = 1.29
Number of Extracted MUAPs (%)
0
1
2
3
4
5
6
7
8
0
20
40
60
80
100
120
Peak Amplitude (μV)


Histogram of Extracted MUAP Distance Measures (Study 4)
N = 1835
Mean = 207
St. Dev = 131
Skewness = 1.50
Number of Extracted MUAPs (%)
0
1
2
3
4
5
6
7
8
0
100
200
300
400
500
600
700
800
D_T

APPENDIX B TEST RESULT SUMMARIES

B.1 Test Result Summaries for Study 3

Study 3 (MAMUCS 1)

Subject #1 Right Thenar

Test results - Extrapolation Method #1

Test #	No. of Alternations	MEP Area (mV*mS)	AMUAP Area (mV*mS)	Estimate By Area	EFI (%)
1	0	28.50	0.0725	392	17.0
2	0	27.90	0.0715	388	21.2
3	0	26.10	0.0474	550	24.2
4	0	26.80	0.0468	572	26.7
5	0	32.10	0.1375	232	25.5
6	1	31.70	0.1347	235	22.5
7	0	30.60	0.0406	753	18.0
8	0	29.70	0.0477	622	25.6
9	0	29.40	0.0364	808	34.5
10	0	30.90	0.0247	1250	38.1
			Mean EFI		25.3

Session averages

Session #	MEP Area (mV*mS)	AMUAP Area (mV*mS)	Estimate By Area
1	28.20	0.0720	390
2	26.45	0.0471	561
3	31.90	0.1361	233
4	30.15	0.0441	687
5	30.15	0.0306	1029
Mean	29.37	0.0660	580
St. Dev.	2.0924	0.0420	304
CV1	0.0712	0.6359	0.5240
Intra-session			
CV2	0.0198	0.0838	0.0965

Study 3 (MAMUCS I)

Subject #1 Left Thenar

Test results - Extrapolation Method #1

Test #	No. of Alternations	MEP Area (mV*mS)	AMUAP Area (mV*mS)	Estimate By Area	EFI (%)
1	1	24.10	0.0837	288	28.6
2	1	25.40	0.0858	295	26.8
3	0	32.40	0.1115	290	22.3
4	0	33.30	0.0630	528	21.5
5	0	21.20	0.0710	297	12.7
6	1	22.40	0.0858	261	17.9
7	0	22.40	0.0770	290	29.9
8	0	22.50	0.0790	284	29.6
9	3	27.30	0.0641	427	30.3
10	2	27.40	0.0739	372	21.0
			Mean EFI		24.1

Session averages

Session #	MEP Area (mV*mS)	AMUAP Area (mV*mS)	Estimate By Area
1	24.75	0.0847	291
2	32.85	0.0873	409
3	21.80	0.0784	279
4	22.45	0.0780	287
5	27.35	0.0690	399
Mean	25.84	0.0795	333
St. Dev.,	4.4839	0.0071	65
CV1	0.1735	0.0892	0.1954
Intra-session			
CV2	0.0202	0.1325	0.1264

Study 3 (MAMUCS I)

Subject #2 Right Thenar

Test results - Extrapolation Method #1

Test #	No. of Alternations	MEP Area (mV*mS)	AMUAP Area (mV*mS)	Estimate By Area	EFI (%)
1	1	44.70	0.0716	626	146.0
2	0	45.20	0.0780	581	137.0
3	0	55.40	0.0880	629	53.7
4	0	58.20	0.1110	523	63.1
5	0	52.70	0.0855	614	174.0
6	0	52.70	0.0473	1120	162.0
7	1	49.70	0.0905	549	131.0
8	0	52.60	0.0695	754	137.0
9	0	52.30	0.0755	693	173.0
10	1	52.50	0.0637	824	180.0
			Mean EFI		135.7

Session averages

Session #	MEP Area (mV*mS)	AMUAP Area (mV*mS)	Estimate By Area
1	44.95	0.0748	603
2	56.80	0.0995	576
3	52.70	0.0664	867
4	51.15	0.0800	651
5	52.40	0.0696	758
Mean	51.60	0.0781	691
St. Dev.	4.2812	0.0131	120
CV1	0.0830	0.1673	0.1741
Intra-session			
CV2	0.0171	0.1874	0.1880

Study 3 (MAMUCS I)

Subject #2 Left Thenar

Test results - Extrapolation Method #1

Test #	No. of Alternations	MEP Area (mV*mS)	AMUAP Area (mV*mS)	Estimate By Area	EFI (%)
1	0	42.20	0.1025	411	24.1
2	0	43.60	0.1000	437	23.1
3	0	48.70	0.0470	1040	51.6
4	0	50.70	0.0700	723	57.4
5	0	58.40	0.0755	774	37.4
6	0	58.50	0.0930	628	29.2
7	0	47.20	0.0461	1030	110.0
8	0	48.40	0.0442	1090	125.0
9	0	53.60	0.1485	361	22.2
10	3	54.70	0.1194	458	29.4
			Mean EFI		50.9

Session averages

Session #	MEP Area (mV*mS)	AMUAP Area (mV*mS)	Estimate By Area
1	42.90	0.1013	424
2	49.70	0.0585	881
3	58.45	0.0843	701
4	47.80	0.0451	1060
5	54.15	0.1340	409
Mean	50.60	0.0846	695
St. Dev.	5.9616	0.0352	284
CV1	0.1178	0.4160	0.4087
Intra-session			
CV2	0.0170	0.1253	0.1305

Study 3 (MAMUCS I)

Subject #3 Right Thenar

Test results - Extrapolation Method #1

Test #	No. of Alternations	MEP Area (mV*mS)	AMUAP Area (mV*mS)	Estimate By Area	EFI (%)
1	1	54.40	0.2474	219	27.9
2	1	51.50	0.2321	221	26.9
3	2	68.50	0.3089	221	23.5
4	0	68.80	0.3325	206	22.0
5	2	69.60	0.3367	206	28.9
6	2	69.80	0.1872	372	27.8
7	2	83.20	0.3578	232	23.9
8	2	83.10	0.3611	230	24.7
9	1	62.50	0.2732	228	33.2
10	0	59.00	0.2505	235	33.4
			Mean EFI		27.2

Session averages

Session #	MEP Area (mV*mS)	AMUAP Area (mV*mS)	Estimate By Area
1	52.95	0.2397	220
2	68.65	0.3207	213
3	69.70	0.2619	289
4	83.15	0.3594	231
5	60.75	0.2618	231
Mean	67.04	0.2887	237
St. Dev.	11.2616	0.0497	30
CV1	0.1680	0.1720	0.1268
Intra-session			
CV2	0.0171	0.1136	0.0980

Study 3 (MAMUCS I)

Subject #3 Left Thenar

Test results - Extrapolation Method #1

Test #	No. of Alternations	MEP Area (mV*mS)	AMUAP Area (mV*mS)	Estimate By Area	EFI (%)
1	0	58.50	0.0466	1260	18.3
2	0	56.70	0.0397	1430	30.0
3	0	64.20	0.0243	2640	50.7
4	0	59.70	0.0202	2950	99.8
5	0	68.50	0.0208	3290	42.5
6	0	65.40	0.0282	2320	32.4
7	0	70.10	0.0202	3480	32.1
8	0	68.40	0.0261	2620	30.4
9	0	57.50	0.0241	2390	30.4
10	0	56.10	0.0319	1760	30.6
			Mean EFI		39.7

Session averages

Session #	MEP Area (mV*mS)	AMUAP Area (mV*mS)	Estimate By Area
1	57.60	0.0432	1345
2	61.95	0.0223	2795
3	66.95	0.0245	2805
4	69.25	0.0232	3050
5	56.80	0.0280	2075
Mean	62.51	0.0282	2414
St. Dev.	5.5265	0.0086	700
CV1	0.0884	0.3061	0.2900
Intra-session			
CV2	0.0282	0.1677	0.1653

Study 3 (MAMUCS I)

Subject #4 Right Thenar

Test results - Extrapolation Method #1

Test #	No. of Alternations	MEP Area (mV*mS)	AMUAP Area (mV*mS)	Estimate By Area	EFI (%)
1	0	30.30	0.0205	1480	63.4
2	0	29.70	0.0215	1380	56.7
3	0	26.80	0.0400	671	28.3
4	0	25.40	0.0289	879	31.4
5	0	35.90	0.0178	2010	93.3
6	0	34.90	0.0190	1840	60.0
7	0	41.20	0.0252	1630	80.0
8	0	37.90	0.0212	1790	84.4
9	0	46.50	0.0379	1230	33.2
10	0	45.20	0.0250	1810	46.6
			Mean EFI		57.7

Session averages

Session #	MEP Area (mV*mS)	AMUAP Area (mV*mS)	Estimate By Area
1	30.00	0.0210	1430
2	26.10	0.0344	775
3	35.40	0.0184	1925
4	39.55	0.0232	1710
5	45.85	0.0314	1520
Mean	35.38	0.0257	1472
St. Dev.	7.7793	0.0069	433
CV1	0.2199	0.2686	0.2945
Intra-session			
CV2	0.0302	0.1442	0.1275

Study 3 (MAMUCS I)

Subject #4 Left Thenar

Test results - Extrapolation Method #1

Test #	No. of Alternations	MEP Area (mV*mS)	AMUAP Area (mV*mS)	Estimate By Area	EFI (%)
1	0	30.60	0.0433	705	27.5
2	0	29.70	0.0416	715	24.0
3	0	31.60	0.0730	433	14.1
4	0	28.50	0.0495	575	20.8
5	0	34.30	0.0336	1022	48.5
6	0	34.70	0.0474	732	56.7
7	0	32.90	0.0565	583	34.4
8	0	31.70	0.0550	577	34.2
9	0	30.90	0.0227	1360	66.3
10	0	28.20	0.0249	1130	64.8
			Mean EFI		39.1

Session averages

Session #	MEP Area (mV*mS)	AMUAP Area (mV*mS)	Estimate By Area
1	30.15	0.0425	710
2	30.05	0.0612	504
3	34.50	0.0405	877
4	32.30	0.0558	580
5	29.55	0.0238	1245
Mean	31.31	0.0447	783
St. Dev.	2.0729	0.0146	294
CV1	0.0662	0.3267	0.3759
Intra-session			
CV2	0.0386	0.1255	0.1162

Study 3 (MAMUCS I)

Subject #5 Right Thenar

Test results - Extrapolation Method #1

Test #	No. of Alternations	MEP Area (mV*mS)	AMUAP Area (mV*mS)	Estimate By Area	EFI (%)
1	1	35.60	0.0932	382	14.3
2	0	32.40	0.0850	380	12.1
3	0	31.90	0.1395	229	19.9
4	0	28.70	0.1390	206	19.5
5	0	37.00	0.1380	268	23.7
6	0	35.70	0.1260	282	22.6
7	1	43.80	0.1426	306	16.4
8	1	40.90	0.1111	368	19.9
9	0	36.90	0.1460	252	14.7
10	0	36.20	0.1015	357	15.2
			Mean EFI		17.8

Session averages

Session #	MEP Area (mV*mS)	AMUAP Area (mV*mS)	Estimate By Area
1	34.00	0.0891	381
2	30.30	0.1392	217
3	36.35	0.1320	275
4	42.35	0.1268	337
5	36.55	0.1238	304
Mean	35.91	0.1222	303
St. Dev.	4.3931	0.0194	61
CV1	0.1223	0.1589	0.2044
Intra-session			
CV2	0.0457	0.1124	0.0977

Study 3 (MAMUCS I)

Subject #6 Right Thenar

Test results - Extrapolation Method #1

Test #	No. of Alternations	MEP Area (mV*mS)	AMUAP Area (mV*mS)	Estimate By Area	EFI (%)
1	1	47.20	0.0294	1600	32.7
2	0	48.50	0.0386	1260	49.3
3	0	62.60	0.0417	1500	71.7
4	0	66.00	0.0426	1550	89.1
5	0	61.70	0.0430	1430	85.0
6	0	63.90	0.0444	1440	81.2
7	0	65.80	0.0510	1290	83.1
8	0	63.30	0.0294	2150	101.0
9	0	62.30	0.0445	1400	25.8
10	0	59.00	0.0317	1860	74.9
			Mean EFI		69.4

Session averages

Session #	MEP Area (mV*mS)	AMUAP Area (mV*mS)	Estimate By Area
1	47.85	0.0340	1430
2	64.30	0.0422	1525
3	62.80	0.0437	1435
4	64.55	0.0402	1720
5	60.65	0.0381	1630
Mean	60.03	0.0396	1548
St. Dev.	6.9834	0.0038	126
CV1	0.1163	0.0953	0.0814
Intra-session			
CV2	0.0294	0.1688	0.1499

B.2 Test Result Summaries for Study 4

Study 4 (MAMUCS II)

Subject #1 Right Thenar

Test results - Extrapolation Method #1

Test #	No. of Alternations	MEP Area (mV*mS)	AMUAP Area (mV*mS)	Estimate By Area	EFI (%)
1	2	28.90	0.0830	348	13.5
2	1	30.56	0.1030	296	18.3
3	1	28.03	0.0722	388	25.9
4	0	28.37	0.0713	397	20.6
5	1	34.78	0.1470	236	24.1
6	2	32.96	0.1371	240	24.9
7	1	31.53	0.0647	487	24.5
8	0	31.07	0.0727	427	19.8
9	2	30.36	0.0763	397	37.4
10	2	28.33	0.0591	479	27.7
			Mean EFI		23.7

Session averages

Session #	MEP Area (mV*mS)	AMUAP Area (mV*mS)	Estimate By Area
1	29.73	0.0930	322
2	28.20	0.0718	392
3	33.87	0.1421	238
4	31.30	0.0687	457
5	29.35	0.0677	438
Mean	30.49	0.0887	369
St. Dev.	2.1897	0.0316	90
CV1	0.0718	0.3563	0.2437
Intra-session			
CV2	0.0291	0.0943	0.0735

Study 4 (MAMUCS II)

Subject #1 Left Thenar

Test results - Extrapolation Method #1

Test #	No. of Alternations	MEP Area (mV*mS)	AMUAP Area (mV*mS)	Estimate By Area	EFI (%)
1	1	25.33	0.1063	238	18.7
2	0	25.96	0.0833	311	25.4
3	2	32.10	0.1097	292	24.8
4	1	32.19	0.1059	303	26.8
5	1	23.17	0.1086	213	18.8
6	3	22.60	0.1174	192	18.4
7	0	22.61	0.1001	225	27.1
8	0	23.08	0.1013	227	25.8
9	0	27.84	0.1038	268	18.1
10	2	28.97	0.1000	289	18.5
			Mean EFI		22.2

Session averages

Session #	MEP Area (mV*mS)	AMUAP Area (mV*mS)	Estimate By Area
1	25.65	0.0948	274
2	32.15	0.1078	297
3	22.89	0.1130	202
4	22.85	0.1007	226
5	28.41	0.1019	278
Mean	26.39	0.1037	255
St. Dev.	3.9552	0.0070	39
CV1	0.1499	0.0674	0.1555
Intra-session			
CV2	0.0159	0.0572	0.0694

Study 4 (MAMUCS II)

Subject #2 Right Thenar

Test results - Extrapolation Method #1

Test #	No. of Alternations	MEP Area (mV*mS)	AMUAP Area (mV*mS)	Estimate By Area	EFI (%)
1	0	41.65	0.0790	527	135.0
2	3	41.71	0.0920	453	135.7
3	0	56.83	0.0861	659	61.7
4	0	55.30	0.1318	419	80.5
5	1	53.73	0.0892	601	151.7
6	2	55.02	0.0898	612	155.9
7	0	51.67	0.0930	555	121.0
8	0	53.68	0.0966	555	146.5
9	1	51.32	0.0952	538	141.9
10	1	53.81	0.0843	638	131.9
			Mean EFI		126.2

Session averages

Session #	MEP Area (mV*mS)	AMUAP Area (mV*mS)	Estimate By Area
1	41.68	0.0855	490
2	56.06	0.1089	539
3	54.37	0.0895	606
4	52.67	0.0948	555
5	52.56	0.0898	588
Mean	51.47	0.0937	555
St. Dev.	5.6582	0.0091	45
CV1	0.1099	0.0975	0.0816
Intra-session			
CV2	0.0195	0.1042	0.1109

Study 4 (MAMUCS II)

Subject #2 Left Thenar

Test results - Extrapolation Method #1

Test #	No. of Alternations	MEP Area (mV*mS)	AMUAP Area (mV*mS)	Estimate By Area	EFI (%)
1	0	39.40	0.1026	384	25.5
2	0	39.74	0.1136	349	20.0
3	0	48.81	0.0472	1033	81.4
4	0	48.53	0.0585	829	45.4
5	0	57.07	0.1118	510	29.1
6	0	56.02	0.1296	432	14.9
7	0	48.85	0.0675	724	96.4
8	0	49.07	0.0551	889	116.3
9	1	54.99	0.1108	496	55.7
10	1	54.78	0.1022	536	31.0
			Mean EFI		51.6

Session averages

Session #	MEP Area (mV*mS)	AMUAP Area (mV*mS)	Estimate By Area
1	39.57	0.1081	366
2	48.67	0.0529	931
3	56.54	0.1207	471
4	48.96	0.0613	806
5	54.89	0.1065	516
Mean	49.73	0.0899	618
St. Dev.	6.6696	0.0306	239
CV1	0.1341	0.3404	0.3868
Intra-session			
CV2	0.0058	0.1053	0.1078

Study 4 (MAMUCS II)

Subject #3 Right Thenar

Test results - Extrapolation Method #1

Test #	No. of Alternations	MEP Area (mV*mS)	AMUAP Area (mV*mS)	Estimate By Area	EFI (%)
1	3	53.18	0.3462	153	26.5
2	3	55.69	0.3651	152	26.6
3	3	67.15	0.4062	165	21.7
4	6	66.59	0.3714	179	22.9
5	5	69.77	0.4232	164	23.4
6	4	66.39	0.4058	163	24.3
7	5	79.46	0.5644	140	22.8
8	3	80.40	0.5092	157	21.1
9	0	50.46	0.3218	156	31.3
10	2	55.62	0.3767	147	31.9
			Mean EFI		25.2

Session averages

Session #	MEP Area (mV*mS)	AMUAP Area (mV*mS)	Estimate By Area
1	54.43	0.3556	152
2	66.87	0.3888	172
3	68.08	0.4145	163
4	79.93	0.5368	148
5	53.04	0.3493	151
Mean	64.47	0.4090	157
St. Dev.	11.0591	0.0761	9
CV1	0.1715	0.1862	0.0625
Intra-session			
CV2	0.0301	0.0629	0.0379

Study 4 (MAMUCS II)

Subject #3 Left Thenar

Test results - Extrapolation Method #1

Test #	No. of Alternations	MEP Area (mV*mS)	AMUAP Area (mV*mS)	Estimate By Area	EFI (%)
1	1	60.34	0.0362	1668	11.3
2	1	60.01	0.0489	1228	13.2
3	0	59.30	0.0323	1835	43.1
4	1	58.77	0.0259	2265	39.7
5	0	74.08	0.0371	1999	28.7
6	0	73.94	0.0352	2101	30.2
7	0	69.35	0.0237	2932	63.3
8	4	70.02	0.0347	2020	28.8
9	0	56.93	0.0363	1568	32.9
10	0	58.63	0.0312	1881	19.6
			Mean EFI		31.1

Session averages

Session #	MEP Area (mV*mS)	AMUAP Area (mV*mS)	Estimate By Area
1	60.18	0.0425	1448
2	59.04	0.0291	2050
3	74.01	0.0361	2050
4	69.69	0.0292	2476
5	57.78	0.0337	1724
Mean	64.14	0.0341	1949
St. Dev.	7.2530	0.0056	387
CV1	0.1131	0.1633	0.1986
Intra-session			
CV2	0.0078	0.1554	0.1574

Study 4 (MAMUCS II)

Subject #4 Right Thenar

Test results - Extrapolation Method #1

Test #	No. of Alternations	MEP Area (mV*mS)	AMUAP Area (mV*mS)	Estimate By Area	EFI (%)
1	0	28.86	0.0206	1401	55.3
2	1	27.49	0.0290	947	52.4
3	0	25.20	0.0541	465	32.4
4	0	25.33	0.0423	598	40.5
5	0	36.65	0.0360	1018	40.4
6	1	38.04	0.0506	752	30.3
7	0	39.26	0.0318	1234	37.8
8	2	39.94	0.0308	1296	50.8
9	3	43.34	0.0347	1248	31.7
10	0	44.42	0.0305	1455	40.3
			Mean EFI		41.2

Session averages

Session #	MEP Area (mV*mS)	AMUAP Area (mV*mS)	Estimate By Area
1	28.17	0.0248	1174
2	25.26	0.0482	531
3	37.34	0.0433	885
4	39.60	0.0313	1265
5	43.88	0.0326	1351
Mean	34.85	0.0360	1041
St. Dev.	7.8541	0.0095	334
CV1	0.2254	0.2633	0.3214
Intra-session			
CV2	0.0188	0.1528	0.1612

Study 4 (MAMUCS II)

Subject #4 Left Thenar

Test results - Extrapolation Method #1

Test #	No. of Alternations	MEP Area (mV*mS)	AMUAP Area (mV*mS)	Estimate By Area	EFI (%)
1	3	27.61	0.0579	476	15.6
2	1	30.40	0.0588	516	21.0
3	0	27.09	0.0659	411	15.5
4	0	28.32	0.0678	417	16.0
5	2	31.14	0.0630	494	44.4
6	0	29.60	0.0550	538	36.5
7	1	32.53	0.0833	390	15.1
8	3	29.82	0.0674	442	30.3
9	0	28.11	0.0379	740	62.9
10	1	30.44	0.0379	803	63.6
			Mean EFI		32.1

Session averages

Session #	MEP Area (mV*mS)	AMUAP Area (mV*mS)	Estimate By Area
1	29.00	0.0584	496
2	27.71	0.0668	414
3	30.37	0.0590	516
4	31.17	0.0754	416
5	29.27	0.0379	771
Mean	29.50	0.0595	522
St. Dev.	1.3288	0.0139	146
CV1	0.0450	0.2337	0.2803
Intra-session			
CV2	0.0506	0.0552	0.0547

Study 4 (MAMUCS II)

Subject #5 Right Thenar

Test results - Extrapolation Method #1

Test #	No. of Alternations	MEP Area (mV*mS)	AMUAP Area (mV*mS)	Estimate By Area	EFI (%)
1	1	32.45	0.0992	327	13.5
2	1	33.70	0.1026	328	13.0
3	0	30.57	0.1216	251	17.2
4	0	30.14	0.1453	207	18.9
5	1	32.52	0.1645	197	25.3
6	1	32.44	0.1590	204	23.3
7	1	34.29	0.1073	319	12.4
8	0	37.89	0.1327	285	20.5
9	0	35.13	0.1663	211	16.0
10	0	36.11	0.0976	370	21.1
			Mean EFI		18.1

Session averages

Session #	MEP Area (mV*mS)	AMUAP Area (mV*mS)	Estimate By Area
1	33.08	0.1009	327
2	30.35	0.1334	229
3	32.48	0.1618	200
4	36.09	0.1200	302
5	35.62	0.1320	290
Mean	33.52	0.1296	269
St. Dev.	2.3621	0.0222	53
CV1	0.0705	0.1713	0.1966
Intra-session			
CV2	0.0257	0.1383	0.1259

Study 4 (MAMUCS II)

Subject #6 Right Thenar

Test results - Extrapolation Method #1

Test #	No. of Alternations	MEP Area (mV*mS)	AMUAP Area (mV*mS)	Estimate By Area	EFI (%)
1	3	52.59	0.0646	813	58.7
2	1	55.28	0.0575	961	20.9
3	2	62.99	0.0636	990	86.6
4	0	65.89	0.0483	1362	95.9
5	3	63.40	0.0516	1228	85.5
6	1	64.95	0.0451	1439	92.3
7	1	59.11	0.0474	1247	87.0
8	0	57.60	0.0409	1409	97.8
9	0	59.56	0.0752	792	61.3
10	0	56.71	0.0554	1023	65.6
			Mean EFI		75.2

Session averages

Session #	MEP Area (mV*mS)	AMUAP Area (mV*mS)	Estimate By Area
1	53.94	0.0611	887
2	64.44	0.0560	1176
3	64.18	0.0484	1333
4	58.35	0.0441	1328
5	58.13	0.0653	907
Mean	59.81	0.0550	1126
St. Dev.	4.4700	0.0087	218
CV1	0.0747	0.1590	0.1941
Intra-session			
CV2	0.0274	0.1379	0.1440

B.3 Test Result Summaries for Study 5

Study 5 (Manual)

Subject #1 Right Thenar

Test results - Manual Estimation

Test #	MEP Peak (mV)	Estimated count
1	6.90	184
2	6.70	149
3	7.10	222
4	6.90	263
5	9.60	163
6	8.40	195
7	7.40	247
8	8.00	229
9	7.40	329
10	7.20	206

Session averages

Session #	MEP Peak (mV)	Estimated count
1	6.80	166
2	7.00	242
3	9.00	179
4	7.70	238
5	7.30	267
Mean	7.56	218.70
St. Dev.	0.87	43.65
CV1	0.1155	0.1996
	Intra-session	
CV2	0.0420	0.1546

Study 5 (Manual)

Subject #1 Left Thenar

Test results - Manual Estimation

Test #	MEP Peak (mV)	Estimated count
1	6.80	222
2	6.40	185
3	7.00	144
4	6.80	165
5	6.40	160
6	6.80	136
7	5.90	197
8	6.00	222
9	7.00	226
10	7.00	273

Session averages

Session #	MEP Peak (mV)	Estimated count
1	6.60	203
2	6.90	154
3	6.60	148
4	5.95	209
5	7.00	249
Mean	6.61	193.00
St. Dev.	0.41	42.08
CV1	0.0620	0.2180
Intra-session		
CV2	0.0236	0.1114

Study 5 (Manual)

Subject #2 Right Thenar

Test results - Manual Estimation

Test #	MEP Peak (mV)	Estimated count
1	10.80	218
2	9.80	196
3	14.00	200
4	14.00	212
5	15.50	271
6	15.00	250
7	13.00	289
8	12.80	256
9	16.00	307
10	13.00	213

Session averages

Session #	MEP Peak (mV)	Estimated count
1	10.30	207
2	14.00	206
3	15.25	260
4	12.90	272
5	14.50	260
Mean	13.39	241.20
St. Dev.	1.93	32.07
CV1	0.1439	0.1330
Intra-session		
CV2	0.0498	0.1029

Study 5 (Manual)

Subject #2 Left Thenar

Test results - Manual Estimation

Test #	MEP Peak (mV)	Estimated count
1	10.60	212
2	10.40	223
3	12.80	256
4	12.80	256
5	14.00	327
6	13.50	270
7	15.50	291
8	15.00	293
9	15.00	225
10	16.00	206

Session averages

Session #	MEP Peak (mV)	Estimated count
1	10.50	217
2	12.80	256
3	13.75	298
4	15.25	292
5	15.50	215
Mean	13.56	255.90
St. Dev.	2.04	39.45
CV1	0.1502	0.1542
Intra-session		
CV2	0.0216	0.0476

Study 5 (Manual)

Subject #3 Right Thenar

Test results - Manual Estimation

Test #	MEP Peak (mV)	Estimated count
1	14.00	66
2	13.00	76
3	13.50	71
4	13.50	93
5	15.50	98
6	15.50	95
7	16.00	102
8	16.00	121
9	13.00	97
10	12.50	88

Session averages

Session #	MEP Peak (mV)	Estimated count
1	13.50	71
2	13.50	82
3	15.50	96
4	16.00	111
5	12.75	92
Mean	14.25	90.70
St. Dev.	1.41	15.27
CV1	0.0992	0.1684
Intra-session		
CV2	0.0160	0.1001

Study 5 (Manual)

Subject #3 Left Thenar

Test results - Manual Estimation

Test #	MEP Peak (mV)	Estimated count
1	17.00	785
2	16.00	549
3	14.50	655
4	14.00	723
5	16.00	706
6	16.00	632
7	18.50	816
8	16.50	643
9	14.50	709
10	14.00	636

Session averages

Session #	MEP Peak (mV)	Estimated count
1	16.50	667
2	14.25	689
3	16.00	669
4	17.50	729
5	14.25	672
Mean	15.70	685.40
St. Dev.	1.43	26.13
CV1	0.0911	0.0381
Intra-session		
CV2	0.0347	0.1285

Study 5 (Manual)

Subject #4 Right Thenar

Test results - Manual Estimation

Test #	MEP Peak (mV)	Estimated count
1	8.00	366
2	7.80	390
3	6.80	408
4	6.80	378
5	9.80	470
6	10.00	553
7	11.40	597
8	10.20	567
9	11.20	535
10	11.40	597

Session averages

Session #	MEP Peak (mV)	Estimated count
1	7.90	378
2	6.80	393
3	9.90	511
4	10.80	582
5	11.30	566
Mean	9.34	486.10
St. Dev.	1.92	95.63
CV1	0.2060	0.1967
Intra-session		
CV2	0.0247	0.0655

Study 5 (Manual)

Subject #4 Left Thenar

Test results - Manual Estimation

Test #	MEP Peak (mV)	Estimated count
1	8.20	301
2	7.80	306
3	9.20	230
4	9.00	266
5	8.20	312
6	8.00	320
7	8.80	299
8	8.40	269
9	7.80	300
10	7.60	355

Session averages

Session #	MEP Peak (mV)	Estimated count
1	8.00	303
2	9.10	248
3	8.10	316
4	8.60	284
5	7.70	327
Mean	8.30	295.80
St. Dev.	0.55	31.21
CV1	0.0665	0.1055
Intra-session		
CV2	0.0239	0.0651

Study 5 (Manual)

Subject #5 Right Thenar

Test results - Manual Estimation

Test #	MEP Peak (mV)	Estimated count
1	9.00	130
2	9.40	101
3	8.40	183
4	8.40	202
5	8.00	123
6	8.60	166
7	9.20	207
8	9.20	178
9	9.40	192
10	9.40	246

Session averages

Session #	MEP Peak (mV)	Estimated count
1	9.20	115
2	8.40	192
3	8.30	144
4	9.20	192
5	9.40	219
Mean	8.90	172.80
St. Dev.	0.51	41.82
CV1	0.0573	0.2420
Intra-session		
CV2	0.0164	0.1477

Study 5 (Manual)

Subject #6 Right Thenar

Test results - Manual Estimation

Test #	MEP Peak (mV)	Estimated count
1	8.80	229
2	8.80	249
3	14.00	498
4	13.50	431
5	11.20	336
6	12.00	391
7	11.80	343
8	11.40	342
9	11.80	327
10	11.40	343

Session averages

Session #	MEP Peak (mV)	Estimated count
1	8.80	239
2	13.75	464
3	11.60	363
4	11.60	342
5	11.60	335
Mean	11.47	348.90
St. Dev.	1.76	80.45
CV1	0.1534	0.2306
Intra-session		
CV2	0.0246	0.0608

REFERENCES

Ballantyne, J.P. and S. Hansen. "A new method for the estimation of the number of motor units in a muscle.
1. Control subjects and patients with myasthenia gravis", Journal of Neurology, Neurosurgery and Psychiatry, 37, 1974, 907-915.

Basmajian, J.V. Muscles Alive: Their function revealed through electromyography, 4th Ed. Baltimore: Williams and Wilkins Co., 1979.

Brown, W.F. and H.S. Milner-Brown. "Some electrical properties of motor units and their effects on the methods of estimating motor unit numbers", Journal of Neurology, Neurosurgery and Psychiatry, 39, 1976, 249-257.

De Koning, P., G.H. Wiencke, D. Van der Most van Spijk, A.C. Van Huffelen, W.H. Gispen, and F.G.I. Jennekens. "Estimation of the number of motor units based on macro-EMG", Journal of Neurology, Neurosurgery and Psychiatry, 51, 1988, 403-411.

Feasby, T.E. and W.F. Brown. "Variation of motor unit size in the human extensor digitorum brevis and thenar muscles", Journal of Neurology, Neurosurgery and Psychiatry, 37, 1974, 916-926.

Jasechko, J.G. Automatic estimation of the number of muscle motor units, Master's Thesis. Hamilton: McMaster University, 1987.

Kadrie, H.A., S.K. Yates, H.S. Milner-Brown, and W.F. Brown. "Multiple point electrical stimulation of ulnar and median nerves", Journal of Neurology, Neurosurgery and Psychiatry, 39, 1976, 973-985.

Leifer, L.J. "Nerve-fiber conduction velocity distributions: motor nerve studies using collision neurography", Conduction velocity distributions: A Population Approach to Electrophysiology of Nerve. New York: Alan R. Liss, Inc., 1981.

McComas, A.J., P.R.W. Fawcett, M.J. Campbell, and R.E.P. Sica. "Electrophysiological estimation of the number of motor units within a human muscle", Journal of Neurology, Neurosurgery and Psychiatry, 34, 1971, 121-131.

Milner-Brown, H.S. and W.F. Brown. "New methods of estimating the number of motor units in a muscle," Journal of Neurology, Neurosurgery and Psychiatry, 39, 1976, 258-265.

Panayiotopoulos, C.P., S. Scarpalezos, and Th. Papapetropoulos. "Electrophysiological estimation of motor units in Duchenne muscular dystrophy", Journal of Neurological Sciences, 23, 1974, 89-98.

Plonsey, R. Bioelectric Phenomena. New York: Mcgraw-Hill, 1969.

Principe, J.C. and J.R. Smith. "Design and implementation of linear phase FIR filters for biological signal processing", IEEE Transactions on Biomedical Engineering, vol. BME-33, no. 6, 1986, 550-559.

Rasminski, M. and T.A. Sears. "Internodal conduction in undissected demyelinated nerve fibres", Journal of Physiology, 227, 1972, 323-350.

Sica, R.E.P., A.J. McComas, A.R.M. Upton, and D. Longmire. "Motor unit estimation in small muslces of the hand", Journal of Neurology, Neurosurgery and Psychiatry, 37, 1974, 55-67.

Snedecor, G.W. and W.G. Cochran. Statistical Methods 7th Ed. Iowa State University Press, 1980.