Development of thumb-force-measurement system for single human thenar motor unit twitch tension measurements
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twitch tension measurements

Ellen Olmer
February 1995

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single human thenar motor unit
twitch tension measurements

Ellen Olmer*,#
February 1995

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Preface

A dream has come true for me. Being so lucky to get an invitation of Prof. A. Pedotti in Milano, Italy and one of Dr. J. Fozard in Baltimore, I was able to do the internships, necessary for my study Medical Mechanical Engineering", abroad which have been a great experience.

The Dutch Heart Foundation, "de Nederlandse Hartstichting", has made the internships financial possible by giving me a student fund, for which I am very grateful.

I would like to thank Jeffrey and Elayne Metter for their welcome and introduction in the USA. Also the time spent with Caroline Nelka, a BLSA participant, was wonderful.

During the time in Baltimore at the Baltimore Longitudinal Study of Aging, I have had the good fortune to work with many people who have contributed significantly to the completion of this internship.

Excellent technical support was provided by Reginald Quilter from the National Institute of Health at Baltimore. His efforts and talents are gratefully acknowledged.

1994 was a year of great experience and the support of my family and friends helped me abroad. Finally I would like to thank Fred for all his stimulation and support. I can look backward to a wonderful year, in which I came in contact with many people in a medical and technical environment, and who made this of such a great experience for me.
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List of Abbreviations

BLSA : Baltimore Longitudinal Study of Aging
CT : Contraction Time
3-D : 3-dimensional
EMG : Electromyography, Electromyographic
IGF-1 : Insulin Growth Factor-I
MCR : Maximum Contraction Rates
MF : Muscle Fiber
MPS : Multiple Point Stimulation
MU : Motor Unit
sMU : single Motor Unit
MUP : Motor Unit Potential
sMUP : single Motor Unit Potential
MUAP : Motor Unit Action Potential
sMUAP : single Motor Unit Action Potential
MVC : Maximum Voluntary Contraction
½RT : One-half Relaxation Time
SD : Standard Deviation
STA : Spike Triggered Averaging
TFM-system : Thumb-Force-Measurement system
TMP : Transmembrane Potential
VO₂max : Maximum Oxygen Uptake
# Metric Units and Prefixes

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Unit</th>
<th>Definition</th>
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<tbody>
<tr>
<td>A</td>
<td>ampere</td>
<td>current</td>
</tr>
<tr>
<td>c</td>
<td>centi</td>
<td>$= 10^2$</td>
</tr>
<tr>
<td>c/s</td>
<td>cycles per second</td>
<td></td>
</tr>
<tr>
<td>dB</td>
<td>decibel</td>
<td>charge</td>
</tr>
<tr>
<td>g</td>
<td>gram</td>
<td>mass</td>
</tr>
<tr>
<td>Hz</td>
<td>Hertz</td>
<td>frequency</td>
</tr>
<tr>
<td>&quot;</td>
<td>inch</td>
<td>length</td>
</tr>
<tr>
<td>k</td>
<td>kilo</td>
<td>$= 10^3$</td>
</tr>
<tr>
<td>m</td>
<td>milli</td>
<td>$= 10^{-3}$</td>
</tr>
<tr>
<td>m</td>
<td>meter</td>
<td>length</td>
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<tr>
<td>μ</td>
<td>micro</td>
<td>$= 10^{-6}$</td>
</tr>
<tr>
<td>N</td>
<td>Newton</td>
<td>kgm/s²</td>
</tr>
<tr>
<td>s</td>
<td>second</td>
<td>time</td>
</tr>
<tr>
<td>V</td>
<td>Volt</td>
<td>electric potential</td>
</tr>
<tr>
<td>O</td>
<td>Ohm</td>
<td>electrical Ohm</td>
</tr>
<tr>
<td>yr</td>
<td>year</td>
<td>time</td>
</tr>
</tbody>
</table>
List of symbols

A  cross-sectional area
b  width
E  modulus of elasticity; Young's modulus
F  force
F_v  vertical load
F_v * l  bending moment
GF  gage factor
h  thickness
l  length
rms  root mean square average
Z  sectional

ε  strain
ε_B  bending strain
σ  stress
σ_B  moment stress
### Definition of terms

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Action potential</td>
<td>Brief, regenerative, &quot;all-or-nothing&quot; electrical potential that propagates along an axon or muscle fiber.</td>
</tr>
<tr>
<td>Contraction time (CT)</td>
<td>Time from onset of muscle force response to peak twitch tension.</td>
</tr>
<tr>
<td>Electromyogram</td>
<td>Muscle electrical recording detected by external electrodes.</td>
</tr>
<tr>
<td>Electromyography (EMG)</td>
<td>Electromyography is the study and use of the EMG signal that originates in the membrane of muscle fibers as they contract.</td>
</tr>
<tr>
<td>F-response</td>
<td>Recurrent potential produced by re-excitation of the motor neuron cell body or initial segment following activation of the motor axon in the periphery.</td>
</tr>
<tr>
<td>M-potential</td>
<td>Surface-detected compound muscle action potential.</td>
</tr>
<tr>
<td>Motor unit (MU)</td>
<td>A single motor neuron, its motor axon, and the muscle fibers it innervates.</td>
</tr>
<tr>
<td>One-half relaxation time (½RT)</td>
<td>Recovery time from peak muscle twitch force to a value one-half of the peak.</td>
</tr>
<tr>
<td>MUAP</td>
<td>The action potential produced by a single motor unit, voluntary or electrically evoked.</td>
</tr>
<tr>
<td>S-MUAP</td>
<td>Surface-detected motor unit action potential.</td>
</tr>
<tr>
<td>Twitch contraction</td>
<td>A brief muscular contraction produced by a single motor unit action potential.</td>
</tr>
</tbody>
</table>
Changes in cardiovascular and muscular performance with advancing age can affect functional capacity. The growing group of elderly may be at risk for being functionally limited due to declines in muscle mass and the associated loss in muscle strength with advancing age. Muscle strength begins to decrease after the fifth decade. Causes of muscle atrophy, declining strength, and physical frailty with advancing age are not completely known. The Baltimore Longitudinal Study of Aging is developing several research protocols which focus on the general area of frailty and physical independence. Relationships between physiological factors and age associated loss of muscle strength will be investigated by motor nerve and twitch tension measurements.

Electrophysiological and contractile properties of human thenar motor units (MUs) -The MU is comprised of an α motor neuron with its cell body in the ventral horn of the spinal cord, its single motor axon, and the population of muscle fibers innervated by that axon- will be studied. Studies have shown that the number of thenar MUs of the elderly was reduced in comparison to the younger age groups. Additionally, along with reduced MU number, studies have reported significant reductions in the electrically evoked and voluntary contractile force in the muscles of older subjects.

The Advantage EMG system records the electrophysiological properties of single MUs which are stimulated by surface electrodes. The multiple point stimulation method is used to detect single human thenar MUs. To detect and record also the contractile properties of the thenar MUs, a device, the Thumb-Force-Measurement-system, has been developed (also because there wasn't one commercial available).

Because twitch forces of single thenar MUs are forces of 3-40 mN, the device has to be very sensitive. Moreover, twitch forces are mixed with respiratory forces (10-150 mN), pulse pressure waves (5-30 mN), and body movements. To reduce body movement artifacts, a handholder has been developed which immobilizes the forearm and the hand. The pulse pressure waves will have to be detected by an optical pulse detector attached to the subjects middle finger. Respiratory artifacts will be reduced through the experimental set-up.

The first experiments with and without electrical stimulation, showed that the device seems suitable to use. But first, further development as elimination of respiratory artifacts and pulse pressure waves, signal processing and data presentation, integration of the force and electromyographic signals, and definition of the final experimental procedure, is neccesary.
1. Introduction

Everybody ages. Every passed minute has been one of your life. We all wish to get older and older and to stay physically independent. However, the aging process is often accompanied with disabilities and diseases. By expanding our knowledge of the human aging process, we ultimately acquire the knowledge needed to enhance the quality of life in our later years.

Research on the aging process is important to develop interventions to restore or maintain body functions and to develop new knowledge to prevent or treat age associated diseases and disabilities. The Baltimore Longitudinal Study of Aging (BLSA) seeks a better understanding of how and why we age. The study follows a group of men and women between 20 and 100 years of age who return to Baltimore every two years for an intensive health evaluation. Each assessment will add detail and focus to the BLSA's slowly growing picture of how we age.

The BLSA encompasses over 50 ongoing research projects, including studies that investigate changes in sensory and perceptual functions, oral physiology, pulmonary function, response speed, strength and physical functioning, and analyses of risk factors indicating morbidity and mortality. The BLSA aims are to measure the usual or universal changes that occur as people age and to learn how these changes relate to the fundamental causes of aging and to the diseases that sometimes accompany aging. One of the BLSA's objectives is to relate aging processes to one another.

Aging in humans is associated with a decline in neuromuscular performance. Characteristic of this decline is an age related reduction in skeletal muscle mass, leading to decreased voluntary and electrically evoked contractile strength. It is suggested that age associated reductions in muscle mass are primarily a consequence of losses of alpha motor neurons in the spinal cord and secondary denervation of their muscle fibers. The decline in muscle mass, which is characterized by skeletal muscle atrophy and weakness, is in part attributable to losses of motor units (MUs).

The MU is the basic functional component of the mammalian motor system. It is comprised of an α motor neuron with its cell body in the ventral horn of the spinal cord, its single motor axon, and the population of muscle fibers innervated by that axon.

Using an electrophysiological technique, it was shown that the number of MUs in the thenar muscles of subjects between 60 and 80 years of age were reduced compared to subjects between 20 and 40 years of age (Doherty, 1993a). Additionally, along with reduced MU number, studies have reported significant reductions in the electrically evoked and voluntary contractile force in the muscles of older subjects (Doherty et al., 1994a). In general, electrophysiologic studies have shown age associated reductions in the maximum compound muscle action potential size coupled with increases in the mean motor unit action potential (MUAP) size. These findings suggested that there were, on average, fewer yet larger MUs in the muscles of the elderly.
However, investigations of age-related changes in MU contractile properties have been limited. Further study is required to provide a more thorough understanding of the underlying changes and adaptive capabilities of MUs in older adults. Additionally, it would be of considerable interest to relate the contractile properties of the MU to the electrophysiologic characteristics of the MU and whole muscle.

The BLSA would like to investigate also the contractile and electrophysiological properties of human thenar MUs in a representative sample of healthy subjects of different age groups to provide a better understanding of the effects of the normal aging process on the neuromuscular system. Because there isn't a device commercial available to examine the contractile properties of human thenar MUs, the purpose of the current study was to develop such a device.

First of all an introduction in electromyography, electrophysiological and contractile properties, is given in chapter 2. A literature search concerning aging and the MU has been performed and described in chapter 3. In chapter 4, a description of the BLSA study protocol for neuromuscular studies is presented. For this study, the development of the Thumb-Force-Measurement-system (TFM-system) was necessary (chapter 5). The first sets of experiments with the TFM-system (chapter 6) showed good results and it seems to be suitable for the neuromuscular study. However, further development is necessary. Because of the limited time, the data processing and presentation and further experiments have still to be done (chapter 5). General conclusions and recommendations are finally presented in chapter 7 and 8 respectively.
2. **Basic of Electromyography**

2.1 **The human motor unit**

The structural unit of contraction is the muscle fiber. In normal skeletal muscles, the fibers never contract as individuals. Instead small groups of them contract at the same moment. These groups of muscle fibers (MFs) are supplied by the terminal branches of one nerve fiber or axon whose cell body is in the anterior horn of the spinal grey matter. The motor neuron with its cell body, its single motor axon, and all the MFs innervated by the branches of that axon, together constitute a MU (figure 1). MU are the motor "output" of the nervous system and are responsible for both movements and the maintenance of posture. The number of MFs in one MU varies widely depending on the movement to be controlled.

![Fig. 1 Scheme of a motor unit](image)

2.2 **The motor unit action potential**

Under normal conditions, an impulse, action potential, propagating down a motor neuron, reaches the MU endplate and activates all the branches of the motor neuron; these activate all the MFs of one MU almost simultaneously. A wave of contraction spreads over the fiber resulting in a brief twitch contraction followed by rapid and complete relaxation. The duration of the twitch contraction and relaxation varies from a few ms. to as much as 0.2 s depending on the type of fiber involved (fast or slow). MUs normally contract upon the arrival of such nervous impulses at various frequencies usually below 50 per second, the upper physiological limit. When the postsynaptic membrane of a MF is depolarized, the depolarization propagates in both directions along
the fiber. The membrane depolarization, accompanied by a movement of ions, generates an electromagnetic field in the vicinity of the MFs. A recording electrode will detect the potential or voltage with respect to ground, whose time excursion is known as action potential.

During the twitch contraction a minute electrical potential, with a duration of 1-4 ms, is generated which is dissipated into the surrounding tissues. Since all the MFs of a MU do not contract at exactly the same time—some being delayed for several milliseconds—the electrical potential developed by the single twitch contraction of all the fibers in the MU is prolonged to about 5 to 12 ms. The electrical result of the MU twitch contraction then is an electrical discharge with a median of 9 ms, and a total amplitude measured in microvolts with needle or surface electrodes. A schematic representation of this situation is presented in figure 2.

**MOTOR UNIT ACTION POTENTIAL**

[Diagram of motor unit action potential]

Fig. 2 Schematic representation of the generation of the motor unit action potential.

In the diagram, the integer n represents the total number of MFs of one MU of which the action potentials are detected by the electrode.
2.3 Motor unit firing rates

It generally has been accepted that the normal upper limit of activation of MUs is about 50 times per second. The rate of firing rate of MUs is increased with stronger contractions (Dorfman et al., 1988; Fuglsang-Frederiksen et al., 1987; McGill et al., 1985). Fuglsang-Frederiksen et al. (1987), showed no relation between the maximum force and the MU firing intervals in controls or patients. The expected firing rate of a typical MU decreases with time during an isometric contraction at low force levels. The probability of a MU firing after a previous firing has occurred, increases exponentially with respect to elapsed time.

2.4 Motor unit recruitment

Under normal conditions with a slight voluntary contraction, the smaller potentials, i.e. the smaller MUs, appear first and increasing force larger MUs are subsequently recruited (larger motor unit potentials (MUPs) are seen), and all MUs increase their frequency of firing (Dorfman et al., 1988; Jones et al., 1989; Thomas et al., 1986; Thomas et al., 1987). The stimulation threshold for motor fibers in the same nerve are lower for those of a small diameter than for those of large diameter. The smaller fibers supply the smaller MUs which appear to be the most easily recruited in normal voluntary contraction. In general, the lower the input resistance of the motor neurons, the higher the threshold for recruitment in response to peripheral and central inputs, the larger the twitch tension of the MU, and the less resistance the MU is to fatigue (Brown et al., 1988).

2.5 Force of motor units

The force MUs can generate vary widely. This is probably mainly because of the larger numbers of the MFs in the higher-tension MUs. The number of contractile elements is approximately related to the cross-sectional area of the MF. The type of MF is also important because the force generated per unit cross-sectional area is higher in fast compared to slow MFs. Firing frequency is important because in slow MFs no significant change in force output occurs in a train of twitches, whereas in fast MUs, appreciable force decrements may occur. Both the number of active MUs and the firing rate of the MUs correspond to the force produced by the muscle. Characteristics of the forces generated by MUs are:

* Number of MFs per MU.
* Diameters of MFs.
* Force output per unit cross-sectional area of the MF.
* Types of MFs.
* Discharge frequency of MUs.
* Initial length of MFs.
To increase the force output, the firing rate of active MUs increases and increasingly larger MUs are recruited. Also the amplitude of the surface electromyographic (EMG) signal will increase and the number of action potentials per unit time (Brown et al., 1988; Dorfman et al., 1988; McGill et al., 1985). Contractile force is highly correlated to MUAP shape, behavior properties, and correlated to effects of age, gender differences, and, intermuscular variability (Dorfman et al., 1988).

### 2.6 The electromyographic signal

Electromyography (EMG) is the study and use of the EMG signal that originates in the membrane of MFs as they contract. EMG signals detected noninvasively on the surface of the skin are referred to as surface EMG.

The EMG signal is affected by the anatomical and physiological properties of muscles, the control scheme of the peripheral nervous system, as well as the characteristics of the instrumentation that is used to detect and observe it. Using EMG equipment several physiological properties, maximum M-potential (sum of all MUAPs of the muscle), single motor unit action potential (sMUAP), estimation of the number of MUs, conduction velocities (CVs) firing rates, can be measured and determined. These factors are determined using stimulation electrodes or voluntary contraction to activate the MUs and the EMG signal is recorded with surface or needle electrodes. The two main types of electrodes used to stimulate human peripheral nerves in situ are needle electrodes inserted near the nerve and surface electrodes.

The surface EMG signal is an expression of anatomical, biochemical, physiological, and electrical factors. The signal is affected by the distance it must travel between the source and the electrode as well as the geometric and electrical characteristics of the electrode. The surface EMG signal differs from the needle EMG signal: The MUAPs originate from the membrane of the MFs and propagate radially through muscle, fascia, fat and skin tissues (which acts as a filter) to reach the electrode placed on the surface of the skin. With the needle arrangements, the signal presents a superposition of the MUAPs of all active MUs in the detectable vicinity of the electrode. So the surface EMG signal does not always provide the sMUAPs which are available via needle EMG (De Luca, 1994).

### 2.7 Threshold

A MU will contract when the stimulus current is above its threshold and a MUP will be detected. In electrochemical terms, threshold is that level of transmembrane potential (TMP) at which a depolarization in TMP will trigger an irreversible escalation in the proportion of open sodium channels. Threshold is normally between -55 and -60 mV in mammalian muscle (Brown, 1984). So, for a motor nerve fiber, threshold is the stimulus intensity at which the motor axon generates an "all-or-nothing" action potential in response to the stimulus. This stimulus intensity is not a single level, but a range over which the probability of the "all" response increases from 0 to 100 percent. The thresholds of individual motor nerve fibers at or just above motor threshold often
appear to overlap to some extent, and fire in different combinations, such that at any particular stimulus intensity the amplitude of the M-potential fluctuates in incremental steps. When the thresholds of two or more motor axons overlap, the number of these motor axons that develop an "all" response fluctuate from stimulus to stimulus, and depending on their number and the amplitudes of their MUPs, the M-potential amplitude will fluctuate, this is called alternation among motor axons (Brown, 1984; Galea et al., 1991; McComas, 1994; Stein et al., 1990).

2.8 F-response

Sometimes a F-response is detected, which is a late potential from a muscle through activation of its motor axon in the periphery. It is a result of reexcitation of the motor neuron at its first node. The probability of a F-response occurring in any one MU following peripheral excitation of its motor axon is low, about 1-10% (Doherty et al., 1994a). The F-response of one single motor unit (sMU) is similar to the sMUAP in size and shape.

2.9 Influences on the recorded motor unit action potential

Distance of the MU from the electrode, the type of electrodes and the equipment used, etc., influence the final size of individual MUs recorded. The amplitudes of MUPs depend on a number of factors (Brown, 1984; Kilgore et al., 1990; De Luca, 1994; De Luca et al., in press):

1. Number of MFs per MU.
2. The number of MFs belonging to individual MUs that are nearest to the recording electrode.
3. Characteristics of the electrode, including the area of the recording surfaces, location of the reference electrode, and impedance electrode(s).
4. Orientation of the electrode(s) with respect to the MFs
5. Diameters of the MFs.
6. The degree of synchronization in the summation of the compound single motor unit potential (sMUP).
7. Stimulus intensity or percentage of maximum voluntary contraction (MVC).

Of the above factors, the most important is the number of MFs nearest to the detection area of the recording electrode. The diameters of MFs are important because the larger the diameters of the MFs generating the potential, the larger the amplitude of the recorded action potential. Generally, the larger the MUP recorded, the larger is the MU producing it. Increasing the stimulus intensity or the percentage of MVC will activate the MU with a higher threshold; these are the larger MUs and they have a larger amplitude. Rise times are shorter and the amplitudes higher in recorded action potentials generated by fast-twitch compared to slow-twitch MFs.

The amplitude (or area) of the M-potential depends on three main variables, namely:

1. Position(s) and orientation of the electrodes in respect to the muscle.
2. Numbers and diameters of MFs generating action potentials.
3. Distances between these potential sources and the electrodes.
Ad3: The CVs of MFs are much slower (<5 m/s) than those of the parent motor axons. To avoid introducing an error in measuring motor terminal latency, as a consequence of this, is to position the intramuscular or surface recording electrode as close to the innervation zone as possible.

Influence of environmental temperature on the nerve is that the cooler the nerve, the slower are the time courses of the transmembrane ionic currents accompanying the impulse. This not only slows conduction of the impulse but prolongs the duration of the potential and tends to increase the amplitude of the action potential.

Howard et al. (1988) have shown that men had significant greater mean MUAP amplitudes, and longer mean MUAP durations which might reflect larger mean diameter of MFs.

2.10 Correlations between motor unit action potential and twitch tension

In the human, clear correlations have been shown between the amplitudes of MUPs and the tensions of these same MUs for the first dorsal interosseus muscle. These correlations have been shown between intramuscular recorded MUPs and tension, and between the surface MUP amplitudes and tension. The twitch tension of MUs in the first dorsal interosseus muscle in the human increases linearly with threshold force at which MUs are recruited, and the corresponding surface amplitudes of their MUPs increases as the square root of the tensions of the MUs. So, the amplitude of MUPs recorded by either an intramuscular of surface electrode correlates with the tension of the MUs (Basmajian, 1978; Brown, 1984; Thomas et al., 1986; Thomas et al., 1987).

The force of muscle contraction depend on the following main factors:
1. The number and sizes of MUs recruited.
3. Patterns and firing frequencies of the MUs.
4. Especially in primary diseases of muscle, the presence of any abnormalities in the contractile process.

The relative importance of these factors varies among the different muscles and the character of the movement. The recruitment of MUs is the most important factor by which the force of a muscle contraction is increased in weak contractions. As the strength of the contractions increases, the firing frequencies of MUs become more and more important, and once all or most of the MUs are recruited, it is the only mechanism for increasing the force.

2.11 Motor unit estimation

More researchers study the number of MUs because these can provide indications of motor neuron or motor axon losses in serial studies, and the rates at which they are being lost. The number of MUs, however estimate, is the number of functioning MUs (Basmajian, 1987; Brown, 1984; De Luca, 1994; Stein et al., 1990). An estimate of the number of MUs present in the muscle can be made by division of the maximum M-potential amplitude (or area)—the sum of all MUPs generated by those motor axons excited by the stimulus—and the mean MUP amplitude:
The mean sMUP amplitude is obtained by collecting a sample of several sMUPs and average the amplitudes of the sMUP amplitudes. In practice, a way to collect sMUP is to stimulate at 1 Hz and steadily increase the current. Once, motor threshold is reached, the characteristic "all-or-nothing" potential corresponding to the activation of one MU can be detected. Further increases in the stimulus intensity excite more other motor axons in the order of their thresholds, and the amplitude of the M-potential correspondingly increases with the addition of successively recruited MUPs.

MU number estimation has made contributions to neuromuscular physiology in (McComas, 1994):
1) Establishing sizes of various motor neurons.
2) Aging.
3) Amyotrophic lateral sclerosis and spinal muscular atrophy.
4) Collateral reinnervation.
5) EMG diagnosis and assessment.

In the future, MU number estimation studies should be complemented by force measurements, both of sMUs and the entire muscle to complete more the neuromuscular physiology study of the muscle. With this added information, it should be possible to determine the balance of fast-twitch and slow-twitch MUs and to what extent collateral innervation has taken place (McComas, 1994).
3. Aging effects on the motor unit

Very few researchers have investigated single human MU electrophysiologic and contractile properties in relation to aging. Electrophysiologic measures are influenced by multiple factors namely temperature, height, as well as age (Robinson, 1994). Over the past few years, techniques have become available to estimate the number of MUs in human muscles. From the very few human studies, age-related changes in the number and physiological properties of human MUs have been shown. In this chapter a summary of a literature search concerning aging and the MUs is described. Because of the particular interest in thenar MUs, thenar MU properties are mentioned in part 3.7.

3.1 Motor neuron

Age is known to be associated with losses of motor neurons, alteration in neuron size (i.e., atrophy) (Brown, 1994; Doherty et al., 1994a; Dyck, 1994) and other structural alterations and a variable degree of functional and nonfunctional regeneration (i.e., sprouting). The decrease of neurons is not uniform among classes of neurons. With losses of motor neurons, the remaining MUs are enlarged as reflected by increased mean sMUAP sizes (Booth et al., 1994; Brown, 1984; Brown, 1994; Doherty et al., 1994a; Dyck, 1994). Rates of motor neuron cell loss based on physiological studies are similar to those derived from anatomical studies of losses of cells (Brown et al., 1988). The magnitude of the losses varies widely with the motor neuron cell or muscle studied and the methods used to derive the numbers of motor neurons. Besides aging, other factors can contribute to the losses of motor neurons. Losses in spinal motor neurons and MUs in lower limb muscles became apparent by 60 years of age (Booth et al., 1994; Doherty et al., 1993b). No evidence of ventral horn cell body loss was detected until 60 year of age when their numbers began to decrease progressively (Booth et al., 1994; Doherty et al., 1993b). However, these findings were collected on different subjects and longitudinal data can show the variability in the numbers of motor neurons present in any age group. These findings suggest age-associated losses of motor neurons and the subsequent degeneration of their axons.

3.2 Conduction velocities

The functioning of the peripheral motor system is often investigated by measuring the maximum motor CV of a given nerve. It is well known that aging is associated with reduced maximum motor CV in peripheral nerves supplying various muscles (Basmajian, 1978; Brown, 1994; Doherty et al., 1993b; Dyck, 1994; Robinson, 1994). These reductions could be the result of selective losses of the largest and fastest conducting motor fibers or simply losses of the same
fibers through natural random attrition or, as is found by Doherty et al. (1994a) and Brown 1994, a more or less uniform slowing of the motor axon CVs of all nerve fibers. The cause of reductions in the motor CVs of all nerve fibers with aging might reflect variety of changes in the underlying nerve fibers such as reductions in axonal diameter, and reductions in internode length. Motor nerve CVs generally drop about 0.2 m/s/yr (Robinson, 1994).

Doherty et al. (1994a), studying the thenar muscles, showed that in older subjects (age 68 ± 3 yr), the total range of MU CVs (38-61 m/s; mean 52 ± 3) of the older subjects is similar to the young; however, the distribution of CVs was shifted toward lower values, reflecting a slower population of MF. There was a significant reduction in the mean MU CV in older subjects. Thus suggesting that age-related axonal slowing may affect all median nerve MF (Doherty et al., 1994a).

3.3 Motor unit action potential

The few studies investigating human muscles with EMG in older subjects, documented age-related changes in the MUAPs; the amplitudes and the durations of the MUAP (Basmajian, 1978; Booth et al., 1994; Brown, 1984; Brown, 1994; Doherty et al., 1993b; Doherty et al., 1994b; Dyck, 1994; Howard et al., 1988; McComas, 1994; Robinson, 1994). There is an increase in MUAP durations of about 0.05 ms/yr shown for the biceps brachii muscle (Robinson, 1994). Brown et al. (1988), studied the biceps and brachialis muscles and showed that in subject of 60 years of age or older that there was a significant increase in mean surface MUAP size, but the range of values was wide at all ages. For the thenar muscles, the sMUAP size were significant larger (39%) in older subjects (age 68 ± 3 yr) compared to the young (Doherty, 1994a). Also they showed that in older subjects, there was besides a significant increase in the mean sMUAP size as sampled with both the "F-response" and "multiple point stimulation" (MPS) methods, a shift in the distributions toward greater numbers of larger sMUAPs.

3.4 Motor unit estimation

Subjects over 60 years of age had less than half the number of MUs in the thenar muscles when compared to the younger subjects. Also in the biceps brachii and brachialis muscles and the extensor digitorum brevis muscle, age-related reductions in number of MUs has been shown (Brown et al., 1988; Doherty et al., 1993b; McComas, 1994) besides a significant increase in mean surface MUP size. MU loss in the thenar muscles seems to begin between the ages of 50 and 60 years (Booth et al., 1994; Brown et al., 1988; Doherty et al., 1993a). Losses of MUs of the order of 30%-50% in the latter decades of life have been found (Brown, 1994).

As a result of the loss of MUs, it is thought that some of the MFs from the lost MU becomes reinnervated by the other remaining MUs. The reasoning for this inference is based upon:

a) The enlargement of MU size with aging.
b) MFs within a given area of the muscle becoming more homogeneous in fiber type (i.e., fiber type grouping).
c) The endplates in aged muscles are more complex (Booth et al., 1994, 556-560; Brooks et al., 1994; Brown, 1994; Doherty et al., 1993b; Dyck, 1994; Fielding, 1994; McComas, 1994).
Suggested is that the underlying mechanism is not only failure of nerves to reinnervate MFs in the cycle of denervation-reinnervation, but also motor neurons are degenerating. If MFs are lost prior to the degeneration of spinal motor neurons, then the primary lesion may originate in the MF and/or neuromuscular junction. However, an accelerated loss of total muscle area and a decrease in MF number begins about 50 years of age, losses of MUs are present in men and women by the seventh decade. The aforementioned electrophysiological studies provide evidence for reinnervation, fiber grouping, and increases in MU size.

### 3.5 Contractile properties

The age-related reductions in MU number are accompanied by significant reductions in both maximum twitch and maximum voluntary contractile forces of the following muscles: thenar, biceps brachii, brachialis, and extensor digitorum brevis (Booth et al., 1994; Brooks et al., 1994; Brown, 1994; Doherty, 1993a; Howard et al., 1988; McComas, 1994). Thus, losses of MUs is accompanied with increases in sizes of both surface and macro-recorded MUAPs and with larger twitch tensions in the remaining MUs. Additionally prolonged MU contraction times (CTs) along with reductions in the threshold MU firing rate have been shown in the first dorsal interosseous muscle (Doherty, 1993a; Doherty et al., 1993b; Fielding, 1994; Howard et al., 1988) showed that aging affects low-threshold and higher threshold MUs comparably.

(Brown et al., 1988) MUs that generate larger MUPs not only generate larger twitch tensions but are recruited at higher thresholds in voluntary contractions as compared with MUs generating smaller-sized potentials and lower tensions. The increased MUAP and the increased twitch tension in aged MU may provide evidence for reinnervation of MFs which increases MU size. Additionally, MUs exhibit significant prolonged CTs and one-half relaxation times ($\frac{1}{2}$RTs) (Brown, 1994; Doherty, 1993a; Dyck, 1994) which is associated with the reductions in strength. Consistent with these differences are the results of a number of studies that have reported decreases in MU firing rate with aging (Brown, 1994; Doherty, 1993a; Howard et al., 1988; McComas, 1994). These results are in agreement with the reported increases in CTs and $\frac{1}{2}$RTs in the aforementioned studies. Whether these reductions in firing rates represent an adaptation to the slower contractile speeds of elderly MUs or simply a reduced capacity of the central nervous system to drive motor neurons at higher firing rates is unknown. Thomas et al. (1987) showed for the abductor pollicis brevis muscle and first dorsal interosseous that units with slow CTs tended to generate small twitch tensions, whereas those with fast CTs generated large twitch tensions.

### 3.6 Conclusions

Aging in humans is associated with reduction in muscle mass (atrophy) and the loss of functioning motor neurons resulting in changes in muscle strength, muscle twitch, and size of the compound MUAP. There are greater numbers of MFs per MU, resulting in larger amplitude potentials and twitch tensions. The underlying cause is thought to be an ongoing denervation/reinnervation
process that contributes to increase in the numbers of MFs per recruited MU through axonal sprouting.

3.7 Thenar motor unit properties

3.7.1 Twitch forces

Fig. 3 Schematic of twitch and differentiated force defining contraction time, one-half relaxation time, and maximum contraction rate.

Thomas et al. (1990a) showed that initial twitch forces ranged from 2.9 to 34.0 mN with a positively skewed distribution—the force from > 50% of the units was < 10 mN. Most units (86%) produced force between abduction and flexion. CTs (figure 3) ranged from 34 to 80 ms, and \( \frac{1}{2} \)RTs from 25 to 108 ms. For 80% of all units, \( \frac{1}{2} \)RT was slightly longer than CT.

Resultant twitch forces were positively correlated to normalized maximum relaxation rates, but not to other rate indexes or to CV. The various contraction rate measures were not correlated to relaxation rates. No significant correlations were seen between twitch force and CT, \( \frac{1}{2} \)RT, maximum contraction rates (MCR), or the time at which MCR occurred.

3.7.2 Tetanic forces

At stimulus rates of 8 and 10 Hz, the force responses of all units were partially fused. This significant reduced the amplitudes of force oscillations as well as their CT and \( \frac{1}{2} \)RT, compared to those of twitches elicited individually at 1 Hz (Thomas et al., 1990a).
Twitch and tetanic forces were positively correlated, with a stronger relationship after potentiation. Axon CVs were not significant correlated to initial or potentiated twitch forces or tetanic forces.

Thomas et al. (1991b) showed that the stimulus rate (at 12 ± 4 (SD) Hz) needed to evoke 50% max. tetanic force was correlated to contractile rate, i.e., units with faster twitch CT and twitch (or tetanic) \( \frac{1}{2} \text{RT} \) needed higher stimulation frequencies. It was generally the faster units that showed greater force gradation with stimulus rate. Thus units with slow twitch CTs or tetanic \( \frac{1}{2} \text{RTs} \) showed the largest changes in force with frequency.

### 3.7.3 Fatigue

Most units were fatigue resistant and could not be classified by conventional fatigue index and contractile rate criteria, because fatigue-resistant and fatigue-intermediate units had similar contractile rates (Thomas et al., 1991a).

Most units tended to reduce their contractile rate, i.e., their twitch CT and tetanic \( \frac{1}{2} \text{RT} \) increased. The fatiguing units needed higher stimulation rates to produce any given submaximum force (Thomas et al., 1991b).

### 3.7.4 Thenar motor unit estimation

Galea et al. (1991) found as MU estimation for the thenar muscles: mean 228 ± 93 (SD), this is similar to the value 203 derived from anatomical studies of the recurrent branch of the median nerve.

Stein et al. (1990) also studied the number of MUs in the thenar musculature. The number of MUs in the thenar muscle group was calculated by dividing the surface EMG and twitch force, in maximum stimulation of the median nerve, by estimates of the average EMG and twitch force from sMUs. The five estimates (3 based on EMG and 2 on force) ranged from 116 to 170 MU in the thenar group (table 1). None of these estimates was significant different from any other (in between the methods: Spike Triggered Averaging (STA), McComas method, and microstimulation). The most likely reason for the higher estimates in previous studies using graded whole nerve stimulation is shown to be the cause of alternation of MUs.
Table 1 Summary of results from normal subjects for three different methods used to study MUs (Stein et al., 1990).

<table>
<thead>
<tr>
<th>Unit sizes</th>
<th>Comas</th>
<th>STA</th>
<th>Microstimulation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avg p-p EMG (μV)</td>
<td>102 ± 52</td>
<td>108 ± 38</td>
<td>120 ± 36</td>
</tr>
<tr>
<td>Avg twitch (mN)</td>
<td>116 ± 10</td>
<td>19 ± 12</td>
<td></td>
</tr>
<tr>
<td>Estimated number of units</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Based on EMG</td>
<td>170 ± 62</td>
<td>135 ± 27</td>
<td>122 ± 38</td>
</tr>
<tr>
<td>Based on force</td>
<td>130 ± 39</td>
<td>116 ± 45</td>
<td></td>
</tr>
</tbody>
</table>

Avg = average; p-p = peak-to-peak; EMG = electromyogram
STA = Spike-Triggered Averaging

The peak-to-peak amplitude of the maximum M-potential ranged from 9 to 20 mV, and the corresponding peak twitch force ranged from 0.9 to 3 N in normal subjects (Stein et al., 1990). Doherty (1993a) detected an peak-to-peak amplitude of the maximum M-potential of 16.2 ± 3.0 for subjects of 20-40 years of age and 11.5 ± 3.0 for subjects of 63-81 years of age. The MU peak-to-peak estimate of the same subjects was for the younger subjects 206 ± 58 and for the older subjects 104 ± 45.

3.7.5 Twitch contractile and electrophysiologic properties of motor units in younger and older subjects

Doherty (1993a) showed the following results, studying the thenar MUs:

<table>
<thead>
<tr>
<th>Variable</th>
<th>Younger (20-40 yr)</th>
<th>Older (60-80 yr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Force (mN)</td>
<td>8.8 ± 7.4</td>
<td>13.4 ± 10.4 *</td>
</tr>
<tr>
<td>CT (ms)</td>
<td>49.5 ± 11.5</td>
<td>56.7 ± 14.0 #</td>
</tr>
<tr>
<td>½RT (ms)</td>
<td>55.2 ± 22.2</td>
<td>69.3 ± 27.6 #</td>
</tr>
<tr>
<td>S-MUAP (μVms)</td>
<td>394 ± 325</td>
<td>459 ± 458 ns</td>
</tr>
<tr>
<td>Max. M (mVms)</td>
<td>45.8 ± 11.3</td>
<td>32.2 ± 838 &quot;</td>
</tr>
</tbody>
</table>

Values are mean +/- SD; CT = contraction time; ½RT = one-half relaxation time; S-MUAP = surface detected motor unit action potential; Max. M = maximum compound muscle action potential; ns = not significant; Younger versus Older: * P < 0.05; # P < 0.01; " P < 0.001.
4. **Racial and Gender Effects on Age-Associated Changes in the Neuromuscular System**

4.1 **Study introduction**

The percentage of Americans over the age of 65 years is growing and this trend heightened interest in aging research (Booth et al., 1994; Fielding, 1994). This rapid growing group of elderly, especially those over 85 years, may be at greatest risk for being functionally limited due to declines in muscle mass and the associated loss in muscle strength. Declines in the functioning of several major systems have been observed such as changes in cardiovascular and muscular performance, which with advancing age can affect functional capacity. Maximum oxygen uptake ($V_{O_{2}}_{\text{max}}$) and total cross-sectional area of leg muscle begin to decline in early adulthood and muscle strength begins to decrease after the fifth decade (BLSA study results, Booth et al., 1994; Brooks et al., 1994; Brown, 1994; Dyck, 1994; Fielding, 1994). These declines in exercise capacity are in parallel to the declines seen in musculoskeletal and cardiorespiratory systems.

All body movements are produced by contractions of skeletal muscles. Consequently, any impairment in the functional properties of skeletal muscles results in some degree of immobility. A loss of mobility inhibits participation in physical activities, as well as successful performance of the necessary activities of daily living. Clarification of the mechanisms responsible for the neuromuscular changes would enhance our understanding of the degree to which they are preventable or treatable.

A consequence of skeletal muscle atrophy with aging is the reduction in muscle strength. Muscle strength appears to be relatively well maintained up through 50 years of age. Muscle atrophy, declining strength, and physical frailty are generally accepted as inevitable concomitants of aging, however, the causes are not completely known. Physical frailty describes the summation of the effects of muscle atrophy, decline in muscle strength and power, fatigue, and injury. The degree to which these changes are preventable and treatable is not clear.

Functional problems with increasing age represent a continuum that over time results in increasing disability. Whether the changes occur because of age-associated factors or early disease or a combination of both is unknown. It is known that significant differences exist between women and men in muscle strength and body mass and may in part account for the greater degree of frailty in elderly women. With increasing age, both sexes lose muscle mass and show a decline in muscle strength. Woman show, around the time of menopause, a dramatic decline in the ability to generate force and this can be prevented by the use of hormone replacement therapy (Phillips et al., 1993).

Several research protocols are being developed to focus on the general area of frailty and physical independence. Causes of frailty are not well understood and the role of race is unknown. The
Development of TFM-system

Neuromuscular Study Protocol

BLSA has the opportunity to investigate the role of biological factors and the natural history of
development of age associated changes in functional abilities that contribute to frailty in a group
of volunteers. The study "Racial and Gender Effects on Age-Associated Changes in the
Neuromuscular System" is designed to examine the role of the peripheral nerve on age associated
loss of muscle strength and the contribution of strength loss to physical independence and other
health factors. To study the relationships between physiological factors and age-associated loss of
muscle strength by age, gender, and race, will be investigated by motor nerve and twitch tension
measurements.

At the neuromuscular level, the loss of muscle strength, muscle mass and muscle efficiency may
be associated with age-related changes in the muscle, in the nervous innervation of the muscle, or
with circulatory factors that are involved with muscle homeostasis. Early studies found that age
differences occur in the distribution of fiber type, muscle metabolism, and in secondary messenger
function (primarily calcium regulation) with decreases in force generation, slower contractions
and increased fatigability (Booth et al., 1994; Dyck, 1994; Fielding, 1994). On the other hand
lower extremity muscles tend to show much greater loss of strength than those in the upper
extremities with increasing age. Also exercise appears to reverse or prevent some of the changes
that can be observed in the elderly. In addition, while the decreases in muscle mass, strength, and
power may be related to decreased activity levels throughout the life time, maintenance of
physical activity does not appear to protect skeletal muscles completely from these age-related
decrements. Even trained world class athletes show similar trends and time courses of decline in
structural and functional properties (Brooks et al., 1994; Brown, 1994; Fielding, 1994).

Although muscle atrophy is attenuated by resistance training with aging, little is known about
effects of resistance training on the loss of spinal motor neurons, MUs, and MF number. An
accelerated loss of total muscle area and a decrease in MF number begins about 50 years of age
(Booth et al., 1994; Brown et al., 1988; Doherty 1993b). Losses in spinal motor neurons and
MUs become apparent at about 60 years of age (Booth et al., 1994; Doherty 1993b).

It is clear that elderly persons who remain physically active have only moderate losses in skeletal
muscle mass, but exactly how much of the decrease in muscle mass is a) a consequence of aging,
b) a reduction in physical activity, or c) both is currently unknown. Studies showing that
individuals aged 60-90 year can increase/maintain muscle mass with resistance training suggest
that the lack of muscle loading could contribute to muscle atrophy in the aged (Booth et al.,
1994).

4.2 Study protocol

The specific goal of the BLSA study is to explore gender and racial effects on age differences in
neural control of muscle function, and to explore whether potential differences in neuromuscular
function are associated with differences in physical activity or functional capability.
Hypotheses:
1. Gender, racial and age differences exist in the amount of neuronal activity required to generate a specified force.
2. There are racial and gender differences in the age associated decline in nerve CV and the number of MUs.
3. Self reported physical activity will correlate with muscle strength, nerve CV, and number of MUs.
4. Differential loss of muscle strength occurs in the upper and lower extremities with age and are correlated to the decline in MUs.

BLSA subjects will be used and at least 20 subjects in each age decade from the 20's to the 80's for four groups based on gender and race. Subjects will be tested at two points in time, 6 years apart in order to measure rates of changes. A standard clinical evaluation to assess overall health status, estimation of muscle mass and functional activity will be examined. Also the VO_{2,\text{max}} data from the cardiovascular laboratory will be used.

4.3 Neuromuscular Studies, system, and methods

For this study, two methods: multiple point stimulation (MPS) for the thenar musculature and computerized decomposition of the MUAP for the proximal muscles, are used. Both methods estimate the number of functional MUs in the muscle. For this estimation, the size of the electrical response to muscle activation using surface electromyogram is examined and divided by the average amplitude (area) of the MU responses analyzed. The methods vary in how the latter measurement is estimated. Commercial equipment, the Advantage EMG system, specially designed to improve the accuracy of MU number estimation, will be used for these purposes. The intramuscular recordings, decomposition method, is described in appendix 3. In the following section, the Advantage EMG system for surface EMG and the MPS method are described.

4.3.1 Principles of the Advantage EMG system for surface Electromyography

Motor neuron diseases and many peripheral neuropathies are characterized by losses of MUs. Reliable, non-invasive techniques exist for estimating the number of MUs in a muscle or muscle group (Doherty et al., 1993b; Galea et al., 1991; McComas, 1991).

The Advantage EMG system can be used for determining the number and the relative sizes of MUs comprising a muscle. Using graded electrical stimulation and a series of algorithms, it collects and identifies individual MUs. It provides information about the innervation and MU composition of muscles, is capable of detecting denervation, and can be used to monitor progress of patients with a variety of neuromuscular disorders.

The estimation of the number of MUs is done by comparing the average MUP with the maximum M-wave (compound action potential) of the same muscle. The sample of MUPs from which the
average area is derived, is obtained by weak, graded stimulation of the motor nerve as will be described.

The number of MUs in individual muscles is a relatively stable quantity that decreases in the elderly. To distinguish the MUs, the stimulus current is gradually increased. When a stimulation site is found which satisfies the criteria for excitation of a single motor axon, the stimulator can be taped in place, subject to minor adjustment thereafter to maintain selectivity. Stimuli are constant current pulses usually of 0.05 ms duration, and delivered at 1 Hz. All the stimuli are submaximum and many are only minimally above threshold. The stimulus intensity is just subthreshold and the corresponding potential samples are stored in memory as "template one". Then the stimulus current is increased until the first muscle response is obtained and "template one" is subtracted from this and the sMUAP and the twitch tension are recorded. The final shape, the sMUAP, is stored and displayed on the screen. Next another stimulation site along the course of the median nerve will be found and so the procedure continues until 10-20 sMUAPs are collected. The detection procedure is carried out using Fourier transformation of the responses.

The responses picked up by the recording electrodes are amplified, using a band-pass of 10 Hz to 1 kHz before being analyzed and simultaneously displayed in real time on a screen. For the analysis, the M-waves and MU responses, after filtering, are sampled by the computer at 4 kHz, and collected on an Advantage EMG system. Comparisons of the responses are made by calculating the Euclidean distances between their Fourier coefficients. An additional algorithm determines whether any composite potentials are the result of "alternation".

### 4.3.2 Multiple Point Stimulation

**Description of the Multiple Point Stimulation Method**

This method will be used for thenar musculature measurements and uses graded stimulation of the median nerve to activate individual thenar MUs. Multiple sites along the median nerve are stimulated to find different sMUs. This technique can also be used to longitudinally follow individual MUs (Doherty et al., 1994b).

Several assumptions underlying the MPS method combined with twitch tension measurements, include:

1) The ability to stimulate percutaneously one sMU, in an "all-or-nothing" manner, and to record the surface-detected sMUAP from the muscle.

2) The sample of the first motor axons excited above threshold and the MUs they innervate, are representative of the relative numbers of sMUAPs of different sizes within the muscle (group) studied.

3) Collecting 10-20 sMUAPs is a sufficient large sample to accurately represent the whole population.

Doherty (1993a) provided evidence that these assumptions are correct.
Self-adhesive surface recording electrodes are cut into strips 1.2 mm x 3.0 mm and used to detect thenar sMUAPs. The "active" electrode is placed over the innervation zone with an inactive electrode on the muscle tendon. This zone is detected by stimulating the nerve to the muscle with electrical current, and moving the electrode around until a maximum recording is obtained. The ground is a metal plate fixed to the back of the hand.

A bipolar electrode (5 mm in diameter spaced 1.8 mm apart) stimulates the median nerve with low current and with the cathode distal. First, a maximum M-potential is elicited by gradually increasing the electric current (manually) during stimulation of the median nerve at the wrist, at 1 Hz. This will continue until the current is 20% greater than the current which gives the maximum size and will then be reduced manually until it is just subthreshold.

To locate sites where a single motor axon can be excited, 0.05-1.0 ms duration pulses at intensities from 0-50 mA are applied at a frequency of 1 Hz to the median nerve. The stimulus intensity is increased to the level at which the first reproducible, "all-or-nothing" sMUAP is detected. If it is impossible to detect a single, repeatable and clear "all-or-nothing" sMUAP, free of alternation, the bipolar electrode will be moved. The stimulation electrode is subsequently moved to points along the course of the median nerve between the thenar motor point and the distal forearm and between the elbow and the axilla, to detect sMUAPs. In the latter sites, it is very important to avoid stimulation of the ulnar nerve as it supplies the finger and hand muscles, which influences the sMUAPs (Doherty, 1993a). Those sMUAPs make no contribution to the maximum M-potential and should therefore be excluded in the sample of sMUAPs from which the thenar MU estimate is derived. At least 20 sMUAPs of the thenar muscles will be identified for the estimation. It is not possible to stimulate the proximal forearm successfully without producing artifacts from stimulation of other muscles and tendons, because the nerve lies deep in this region.

Because the current increases gradually, the interference pattern will change every time another MU is recruited. To be accepted in the study, the responses have to fulfill the following criteria (Brown et al., 1988; Doherty, 1993a; Doherty et al., 1994b; McComas, 1994; Westling et al., 1990):

1) No force or EMG signals will be elicited until the stimulus reached a critical level. Small increases or reductions in the stimulus intensity at motor threshold evoke either an "all" response of constant shape, size, and latency or fail to evoke motor activity, i.e., the "nothing" response.

2) Successive 1 Hz stimuli of an intensity to evoke an "all" response produce no fractionation or subdivision of the same identical sMUAP.

3) Both force and EMG signals appear simultaneously, in an "all-or none" manner.

4) When a F-response evokes, the shape and the magnitude of the direct EMG and the F-responses are identical, with no change in the direction in which the force exerts.

5) All signals remain unchanged as the current intensity will be increased by a considerable margin (i.e., a wide operational current range is required).

6) The characteristic direction in which each unit generates force does not change during the recording period.
Development of TFM-system Neuromuscular Study Protocol

It is important to be sure that all responses continued to originate from the same unit. During repeated stimuli, the operator has to make sure that no unexpected or abrupt changes are seen in the following:
1) The direction of the resultant force.  
2) The amplitude and shape of the EMG signals.  
3) The stimulus current operational range.  
4) The magnitude of mechanical parameters that are not related to the test procedure (e.g., twitch potentiation or tetanic stimulation).

To ensure that the same motor axon will be stimulated in successive studies, additional criteria included (Doherty et al., 1994b):

a) The motor axon is found at approximately the same site along the nerve  
b) The shape of the sMUAP is almost identical on repeated studies.

This method provides the ability to track longitudinally the electrical and contractile properties of sMUs in health and during the course and treatment of disease. In Doherty's study (1994b), five MUs were studied five times each over a period of several months.

sMUs will be identified, by subtraction of the patterns before and after the stimulation and are then recorded and displayed on the screen. To estimate the number of functional units, the onset and the peak amplitudes of the sMUAPs are automatically selected, subject to correction by the operator. Than the average negative peak area and average peak to peak amplitudes of the sample of sMUAPs are calculated and divided into the corresponding values for the maximum M-potential to obtain the MU estimations.

The validity of the MU estimation depends on assumptions underlying the technique. These assumptions include (Brown et al., 1988; Doherty, 1993a; Stein et al., 1990):
1) The sMUAPs collected represent sMUs.  
2) The motor axons excited and the MUs are not biased to any particular size or physiological property.  
3) MPS provides a sufficient sample to derive the average sMUAP size.  
4) The ability of the MPS technique to provide reproducible MU estimations.  
5) The sample of MUs refers to the portion of the thenar group innervated by the median nerve only.

**Side-reflections of the Multiple Point Stimulation method**

Median nerve stimulation can lead to abduction, adduction, and flexion of the thumb. The course of the median and ulnar nerve are shown in figure 4. Stimulation of the median nerve axons to study the thenar MUs and thenar twitch tensions, is chosen because the thenar muscles are primarily innervated by the median nerve and the nerve is suitable for the MPS method—can be stimulated by surface electrodes along its course to activate sMUs (Doherty, 1993a; Doherty et al., 1994a; Doherty et al., 1994b; Stein et al., 1990).
For this study, looking to the anatomy of the arm and the hand (appendix 1), it becomes clear that the median nerve can only be stimulated, using percutaneous stimulation, along the course between the distal forearm and the thenar motor point and between the elbow and the axilla. The proximal forearm is unsuitable as the median nerve lies too deep to stimulate directly. It is very important to avoid stimulation of the ulnar nerve when stimulating between the elbow and the axilla. Because activation of the forearm muscles as well as the hand muscles will heavily disturb sMU twitches from the thenar muscles because of movement artifact. Successful stimulation of the median nerve without producing unacceptable artifacts from direct stimulation of underlying muscles and tendons is not so easy. The median nerve consist of nerve fibers to the thenar muscles, and to the muscles which flex the fingers and the wrist. In the table below, the muscles innervated by the median nerve and the movement they cause are shown (McClintic, 1983).

Fig. 4 Course of median (number 15) and ulnar (number 16) nerve
Table 3  Muscles innervated by the median nerve and the movement they cause.

<table>
<thead>
<tr>
<th>Muscles</th>
<th>Movement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abductor pollicis brevis</td>
<td>Abducts thumb</td>
</tr>
<tr>
<td>Flexor pollicis brevis</td>
<td>Flexes thumb</td>
</tr>
<tr>
<td>Opponens pollicis</td>
<td>Flexes and adducts thumb</td>
</tr>
<tr>
<td>Flexor digitorum superficialis</td>
<td>Flexes fingers</td>
</tr>
<tr>
<td>Flexor digitorum profundus</td>
<td>Flexes fingers</td>
</tr>
<tr>
<td>Flexor carpi radialis</td>
<td>Flexes wrist and abducts it</td>
</tr>
<tr>
<td>Palmaris longus</td>
<td>Flexes wrist</td>
</tr>
</tbody>
</table>

The single efferent fibers to the thenar muscles are homogeneous mixed in fascicles with cutaneous afferents and their relative position in the crosssections are changing along the nerve. Moreover above the elbow, the motor fibers to any particular muscle are widely distributed between different fascicles (Westling et al., 1990). Only 2% of the fibers in the median nerve are efferent to the thenar muscles and these fibers are homogeneous mixed with afferent fibers. The probability of finding the 2% fibers is low and up to 12 sMU may be found using MPS within a respectable time (obtaining more sMUs will be more time consuming). Stimulation of only single thenar MUs may seem unlikely because of the high density of fibers within the nerve fascicle. However, with electrical stimulation, it is possible to activate one sMU on the basis of an "all-or-none" response. The operator will have to be aware of these facts during the experiments.
5. Development of the Thumb-Force-Measurement-System

5.1 Introduction

In the study described in chapter 4, i.e., the neuromuscular study of the thenar musculature, there is also an interest in the force produced by the electrically stimulated sMU which causes movement of the thumb. This is of interest because previous studies have shown an increase of twitch tension of sMUs with aging (chapter 3). Exercise may further increase the twitch tension and may prevent decline of the number MUs. The purpose of this particular study will be to study the effects of exercise and aging on the electrophysiological and contractile properties of sMUs. To study these effects, the EMG signal and twitch tension of sMUs will be examined. So, an extension of the protocol will be to measure the single thenar MU twitch tension and to relate this to age, muscle strength, exercise, size of the MUs, and functional independence. For these force measurements, a device, the Thumb-Force-Measurement-system, has been developed. This prototype measures the single thenar MU twitch tension using strain gages, i.e. force transducers.

In this section, the development of the TFM-system is described. First of all, the purposes and requirements of the TFM-system are described. Then a literature search has been performed to study the devices used by other researchers to measure thenar twitch tension. Then, considerations have been made which are necessary for the development of the device and the final experimental procedure. Finally the design of the TFM-system is described.

5.2 Purposes of the Thumb-Force-Measurement System

Using the MPS method (part 4.3.2), several single thenar MUs will be stimulated and will contract which cause movement of the thumb -flexion, abduction, or a combination of these. The force, twitch tension, and the EMG signal of the sMUs have to be detected for the study described in chapter 4. With the Advantage EMG system and the MPS method, sMUs are detected and the EMG signal is recorded. The TFM-system has been developed to detect and record the sMU force, twitch tension. Relations will be determined between the force and EMG signal, MU size, age, exercise, and so on.

The purpose of the TFM-system is that it accurately measures the force and the force direction produced by the thenar muscles when human thenar sMUs are electrically stimulated by a surface electrode.
5.3 Requirements of the Thumb-Force-Measurement System

→ Detection and recording of single thenar MU twitch tension and the force direction.

→ Immobilize the hand and forearm. A handholder has to be developed which immobilize the arm and forearm to reduce body movement artifacts and to hold the hand every time in the same position during the data acquisition.

→ Detection of respiratory forces and pulse pressure waves. The twitch forces are mixed with these unwanted forces and so these have to be detected and eliminated from the recorded force signal.

→ Useful for several years. About 250 volunteers, both men and women, will be involved and tested at two points in time.

→ Easy in use
→ Low costs
→ Robust
→ Userfriendly
→ Applicable to a large group of participants.
→ Present data readily to analyse.
→ Data obtained should be comparable and realistic.
→ Good reproducibility
→ Good repeatability
→ Good accuracy
→ Good reliability
→ Easy and fast calibration
→ Flexible
5.4 Descriptions of devices used by other researchers

Devices used for twitch tension measurements, as mentioned in the literature are described briefly.

5.4.1 Device of Westling et al. (1990)

The subjects sat with the right arm extended and the hand supinated on an adjustable support. A vacuum cast immobilized the forearm and the fingers, except the thumb, and were constrained by U-shaped clamps. The position of the extended thumb was defined by applying ± 0.5 N force of resting tension in the directions of both abduction and flexion, against a force transducer (figure 5).

![Device of Westling et al. (1990)](image)

Fig. 5 Device of Westling et al. (1990)

A needle electrode was used for the stimulation and surface electrodes for the EMG recording. The two-dimensional strain gage force transducer (Grass Instruments, FT10 force transducers) made contact at the interphalangeal joint and measured the force components generated at right angles in the directions of abduction and flexion. The two force components were displayed on a oscilloscope and the resultant force amplitude and direction were calculated from these. Fluctuations, due to respiration (± 0.1 c/s) and pulse pressure (± 1 c/s) waves, introduced deviations of 10-150 and 5-30 mN respectively, creating a problem measuring the amplified single MU twitch tension. To minimize these fluctuations an analog circuit reset the force signals to zero just before each stimuli delivery. Also the train of stimuli from an infrared blood pressure pulse detector attached to the subject's finger, was recorded. All the signals were monitored continuously on multichannel storage oscilloscopes, digitized and stored on-line within a computer system.
The magnitude of the twitch forces varied between 3-40 mN and the time courses of force development varied widely between units. The direction of force generation was characteristic for each unit.

The force transducer characteristics are: DC-120 Hz, noise <1 mN, stiffness 0.2 mm/N.

5.4.2 Device of Stein et al. (1990)

A strain gage transducer was positioned on the lateral aspect of the thumb at the level of the proximal phalanx, perpendicular to the principal force vector of the thenar group. The wrist, forearm, and fingers were restrained to isolate the force recording from the thumb. The skin temperature was maintained near 37°C with an infrared heating lamp throughout the experiment. The EMG and twitch force in response to 10 maximal stimuli of the median nerve were averaged. This was assumed to represent synchronous activation of all thenar MUs supplied by the median nerve. Since force was measured in one direction only, units with twitch forces divergent from the principal vector only contribute to the component that is in line with the principal vector. The MUs sampled ranged in twitch size from less than 1 mN to 100 mN, and in the size of their surface EMG from less than 10 μV to 1,000 μV peak to peak.

5.4.3 Device of Kilgore et al. (1990)

The subjects were spinal cord injury patients with paralyzed upper extremity. Electrodes were implanted in the forearm and hand muscles of the thumb and the fingers. Forces developed by the electrically stimulated thumb muscles were measured isometrically using a force transducer placed at the distal phalanx. The forearm was held in a restraining apparatus. The thumb was placed into the end of the force transducer beam which was attached to this apparatus (figure 6).

Fig. 6 Device of Kilgore et al. (1990)

Force vectors were measured using a cantilever beam with strain gages placed to measure shear strain in two directions. The two orthogonal force components, the output of the force transducer, were used to calculate the force magnitude and the force direction. The signals were amplified by 500, low-pass filtered at 10 Hz, and sampled at 100 Hz via computer.
They concluded that the direction of force may change as thumb position changes. This is a result of a change in the orientation of the muscle fibers and a change in the relationship between electrode and muscle. The results indicated that for all muscles the predominant change in force direction was due to the change in orientation of the muscle fibers.

5.4.4 Device of Brown & Doherty

Two Grass FT10 force transducers (Grass Instruments, stiffness: 0.2 mm/N) were mounted at right angles to each other (figure 7) on adjustable micrometer stages allowing to be precisely positioned independent of each other.

Bridge excitation and signal amplification were provided by two separate strain gage signal conditioners (Durham Instruments, Pickering ON; DC-6 kHz, 3 dB down). The force transducers contacted the comfortably extended thumb at the level of the interphalangeal joint via slightly curved aluminum cups approximately 3 mm by 10 mm in size, and about 0.5 N of passive force was applied in the direction of thumb abduction and flexion. Fluctuations related to respiration,
pulse pressure waves, and other slight movement exceeded the size of the MU twitches. These fluctuations were minimized in two ways based on methods described by Westling et al. (1990). First, each stimulus was triggered following a delay of 50-150 ms, by the signal produced from an infrared pulse detector attached to the subject's finger. Secondly, a computer algorithm was used which sampled the DC offset in the force signal and reset the baseline to zero in response to the stimulus artifact of the nerve (usually delayed 10-20 ms). The MU twitch tension needed to be averaged. Force and EMG signals were collected on line (12 bit A/D converter) and viewed on a four channel split-screen display. Force data was sampled at 500 Hz. All data was stored on a hard-disk for future analysis. If an F-response occurred, the trial was discarded and restarted as the force record would have been distorted by the recurrent response of the test MU.

5.4.5 Considerations with regard to the development

A device, which is necessary for the single thenar MU twitch tension measurements, has been developed. Because only the device of Westling et al. (1990) and the one of Doherty and Brown, which is based on the device of Westling et al. (1990), is suitable for this study (part 4.2) and both devices are not commercial available. However, the designs of the devices described above, were useful for the development of the TFM-system.

The contact with Dr. Westling pointed out that there are certain difficulties of percutaneous stimulation (part 4.3.2.2) of sMUs and some other aspects which have to be considered (part 5.6). However, W.F. Brown and T.J. Doherty, who used the MPS method for the stimulation of sMUs (which will also be used in this study), showed good results.

For the development of the handholder (part 5.5), for minimizing the fluctuations due to respiration and pulse pressure, the electronical scheme, and the data processing, the description of the device of Westling et al. and of the device of Brown and Doherty have been used for the development of the TFM-system. However, different strain gages have been used because of the high price of the Grass FT10 force transducer.

The device of Kilgore et al. (1990) and of Westling et al. (1990) have been used for the design of the thumbholder. These designs are robust and allow mounting of the chosen strain gages. The results of Stein et al. (1990) and Kilgore et al. (1990) are taken into consideration with regard to the force direction measurements and the position of the thumb.
Development of TFM-system

5.5 Handholder

During the experimental procedure activation of other muscles may occur easily and this will influence the force detection of a single thenar MU. The operator will have to be careful during the stimulation (part 4.3.2) and the participant will be asked not to contract any muscles. Body movement artifacts are reduced through the experimental set-up. The subject will ly relaxed on a table with the left arm extended, and is not allowed to talk or to move during the data acquisition because this influences the force measurements. To reduce artifacts of movement of the fingers, hand, and forearm, a handholder has been developed.

The purposes of the handholder are:
1) to immobilize the forearm and the hand.
2) to position the forearm and the hand for every subject in almost the same position.
3) to held the forearm and the hand in a comfortable way during the data acquisition.

White plastic (E-2-FORM) (6" by 21") is deformed into a mould for the forearm and the hand. This is covered with a blue foam (contour foam). The fingers, except for the thumb, rest on NCM-airputty and are constrained with velcro. A velcro strip is placed around the palm of the hand. The forearm is immobilized by velcro strips and these can be displaced along the handholders side, depending on the arm size of the subject and where the stimulus will be given. The handholder (figure 8) leaves the thumb free for movement and for the force measurement device, and is reported very comfortable by the subjects. The ground electrode, the metal plate, can still be placed on the back of the hand or a saline-soaked ground strip can be wrapped around the upper arm.

Fig. 8 Handholder
Development of TFM-system

5.6 Baseline Artifacts

Twitch forces are mixed with respiratory forces, pulse pressure waves, and body movements. These artifacts are in the region of:

- Twitch forces: 3-40 mN
- Respiratory forces: 10-150 mN
- Pulse pressure waves: 5-30 mN

The unwanted forces are reduced by:
- Subjects lying on a bed with the left arm extended and with the hand fixed in the handholder.
- Pulse pressure detection.
- Breathing analysis.

It is also important to have the thumb in the same position during each recording because in another position the thenar muscle fibers are different orientated, as this will influence the force direction measured (Kilgore et al., 1990).

Kilgore et al. (1990) observed that there was no consistent changes in the force magnitude as a function of thumb position (resting, extended, and abducted position were studied) for any muscle groups. The direction of force changed for all muscle groups when the resting force vectors were compared with those obtained when the thumb was abducted or extended. Their data also shows that the shape of the recruitment curve at the extended and abduction positions is different from the curve at resting position. The direction of force changes as thumb position changes and may be a result of a change in the orientation of the muscle fibers and a change in the relationship between the electrode and muscle. Their results indicated that for all muscles the predominant change in force direction was due to the change in orientation of the muscle fibers. In addition, there may also be a change in the moment arm through which the muscle acts on the joint, and this would also influence the force output. Thomas et al. (1986) showed that the characteristic shapes of sMUPs observed, changed with variations in muscle position.

The handholder will be positioned on a surgery table. A 3-dimensional (3-D) global coordinate system has to be defined to determine the position of the thumb with respect to this global coordinate system. This will allow that the experimental setup can be repeated for the same subject. A local coordinate system has to be defined to determine the direction of the force in the 3-D environment. This local coordinate system will have its origin where the interphalangeal joint contacts the thumbholder. The z-plane will be fixed because the movement of the thumb is two-dimensional (flexion and abduction).
5.7  Force direction measurements of the thumb

Median nerve stimulation can lead to abduction, adduction, and flexion of the thumb. Measurements of force from thenar muscles is complicated because they show diverse origins and insertions and operate across several joints providing multiple degrees of freedom. The joints of the thumb are the metacarpal bone, the distal and proximal phalangeal (appendix 1).

Other researchers measured the force amplitude and direction of the interphalangeal joint. The advantage of measuring the force of this joint is that force transducers can be adjusted on it and that there are no measurement artifacts of soft tissue.

It has been demonstrated by other researchers (Doherty, 1993a; Thomas et al., 1990a; Westling et al., 1990) that sMUs within the same muscle group, generate force in widely different directions. Thus regardless of the strain gage orientation, the forces should be measured two-dimensional otherwise the forces for many units must be reduced when measurements are made only in one direction. The prototype, TFM-system is designed to measure both abduction and flexion force components of the interphalangeal joint of the thumb.

5.8  Design of the Thumb-Force-Measurement System

5.8.1  Thumbholder

![Fig. 9 Thumbholder](image)

An aluminum bar 1.14" square and 5.1/16" in length was formed to hold the thumb in position (figure 9, see also technical drawings in appendix 5). When the median nerve is stimulated causing movement of the thumb, it will stress proportionally the two sets of strain gages which are mounted on a milled surface which is designed to maximize the stress moment created by the thumb pressure moment. A round cup (59/64" diameter) was drilled at one end in which the thumb will be fixed. The bar was than milled to a square diameter of 0.26". A strain gage was
mounted centrally on each of the four planes. The end piece of the 1 1/4" squared bar was drilled and topped to enable the complete thumbholder to be attached to a swivel device which in turn allowed the thumbholder to be calibrated and fixed in the xyz plane. Further a hole was drilled through the centre of the mounting hole to a depth terminating under the strain gage mounting section. This was designed to increase the bending moment which increased the sensitivity of the bridge.

5.8.2 Force measurements

When force is applied to a body, the body deforms. In general, this deformation is called strain. Strain is the deformation per unit length or fractional change in length and is noted as \( \varepsilon \).

\[
\varepsilon = \frac{A L}{L}
\]

Strain may be tensile or compressive as shown in figure 10. A proportional relationship exists between stress and strain, i.e. Hooke's law:

\[
\sigma = E \varepsilon
\]

where \( E \) = modulus of elasticity or Young's modulus  
\( \sigma \) = stress  
\( \varepsilon \) = strain

Fig. 10 Uniaxial tension

This relationship exists only in the special case of uniaxial stress (figure 10) and then only in the direction of maximum stress and within certain limits. The limit is the point where the ratio of stress to strain begins to decrease and the relationship is not linear any longer. This is the elastic limit and beyond this point the material will fail to return to its original dimensions when stress is removed (figure 11). Care has to be taken that the force applied to the TFM-system will not exceed the elastic limit because then the device will be deformed and will not be useful anymore!
A section of the beam is made very small because the strain in this reduced cross-sectional area will be locally higher than in the other parts of the beam. The stress will also be highest in this narrow region because of this reduced cross-sectional area carrying the load.

**Bending strain**

When force is applied to the thumbholder, it will bend, creating a stress and strain within the beam which is detected by the strain gages mounted on the thumbholder.

Figure 12 illustrates a typical bending strain situation. The beam is anchored at one end and free to move at the other end, and is called a cantilever beam. A force is applied perpendicular to the surface at the end of the beam. To examine the state of stress and strain at a point $P'$ of the beam, a small section of the beam at that point has to be examined. The relationship between stress and strain at this point is the same as that for tension and compression.

$$\sigma_x = E \cdot \varepsilon_x$$

This is the strain which can be measured with a strain gage.
The cantilever beam of the thumbholder will be anchored at one end and at the other end where
the screws tighten the thumb, the sMU force is applied. The strain gages are placed at the narrow
part of the beam because the stress and the strain will be higher in this part. The force-strain
relationship (the relationship between the twitch tension and the strain) is as follows:

\[
\varepsilon_B = \frac{\sigma_B}{E} \quad \sigma_B = \frac{(F_v \times l)}{Z}
\]

The bending strain (\(\varepsilon_B\)) is equal to bending stress divided by Young's Modulus of
Elasticity. Moment stress (\(\sigma_B\)) equals bending moment (\(F_v \times l\)) divided by sectional modulus (\(Z\)).
Sectional modulus is a property of the cross-sectional configuration of the beam and in case of the
device is:

\[
Z = \frac{bh^2}{6}
\]

Where

\begin{align*}
\text{b} &= \text{width} \\
\text{h} &= \text{thickness} \\
\text{l} &= \text{length}
\end{align*}

Strain gages measuring the strain, used in bending strain configuration can be used to determine
vertical load (\(F_v\)).

\[
F_v = \frac{E \varepsilon_B Z}{l} = E \varepsilon_B \frac{(bh^2)}{6} \frac{1}{l}
\]

5.8.3 Strain gages and Wheatstone Bridge

For measuring twitch tension, i.e. force, strain gages are widely used in biomedical

Strain gages are devices used for the electrical measurement of mechanical quantities. They are
used for the measurement of strain, tensile and compressive strain caused by forces, pressure,
heat, structural changes of the material and so on. These gages consist of a grid of very fine wire
or foil bonded to the backing or carrier matrix (figure 13). The electrical resistance varies linearly
with strain. In use, the carrier matrix is bonded to a surface, force is applied, and the strain is
found by measuring the change in resistance. The amount of force applied can be calculated from
the known strain.
The three primary factors influencing gage selection are temperature, state of strain (gradient, magnitude, and time dependence) and stability required.

The bonded resistance strain gages of OMEGA, type SG-3/350-LY13 were chosen for this device because of its dimensions, the nominal resistance, the low price, and their suitability for this application. Some characteristics are: temperature characteristics are matched to aluminum, nominal resistance of 350 Ohm, dimensions of the grid are 3.0 * 2.5 mm and of the carrier 8.0 * 6.0 mm, and maximum permitted bridge energizing voltage is 8 [V rms].

Their rugged construction make them suitable for static and dynamic measurements with a high degree of accuracy. The measurement grid is formed by etching constantan foil which is then completely sealed in the carrier of polyamide film. Other characteristics are: mechanically strong, small bending radius 3 mm, broad temperature range, and the hysteresis is negligible. The strain gage has thermal resistance characteristics that compensate for the effects of the mismatch in thermal expansion coefficients between the gage and the specific material. These strain gages have another advantage: the conductor in the foil grid gage has a large surface area for a given cross-sectional area which keeps shear stress low. Shear stress may influence the recording of the force applied in a direction which has a force component perpendicular to the direction measured by the pair of strain gages.

The minute strains caused through the applied force, i.e. twitch tension, will change the resistance of the strain gages which are positioned at the narrow part of the cantilever beam. The strain gages are part of the Wheatstone bridge circuit. This bridge is capable of measuring the small resistance changes, is thus sensitive, and compensates for temperature effects.

The use of two strain gages connected in a bridge configuration is suitable for bending measurements. As shown in figure 9, the strain gages are placed on the cantilever beam and the resistance of each will change in proportion to the bending strain imposed on the beam. The changes will be of opposite sign (tension and compression), and the gages are inserted in the $R_1$ and $R_2$ position. The bridge output will thus be twice that achieved by a single gage. The total strain is represented by a change in the voltmeter (figure 14). The strain gages are positioned in the bridge as indicated by $R_1$ and $R_2$, and the other two resistors are of 2 kOhm, which minimize the current and heat generated (keeps it cool). These two resistors for each bridge are mounted close to the strain gages to minimize temperature effects.
An advantage of the Wheatstone bridge is that it offers an opportunity for temperature compensation of the strain gages. An increase in temperature would cause the thumbholder to expand, increasing the tension on both gages by an equal amount and therefore the net effect on the output voltage of the bridge is negligible. The ratio $R_1/R_4$ is thus unaffected by changes in temperature.

The sensitivity of the strain gages is pertained by the gage factor. The gage factor is defined as the ratio of the fractional change in resistance to the fractional change in length (strain) along the axis of the strain gage, i.e. the ratio of unit change in resistance to unit strain. Gage factor is a dimensionless quantity and the larger the value the more sensitive the strain gage.

$$GF = \frac{\Delta R/R}{\Delta l/l} = \frac{\Delta R/R}{\varepsilon}$$

$GF$ = gage factor

$\varepsilon$ = strain; tensile is (+) and compressive (-)

Thus with a typical gage factor of 2 and strain gage resistance of 350 Ohm, a strain of 1000 would change the resistance of the gage by 0.700 Ohm.

Equation to compute strain from unbalanced bridge voltages:

$$V_r = \frac{V_{out}}{V_i} = \left[\frac{R_3}{R_3 + R_2} - \frac{R_4}{R_4 + R_1}\right] - \frac{4V_i}{-\varepsilon}$$

$$\varepsilon = \frac{-4V_i}{GF \left(1 + 2V_i\right)}$$

The bridge output signal requires amplification before it is applied to a readout instrument. Since interference signals are in the same phase on both input leads, they are not amplified. This is known as "common mode rejection". The chosen amplifier is the 2B31J Strain Gage conditioner with the AC1213 Edge Connector of Analog Devices. This is a high performance, low cost, compact signal conditioning module designed specially for high accuracy interface to strain gages. The 2B31J consist of three basic
sections: a high quality instrumentation amplifier, a three-pole low pass filter, and an adjustable transducer excitation. The input stage is a high input impedance ($10^8$ Ohm), low offset and drift, low noise differential instrumentation amplifier. The design amplifies accurately low level (mV) transducer signals riding on high common mode voltages ($\pm 10$ V), with wide (1-2000V/V), single resistor ($R_C$), programmable gain to accommodate 0.5 mV/V to 36 mV/V transducer spans. The three-pole active filter has a cutoff frequency (-3dB) which is set at 1.5 kHz.

A common power supply is used for both bridges and each amplifier. The bridge excitation voltage level affects both the output sensitivity and the gage self heating. From a measurement standpoint a high excitation level is desirable, but a lower level reduces gage self heating.

The sensitive input and gain setting terminals have to be shielded from noise sources for best performance. To avoid ground loops, the cable shield or signal return is grounded at one point. After installation, the resistance of the strain gages were checked to assure that they were not damaged during the installation.

The leads are shielded and adequately insulated to prevent electrical noise and interference. Magnetic induction is controlled by using twisted lead wires and forming minimum but equal loop areas in each side of the bridge.

A housing around the strain gages and the bridges is made and this cover reduces the environmental noise, and ambient temperature fluctuations.
5.9 Further development and dataprocessing

5.9.1 Suggestions

During the development of the TFM-system, it became clear that still a lot have to be developed before the TFM-system is ready to use. Because of the limited time of this research, some suggestions are presented.

Until now, the experiments are performed just as shown in the scheme below. The output of the 2B31J amplifier went to a chartrecorder and this output was 10mV/mm.

![Diagram of instrumentation chain]

First of all, the way of recording and presenting the data has to be defined (figure 15). Anyway a filter, amplifier, oscilloscope, and a device to store the data is necessary. If during the data acquisition the force signals have to be shown, an oscilloscope may be useful. A summator to determine the force direction an force amplitude is necessary. If the data storage and processing will be done with a computer (eventually the Advantage EMG system), the force signal will be digitized with a analog/digital converter. Also the force and EMG signals have to be integrated. Suggestions are presented in appendix 3.

![Diagram of instrumentation chain]

The "programmable color digital storage oscilloscope with digital persistence" of Harvard apparatus may be suitable as device to store and show the data during the experiments. Software has to be developed for the data analysis. The trigger out of the EMG system can be used to synchronize the data recording.
The force signal includes the sMU twitch tension, influence of gravity, environmental noise, body movement artifacts, respiratory artifacts, and blood pressure waves. These artifacts have to be eliminated from the signal. The cover around the strain gages and the bridges reduces environmental noise. The handholder reduces body movement artifacts. The unwanted forces have to be reduced by subtracting background forces just prior to the stimulation. Because the blood pressure pulsations have a similar shape to the twitches, the background subtraction and stimulation are in turn triggered by the pulsations. According to Dr. G. Westling (private communication), there is a linear decay after the systolic phase of blood pressure during which sMU twitch can be insulated. An optical pulse detector attached to the subjects middle finger can be used for the triggering purpose. A pulse transducer is commercially available from Grass Instruments. Thus, the stimulator will have to be driven at a rate corresponding to the resting heart rate and the force data will be collected in the time period following the delay and before the ensuing pulse pressure wave. Averaging of the sMU twitches may be required.

5.9.2 Force data analysis

Researchers (Doherty, 1993a; Westling et al., 1990) have also recorded single thenar MU force data and presented the following characteristics:
* Peak force
* The resultant force vector
* Contraction time
* One-half relaxation time
* X-Y plot of the abduction vs. flexion force

The force data analysis will have to include at least these characteristics to compare the data of the neuromuscular study with the data presented in literature. The force signal can be analyzed by an algorithm. The algorithm will derive the resultant composite force from the abduction and flexion force components. The peak force, CT, and ½RT can be determined by a computer algorithm from the resultant force record. An X-Y plot of the abduction vs. flexion force can be produced to ensure that monophasic time course and trajectory, indicative of a sMU response. Excitation of two or more motor axons in response to a given stimulus would result in increased twitch tension, a compound action potential, and typically a non-linear abduction vs flexion plot indicative of two MUs with two different time courses. The resultant vector or angle of peak abduction force to peak flexion force, and this angle can be plotted.
5.10 Experimental procedure

In this part some suggestions are presented for the experimental procedure. Because of the limited time, a part of the experimental setup has still to be defined. The 3-D environment and axis have to be defined as basis for the force direction and for the thumb and TFM-system position. The setup for the device and the handholder have to be determined and is dependent on the room used for the experiments.

For the experimental procedure, the device has to be calibrated. This can be done by just putting some weights (10 - 500 g) on it for both directions. Also the position and the angles in the 3-D area has to be measured before starting the experiments in order to know the position of the thumb for a better reproducibility when the subject returns for further tests. This can be done by using a surface gage.

During the experiments, first the M-potential has to be determined without the force measuring device because the thenar MUs will contract simultaneously and that may damage the device. Also the current scale has to be put on maximum 25 mA to prevent stimulation with an intensity which could damage the device (the force generated by the thenar muscle may exceed the elastic limit of the TFM-system, part 5.8.2.1). Then the device can be used with the thumb positioned in the thumbholder and the sMU twitches can then be measured. Body movement artifacts influence the recording and make adequate recording impossible. So, the subject has to be kept comfortable, relaxed, and quiet.

Not every sMU of the sample of sMUAPs recorded, will move the thumb interphalangeal joint and so only the twitch tension of several MUs of the total sample will be recorded. This is because the thenar muscles have diverse origins and insertions and operate across several joints providing multiple degrees of freedom. The MUs detected are not all of muscles which insert across this interphalangeal joint. It is hard to say if the twitch tension of a sMU of a muscle inserting on the metacarpal joint will be detected or not. So, it has to be noticed that there may be a bias towards sMUs in a certain direction or magnitude.

To control the x- and y-force components, the operator will turn the beam with the strain gages, so that the force measured by one pair of gages will be zero. The other amplifier will obtain the force amplitude. The operator has to write down the amplitude and the angle over which the thumbholder has been turned. This is necessary for determining the force direction in 3-D and to control this with the calculated one.
6. **Experiments**

6.1 **Set of experiments without electrical stimulation**

First a set of experiments without electrical stimulation were performed to control if the TFM-system was sensitive enough to detect the sMU force. First, the strain gages were tested if they were not damaged during the installation, and if both force direction measurements didn't influence each other.

![Electrical scheme of experimental set-up.](image)

For these experiments (figure 16), the thumbholder was fixed in a vise. The resistors of the two bridges of Wheatstone were made on a proto-board screwed to the thumbholder. The output of the bridges were each connected to a amplifier which output went to a dynograph recorder (R511A, Sensormedics) with a 16 cycle notch filter. A common power supply was used for both bridges and amplifiers.

![Results of experiment](image)

**Fig. 17 Results of experiment; return to baseline, pulling and pushing detection.**
Several weights (5gr up to 500 gr) were placed on the thumbholder and its influence was detected with a chartrecorder. In summary the following results were shown for both force directions (figure 17):

- The signal returned to the baseline when the weights were taken off.
- Pulling and pushing were detected.
- Pulling, pushing, or putting a weight on the thumbholder in a direction perpendicularly to the direction the strain gages would measure, caused no changes in the bridge resistance and so nothing had been recorded.
- The weight of 5 gr and forces by pushing with the finger on the thumbholder or just touching it, were recorded.
- When tapping on one side of the device, changes in the resistance in the direction perpendicular to it were seen. This is due to the characteristics of the tapping which is like a shock wave.

The results showed that the TFM-system seems sensitive enough to detect sMU forces. When a force is applied perpendicular to the thumbholder, one pair of strain gages measured its amplitude and the other pair detected nothing. Experiments have to prove if the twitch of a sMU have the same characteristics as a shock wave. If so, an error will be introduced in the data. However, these results were satisfying and experiments with electrical stimulation could be performed with the device.

6.2 Set of experiments with electrical stimulation

As the TFM-system seemed good enough in use, experiments with electrical stimulation of the median nerve (MPS method) and measuring the sMU force with the TFM-system were performed. These set of experiments would have to prove if the TFM-system can detect several sMU twitches, satisfies the criteria of detecting one sMU, will be suitable for research, and records the artifacts due to respiration, body movements, and pulse pressure waves.

The handholder was used to immobilize the forearm and the hand, leaving the thumb free. First a single thenar MU, causing movement of the interphalangeal joint, had to be found using the Advantage EM6 system and the MPS method.

Pieces of plastic and the two screws in the thumhole were used to fix the thumb of the subject. The side (skin) of the thumb in which direction it would produce the force (flexion and abduction), made contact with the aluminum thumbhole.

The results (figure 18) showed that the force shape was almost every time the same when there was a electrical stimulation of the same sMU. Those were not totally identical because of the respiration and blood pressure artifacts. Also talking and body movements of the subject influenced the recorded signal. The twitch tension of a small sMU was also detected and so the device seemed sensitive enough.
**Development of TFM-system Experiments**

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<th>NParea (μVms)</th>
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<th>NPdur (ms)</th>
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<td>99</td>
<td>13.3</td>
<td>100</td>
</tr>
</tbody>
</table>

Fig. 18 Force recorded of one sMU during repeated stimulation. The MUAP of a small and larger sMU.
In summary the following conclusions could be taken:

- Device seemed sensitive enough.
- The handholder was very comfortable according to the volunteers. However, the handholder need to be more stabilized. To prevent finger movement, the velcro strip seems satisfying. It has to be tested if U-shaped clamps will further decrease artifacts of finger movement.
- Force can be detected in both directions.
- sMU twitch tension of small and larger MU were detectable.
- The device showed that the shape of the force signal was almost identical and occurred at a "all-or-none" response and with the same frequency of the stimulation.
- Respiratory and blood pressure waves are detected as expected and with the expected amplitude levels.
- Body movements (moving of a body segment, talking and so on) resulted in movement artifacts which influenced accurate detection of sMU twitch tension.
- The immobilizing of the thumb was not satisfying and a better solution has to be found. For example: metal piece on the end of the screws and combined with the plastic pieces when there is much space in the thumbhole left. This solution may be more satisfying.
- Table with the device has to be stable.

So the device seemed suitable for these kind of experiments but will first have to be improved. Elimination of unwanted forces, defining of the experimental setup, experiments to determine the properties of the TFM-system and so on, are necessary before the system can be used in research.

6.3. Linearity experiments

Weights from 10 g up to 130 g with steps of 10 g were placed on the thumbholder at the point were the interphalangeal joint will act on the thumbholder (the screws to tighten the thumb are there). In larger steps the weights were taken of the thumbholder. The gain is 10mV/mm for the tests for linearity. The results showed that the device is linear over this range which is comparable with the range of the thenar forces. The output of the amplifier was 10mV/mm and for 10 g the output is 30 mV as can be seen in figure 19.

![Fig. 19 Results of linearity tests.](image-url)
6.4 Further experiments

More experiments have to be performed to test and improve the TFM system, the experimental set-up, and to know the properties of the system. A summary of the necessary experiments follows:

- The experiments have to be repeated with the same subject to investigate the accuracy and reproducibility.
- The twitch tension characteristics of different MUs have to be detected.
- The position of the thumb in the 3-D environment and definition of the axes have to be determined. In this way, every time the same subject returns, the set-up can be repeated, improving the repeatability, reproducibility, and accuracy of the measurements.
- Rotating the device to be able to measure the force in the direction of the strain gages; obtaining the maximum amount of force and knowing the direction as control. The operator need to write down the angle of the rotation (a scale has to be applied on the device). This procedure can be used as control for the calculated values.
- Measurements to determine the characteristics of the TFM-system.
7. General conclusions

The causes of age associated loss of muscle strength, muscle mass, and muscle efficiency are not completely known. At the neuromuscular level, the losses may be associated with age-related changes in the muscle, in the nervous innervation of the muscle, or with circulatory factors that are involved with muscle homeostasis. Research in this area will give a better understanding of the neuromuscular changes and the aging process. This is important because a loss of mobility inhibits participation in physical activities, as well as successful performance of the necessary activities of daily living.

Electrophysiological and contractile properties of human thenar MUs in relation to aging, will be investigated in the BLSA. A device to measure human thenar sMU twitch forces had to be developed for this study because there wasn't one commercial available. This prototype can detect sMU twitches and measure the force direction in two directions. It showed good results during the first experiments. Twitches of small and larger sMUs were detected, the detection occurred at a "all-or-nothing" response, satisfied the requirements of detecting one sMU, and artifacts due to movement, respiration, and blood pressure waves were seen. The linearity tests for both force directions were satisfying. The TFM-system is now not ready to use in the experimental procedure because the signal processing, integration of force and EMG signals, data analysis and presentation have still to be developed.

Another conclusion of the EMG and force tests is that of the 10-20 MUs detected in a subject only the twitch tension of about 5 sMUs of this sample can be detected which is also shown by Doherty (1993a). The reason is that the eight muscles contributing the thenar eminence have a different origination and act on different joints of the thumb. With this device only force measurements of the interphalangeal joint can be made and so the force caused by movement of the metacarpal bone or the distal phalanx may not be detected. The latter because of its soft tissue and the former because it may not cause movement of the interphalangeal joint. So it might be pretty hard to find an unbiased sample of the twitch tension of sMUs.
8. **Recommendations**

The TFM-system and the handholder are made only for right handed people. For the left handed participants another handholder and TFM-system have to be made.

Until now, the thumbhole diameter seems to be large enough to be used for the experiments (nobody had to be excluded). However, taking the anthropometric data into account of the US army (appendix 2), it may be clear that too many men may be excluded for the experiments. In that case another thumbholder will have to be developed with another diameter.

The way the thumb is fixed in the thumbhole is not satisfying and another solution has to be found. Suggestions are:

1. Taking the anthropometric data into account of the thumb, a tube will consist of two parts just like a pipe which is splitted, to make it suitable for all thumb sizes. The tube will be fixed around the thumb and goes into the thumbhole. This part has to be applicable for all sizes of the human adult hand.

2. Making several adjustable rings of different diameters. Put the ring around the interphalangeal joint and fix the thumb further with the screws in the thumbhole.

To reduce body movement artifacts, a handholder has been developed which immobilizes the forearm and the hand. This handholder is also a prototype and can be further improved by stabilizing the handholder and by the use of U-shaped clamps to immobilize the fingers.

The pulse pressure waves will have to be detected by an optical pulse detector attached to the subjects middle finger. Recording this signal, it can be eliminated from the force signal.

Respiratory artifacts will be reduced through the experimental set-up, the subject can be asked not to breath for a while, or detection of the breathing pattern and stimulation only at a rate corresponding to the resting heart rate, just after the systolic phase of blood pressure. Also subtraction of this unwanted force is necessary.

Further development as signal processing and data presentation, and definition of the final experimental procedure, is neccesary. The EMG and force data have also to be integrated, therefore some software will have to be developed.

CV measurements can show that the motor axons stimulated cover the entire range of thick myelinated fibers within the median nerve (Westling et al., 1990). Including these measurements in the study protocol will give the opportunity to control for any biase in the sample of MUs.
References


Development of TFM-system

References


Appendices

Appendix 1: Anatomy of the hand

Appendix 2: Anthropometric data

Appendix 3: Integration of force measurement devices and the Advantage EMG system

Appendix 4: Technical specifications of the Advantage EMG System

Appendix 5: Technical Drawings
Anatomy of the hand

The wrist (figure 20) is composed of eight carpal bones. The five metacarpals form the bones of the hand, which are numbered 1 to 5 beginning with the lateral or thumb side. The five digits of the hand have a total of 14 phalanges. Four fingers each carry three phalanges, whereas the thumb has two phalanges. In the thumb they are named proximal (first) and distal (second). The carpometacarpal joint of the thumb is a saddle joint. The thumb itself is placed with its palmar surface at about a 90-degree angle to the fingers. Flexion, extension, abduction, adduction, circumduction, and apposition are permitted.

The muscles that move the wrist and the fingers take their origins from the distal ends of the humerus or the proximal ends of the radius and ulna. Functionally they may be divided into two groups: those lying on the anterior aspect of the forearm are primarily flexor of the wrist and fingers; those lying on the posterior forearm are primarily extensor of the wrist and fingers (see figure 21). Abduction and adduction of the wrist are accomplished by cooperation of certain of the anterior and the posterior muscles.
Anthropometric data

Digit 1 length

The length of the first digit measured from its tip to its base (see figure 22, data of the US Army).

Fig. 22 First digit measurement

<table>
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Table 1 The summary statistics of 1-digit length.
Digit 1 interphalangeal joint circumference (D1C)

Dimension was calculated from regression equations based upon survey measurement of Digit 1 Breadth (D1B) (see figure 23).
All equation values are in millimeters.
Males: \[ D1C = 2.20 \times D1B + 19.47 \]
Females: \[ D1C = 1.96 \times D1B + 22.60 \]

Fig. 23 digit 1 interphalangeal joint measurement

<table>
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Table 2 The summary statistics of digit 1 interphalangeal joint
Integration of force measurement devices and the Advantage EMG system

1. Introduction

The study "Effects of Age and Strength Training on Muscle Strength, Body Composition and Health Status" is designed and will start in 1995. Researchers are currently working to establish and optimize measurement protocols. Several adjustments on the equipment are needed for one aspect of the project where force and EMG signal need to be recorded together. In this section, the project is described and the method by which the force and the EMG signals can be integrated is explained.

1.1 Study Description

Causes of frailty are important to understand because of associated high costs of health care needs. The BLSA has developed a study to investigate gender and ethnic related effects on age differences in neural control of muscle function and whether differences in neuromuscular function are associated with differences in physical activity or functional disability. Age-associated loss of muscle strength can result in decreasing physical independence. Past studies have shown that exercise increases muscle strength, functional capacity and independence in the elderly (Booth et al., 1994; Brooks et al., 1994; Brown, 1994; Doherty 1993b; Dyck, 1994; Fielding, 1994; Robinson, 1994). It is also known that significant differences exist between men and women in muscle strength and body mass.

Although muscle atrophy is attenuated by resistance training with aging, little is known about effects of resistance training on the loss of spinal motor neurons, MUs, and MF number. Some of the changes in the neuromuscular system seem reversible through continued activity. It is clear that elderly persons who remain physically active have only moderate losses in skeletal muscle mass, but exactly how much of the decrease in muscle mass is a) a consequence of aging, b) a reduction in physical activity, or c) both is currently unknown. Studies showing that individuals aged 60-90 year can increase/maintain muscle mass with resistance training suggest that the lack of muscle loading could contribute to muscle atrophy in the aged (Booth et al., 1994). A combination of a progressive neurogenic process and a decrease in muscle loading are two contributors to the age effects on skeletal muscle atrophy and decline in motor function.

Exercise may result in endocrine, paracrine or autocrine responses that stimulate muscle growth. A certain concentration of hormones such as insulin and growth hormone or testosterone, may have a permissive action acting in conjunction with local changes associated with working muscles. Localized changes in paracrine hormones such as insulin growth factor-I (IGF-I) may be very important in regulating tissue growth but it has to be determined whether there is a relationship between the production of growth factors and the mechanical activity of the muscle (Booth et al., 1994; Jones et al., 1989).

However, little is known about morphological muscle changes and their biological regulation occurring during strength training programs in younger versus older men and women and how these translate into improved neuromuscular performance.
The study "Effects of Age and Strength Training on Muscle Strength, Body Composition and Health Status" will include 8 weeks of one-leg strength training, detraining (16 weeks), and total body strength training (24 weeks) to determine their effects on muscle strength, muscle function, body composition, and health status. Four groups of untrained subjects with 10 subjects per group—young (20-30 year old) and older (65-75 year olds) women and men—will participate in this study. At specific points in the training program, the following measurements will be made: magnetic resonance imaging and absorptiometry to determine lean body mass; surface EMG and intramuscular EMG to estimate MU size and activity; muscle biopsy to determine distribution of fiber types and muscle biochemistry; serum hormone levels to include testosterone, cortisol, IGF-1; plasma glucose and insulin concentrations in response to an oral glucose tolerance test, serum creatine kinase and creatine kinase-mm isozyme.

1.2 Neuromuscular measures

With aging, changes occur in the neuromuscular system with a decrease in the number and size of the motor neurons and with a slowing of nerve CV. Loss of MFs result in a reduction of MUs which are able to innervate other MFs. With loss of innervation, a MF either atrophies or is innervated from larger fiber sprouts from other MUs. A decline in the number of active MUs can be demonstrated by EMG techniques. In this study, surface and intramuscular EMG recordings are obtained in order to estimate effective MUs.

The Kin-Com system, a muscle testing and training system, is used for the muscle strength measurements and the Advantage EMG system to obtain the EMG signals. The goal is to measure the sizes of surface recorded MUPs during an isometric contraction to recruit MUscoupled with STA techniques to isolate and measure the sizes of a representative sample of surface MUPs selected by a needle electrode inserted into the contracting muscle (Brown et al., 1988).

In the study, force and EMG signals of the muscles of interest are measured as well as other parameters. The muscle group of interest are the vastus medialis and biceps brachii. A needle electrode is placed into the body of the muscle to identify specific MUs. A surface recording is taken simultaneously. By averaging a large number of intramuscular spikes from a sMU, the average surface potential can be determined which is used for the calculation of the MU estimation. To make these measurements, a decomposition algorithm is used that can detect up to 5-10 MUs at a time. To maximize the accuracy of the collection, subjects are asked to generate a percentage of their maximum muscle strength. First, with the Kin-Com system, MVC will be determined. Then, during an isometric contraction of 10-25% of MVC controlled by the Kin-Com system, needle and surface EMG are recorded along with the force signal. The needle electrode records only the MUAPs of the MUs whose motor fibers are in the vicinity of the electrode. With a computerized decomposition technique, sMUAPs are determined from the interference pattern. Analyses of both force and EMG signals will be made. In the future, this part of the study may extend to obtain the twitch tension of sMUs of this muscle group.
Both force and EMG signal can be collected now, but an integrated collection will be better. In the next section, a description of the systems and a solution to achieve this goal is provided. However, it is possible that this goal can not be achieved within the set time.

2. Systems Description

The EMG system and the decomposition program used in this study for analyzing the EMG signals are described. The program is specially developed for these kind of experiments and decomposes the interference pattern to obtain the sMUAPs. Then, the Kin-Com system used for the force measurements is described.

2.1 The Advantage EMG system

The Advantage EMG system —which is manufactured by the Clark Davis Medical Systems Inc., London Ontario Canada— is used for the recording of EMG signals such as sMUAPs, M-potential, F-response, and MU number estimation. This EMG system is specially designed to improve the accuracy of MU number estimation and is convenient to operate in a clinical environment. Several specifications (Advantage EMG system operating manual) are described below.

Technical innovations incorporated into the Advantage EMG system enhance the EMG testing process:
* High graphics processing speed guarantees true real time waveform display, eliminating the need for an external analog monitor.
* Fast data acquisition allows sampling rates up to 350 kHz.
* Continuous background signal monitoring and continuous screen readout of amplifier, stimulator, and list parameters are displayed on the same screen.

Several convenient operating features leave the operator free to focus attention on patient and test procedures. The software package includes real time needle EMG, motor and sensory nerve conduction, quantitative EMG, single fiber EMG, repetitive stimulation, somatosensory evoked potentials, screen storage mode, and other functions. Test data is stored automatically and can be recalled at any time for analysis. New test procedures and other software can be loaded onto the system from 3½ inch diskettes.

Other specifications are:
* Enclosed in a transportable unit, the system includes a swivel-base monitor, dual footswitch controls, dual stimulator outputs, and an adjustable utility table.
* Optically isolated input/output board for external trigger Input/Output and 2 channel external analog Input/Output.
* Provision for safe connection of external devices to the system while maintaining electrical isolation.
* Report and Result files can be stored in standard ASCII format for direct transfer into statistical analysis, data base and other commercial software.

Full technical specifications are shown in appendix 4.
For the study, a computerized decomposition method is used for obtaining sMUAPs and MU number estimation which is not part of the Advantage package. Because it is almost impossible for the subject to activate one sMU, several MUs are recorded in stead of one MU. Then the recorded interference pattern will be decomposed to get the sMUAPs.

2.1.1. Motor Unit Decomposition

Motor Unit Decomposition is a technique which uses voluntary contraction to determine the sizes and shapes of surface detected MUPs. The decomposition method will be used for the proximal muscles including the vastus medialis and biceps brancii. In this technique, voluntary MU recruitment is analyzed by a method based on spike averaging, with a needle electrode inserted in the muscle and used to identify corresponding surface MUAPs. First, the MVC is determined using the Kin-Com system. MVC refers to the condition in which a person attempts to recruit as many fibers in a muscle as possible to develop maximum force, that is, maximum contraction.

Then the maximum M-potential is determined by percutaneous stimulation of the nerve and detecting the signal with surface electrodes. This is necessary for the MU estimation. For this estimation, the peak-to-peak amplitude of the electrical response (M-potential) to muscle activation using surface electromyogram is examined and divided by the average peak-to-peak amplitude of the MUAPs analyzed.

The EMG measurements are recorded during an isometric contraction and the Kin-Com system will be used to control the constancy of force output. An isometric contraction is one where the muscle does not shorten or lengthen. Such a contraction can be either maximum or submaximum. The force is controlled by the subject, and is to be maintained within 5% of the target value.

A concentric needle electrode (DMF 25 TECA) is placed into the body of the muscle and is used to detect the electrical potentials generated by those voluntary recruited MUs lying within the pickup territory of the needle electrode. The surface electrode which also measures the MUAPs is placed over the motor point and the ground electrode is placed near the recording electrode.

The subject, sitting, will extend his/her leg for 30-60 seconds while the needle electrode and a surface electrode record the MUAP of several MUs. The recorded interference pattern is then decomposed by the computer program to identify specific MUs and their firing pattern. The expectations are that it is possible to decompose 5-10 MUs up to 10-25% MVC. If too many MUs are recruited, it will be impossible to decompose the signal. The needle will be placed into several points of the muscle body to find up to 20 distinct MUs.

The program is also able to analyze the force signal together with the surface and the needle EMG.
2.2 The Kin-Com System

The Kin-Com system (Kin-Com 125E Plus, Chattecx Corporation) is designed to provide the user with both assessment of muscle strength, as well as the tools of exercise training. The Kin-Com (Operator's Manual, Kin-Com 125E Plus) provides:

* Comprehensive muscle testing capabilities in the concentric and eccentric spectrum.
* Multiple patient training capabilities: isokinetic, passive isometric, isotonic, and a protocol mode.
* Operation through screen touch technology.
* Visual feedback for both clinician and patient.

When working with subjects, in either a training or evaluation function, the operator monitors and controls the range of movement of the activity that is performed, the muscle tension the subject is to generate, and the speed of the movement.

The load cell measures the direction and amount of force that is applied by the subject. The load cell can accurately measure from one Newton to 2000 Newton of force. For the decomposition setup, the EMG measurements are recorded from 30 to 60 seconds during an isometric contraction. The Kin-Com system measures the MVC, does not show the force versus time, but digitally records the amount of force in real time. The system cannot measure the twitch tension of sMUes. In the appendix the electronical schemes are shown.

For this study, it is desirable to use a system that can calculate and set a baseline (for example 10% of MVC), and the range within which the force has to be maintained. When the force falls outside this range, a buzzer or light will warn the operator and the subject. Also the force signal versus time should be shown on one screen, so the subject will know what time is left in order to maintain the isometric contraction. At the present time, the Kin-Com system can only be used for the digital display of the force signal but software modifications will improve the experimental procedure when the described display features above are possible.

Another solution might be to use other equipment, which has the raw force data of the Kin-Com system as input. This other equipment, that will have to be developed or obtained, can also be used for the twitch tension measurements of the thenar musculature and, in the future, for the twitch tension measurements of the proximal muscles. This equipment needs to be flexible to be suitable for several study setups.
Development of TFM-system

Appendix 3

3. Integration of force and EMG signals

In the following section, the actual case and the necessary changes to achieve the goal are described and the options to solve these are explained by schemes.

3.1 Introduction

During an isometric contraction, the EMG signal will be recorded. From the interference pattern, an estimation of the number of MUs will be calculated by the decomposition technique. The Kin-Com system will be used to measure the produced force of the muscle under control. The produced force has to be at 10%-30% of MVC. To control this, the produced force will be represented in real time, and it has to be ensured that it will stay within a certain range. Therefore, as described earlier, an adaptation in the software of the Kin-Com system will be necessary or other equipment will be used that represents, and stores the force produced by the muscle under control. Eventually, the Kin-Com system may be used for the presentation of the force signal. Once a constant force level is attained, the EMG recording will be initiated using the Advantage EMG system which will then store the force signal.

What is necessary for the study is an application to integrate the force data with the EMG-signals. Therefore the signals need to be synchronized and data processing created for a suitable presentation of both signals. This raises another problem relating to differences in sample frequencies in both systems.

Both the Kin-Com system and the Advantage EMG system are sophisticated pieces of equipment. However, the EMG system is necessary to detect and obtain sMUs. It is flexible, other software can be easily implemented, and is already capable to do the data processing of the force signal within the decomposition program. The EMG system is equipped with a "Trigger Output" port to allow connection with the accessory device you wish to time lock with. Use of this capability will depend on the software/hardware capabilities of the Kin-Com system and also of the decomposition program.

Because the EMG system has only two input channels, it isn't possible to synchronize and store the EMG and force signals at this time but a possible solution to this problem may exist. The force signal of the Kin-Com or the twitch tension device will be transferred to the EMG system during or after the experiments. The raw force signal of the Kin-Com system can be obtained, by taking the signal and AC coupling into the signal cable. For the twitch tension device, a data acquisition system is necessary.
3.2 There are several options to record and integrate the synchronized signals.

In summary, the following has to be done during the course of the experiment:

- Real time display of the force for 30-60 sec.
- Automatic setting of a baseline and a minimum (0.95*baseline) and maximum (1.05*baseline) within which the force has to be maintained.
- A signal, like a buzzer or light, to warn the operator and the subject when the force signal doesn't fall in this range.
- Amplify and filter force signal correctly.
- Synchronized force and EMG signal storage.

3.2.1 Options

**Kin-Com modifications:**

- Develop software to set baseline and determine the minimum/maximum range automatically.
- Show the force versus time graphic on the screen.
- Synchronize data storage with the "Trigger Out" of the EMG system or by pushing a button which is connected to both systems.
- Store the force signal in files which can be transferred to the EMG system with 3½ inch diskettes for data processing and analysis after the experiments.

Some software adjustments might be necessary for the EMG system in this case.

Short term solution might be to display the force signal on the Kin-Com system. The raw force signal will also be amplified, filtered, and eventually displayed on an oscilloscope and stored synchronized by the "Trigger Out". Suitable amplifiers, filters, (A/D converter), and an oscilloscope have to be found. The raw force signal of the Kin-Com system could also be displayed on another device, oscilloscope or computer, and stored with the EMG signal synchronized by the "Trigger Out".

These device might be chosen such that it is also suitable to use to record the thenar twitch tension.

Another option is to collect the needle and surface EMG first and than repeat the measurement, collecting the surface EMG and the force signals with the needle in the same position. The procedure has to be repeated because the EMG systems has only two input channels and recording first the needle and the surface EMG and than the force signal and surface EMG, the data can be analyzed in the following way. Because there is a relationship between the force and the needle EMG and the force and the surface EMG, a functional dependency function can be determined and so it may be possible to reduce the introduced errors and analyze the data. An advantage is that there is not a synchronization problem.

Another option will be that the raw force signal will be recorded on a display device (correctly amplified and filtered) synchronized by the "Trigger Out". After the experiments this analog signal
will be transferred to the Advantage EMG system playing back the stored surface EMG signal. Then, analysis of both the EMG and the force signals can be done in the Decomposition technique. Alternatively the force signal will be stored digitally at "Trigger Out" time and transferred with floppies to the Advantage EMG system.

3.2.2 Flows of alternative data acquisition schemes.

Scheme 1

\[\text{Kin-Com Load cell} \rightarrow \text{Modified Kin-Com for display and synchronized storage} \rightarrow \text{Data on floppies} \]

\[\text{"Trigger Out" of EMG system} \rightarrow \text{Modified EMG system}\]

The Kin-Com and the EMG systems need to be modified to achieve this solution and the modifications are described in part 3.2.1. To synchronize the signals, a button connected to both the Kin-Com system and the EMG system can be used for simultaneously initiating storage. Alternatively, the "Trigger Out" of the EMG system may be connected to the Kin-Com system. The advantage of this solution is that no other equipment is necessary. On the other hand, this requires that both corporations need to modify their systems to interact dependably.

Scheme 2

\[\text{Kin-Com Load cell} \rightarrow \text{capacitor + inductor for isolation} \rightarrow \text{amplifier and filter}\]

\[\text{A/D converter} \rightarrow \text{Data on floppies} \]

\[\text{"Trigger Out" of EMG system} \rightarrow \text{Modified EMG system}\]
The raw force signal of the Kin-Com system can be obtained, by splicing into the signal cable, extracting the force signal and isolating it with a capacitor and an inductor. Then the signal needs to be correctly filtered and amplified, according to yet to be determined specifications. The computer, receiving the digital force signal, will display the force signal and store it digital at "Trigger Out" time. The computer will set a baseline and the range within the force have to be maintained. The subject can see the amount of force produced and the force vs. time signal. With 3½ inch floppies, the data can be transferred for analysis after the experiments. The decomposition program may be modified to analyze this force data input.

Alternatively the Kin-Com system may be used for the display function for the options shown in scheme 2-5. Also for these options correct choices for the inductors, capacitors, amplifiers, filters, and other necessary equipment have to be made.

A choice for equipment has to be made which will display and record the force signal time locked with the EMG system and the data transfer will depend on the chosen equipment. Here the possibility of the use of two different oscilloscopes are described.

A programmable oscilloscope with digital data storage can be used as equipment. This option is almost the same as with the use of a computer. The filtered and amplified signal goes into a sophisticated oscilloscope (Harvard Apparatus) which also can be used for the twitch tension recording. The display of the signal can be done either on the Kin-Com system or on the oscilloscope. The digital data storage will be done by the oscilloscope time locked with the EMG system. With 3½ inch floppies, the data can be transferred for analysis after the experiments. The decomposition program may be modified to analyze this force data input.

Other equipment may be an oscilloscope which displays the force signal and stores it in analog format, time locked with the EMG signal recording. After the experiments the data will be digitized and transferred to the EMG system with floppies.
There are three signals to be correlated: the (raw) force, surface EMG, and needle EMG. If a functional dependency can be determined (e.g., between the surface EMG and force and between the needle EMG and surface EMG) then the three signals can be synchronized and analyzed together. This would involve two trials to correlate each experiment. The first would record the functional relation between force and surface EMG. Then, the force input would be replaced with the needle input and the experiment repeated to record surface and needle relationship. Software modifications have to be made to determine this correlation functions.

A third input will be applied to the EMG system so the force, surface EMG and the needle EMG can be stored and displayed simultaneously. To include the force analysis, some software modifications have to be made.

3.3 Conclusions

Choices need to be made on how to achieve the goal. Option 1 cannot be done within the set time. So choices for the capacitors, inductors, amplifier, filters, storage and display device have to be made.

For a short term solution the Kin-Com can be used for the display and other equipment for the storage. A convenient solution will be the one in which you can use the equipment also for the twitch tension recording. A sophisticated oscilloscope (Harvard Apparatus) might be also useful for other study set-ups.

But the last solution would be the best solution which allows simultaneous data storage and analysis with only one system. The decomposition method has to be modified and decisions for suitable amplifiers and filters have to be made.
Technical Specifications of the Advantage EMG system

Amplifiers
* Fully isolated
* Input impedance: >200 Mohms/25 pF
* Sensitivity: 2 μV/div to 10 mV/div in 12 steps
* High frequency filter: 100 Hz to 15 kHz in 8 steps, 12 dB/octave
* Low frequency filter: 0.5 Hz to 500 Hz in 8 steps, 6 dB/octave
* Notch filter: >30 dB down at 60 Hz
* CMRR: >100 dB at 60 Hz
* Noise: <1 μV rms from 2 Hz-10 kHz with input shorted
* Calibration: 200 Hz squarewave, 2 μV/div to 10 mV/div in 12 steps
* Electrode impedance check: 1-500 kOhms
* Temperature measurements: 20.0-40.0°C

Stimulator
* Fully isolated
* Stimulus output: constant current output to 100 mA adjustable in three ranges (20, 50, 100)
* Stimulus duration: 0.05 to 1 ms in 5 steps
* Repetition rate: 0.1-100 Hz including Single Shot mode
* Patient protection: overcurrent, overduration, and overfrequency, with automatic shutdown
* Stimulus monitor: separate LED bargraph and monitor readouts

Display
* Display CRT: 16-inch diagonal anti-glare screen
* Digital resolution: 1280 x 1024 pixels non-interlaced
* Number of colors: 4096 available
* Graphic display controller: 50 MHz TMS 34010, 32-bit processor with graphics accelerator allowing advanced windowing capabilities
* Vector drawing rate: 100,000 vectors/sec allowing true real time display
* Display memory: 2.5 Mbyte

Data Acquisition
* Resolution: 12 bit
* Maximum sample rate: 350 kHz throughput to memory
* Acquisition memory: 128 kbyte dual port ram
* Delay line: 4-channel hardware delay selectable in 1 division increments from 0 to 10 divisions
* Signal trigger: level or window discriminator controlled
* Time base: 1 msec to 100 sec full sweep
System Architecture
* Central processor: 80386 32-bit processor
* System memory: 5.0 Mbyte
* Mass storage: 44 Mbyte hard disk and 31/2 inch floppy disk drive
* Hardcopy device: laserprinter with 300 dots/inch resolution
* Interfaces: parallel printer port and RS-232
* External outputs: amplifiers, audio, and external trigger
* Keyboard entry: enhanced AT-style keyboard

General
* Dimensions: 56"x30"x30"
* Weight: 250 lbs approximately
* Power supply: 110/220 VAC 50/60 Hz with shielded isolation transformer
* Power consumption: 1000 VA approximately
* Patient safety: complies with CSA C22.2 No. 125 and UL 544 standards
Technical Drawings