Chapter 5

Clinical Quantitative Electromyography

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Additional information is available at the end of the chapter

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1. Introduction

Human muscles are composed of motor units and each motor (MU) unit is composed of a specific α-motor neuron and the muscle fibres it innervates. A motor neuron innervates the muscle fibres of a MU via the neuromuscular junction (NMJ) formed at the terminal end of each branch of its axon. Voluntary muscle contractions are initiated when the central nervous system recruits MUs by activating their motor neurons, which in turn, via their NMJs, activate their muscle fibres. At each NMJ, a region of transmembrane current is produced across the sarcolemma membrane of its corresponding fibre when the motor neuron is activated (i.e. discharges an action potential). This transmembrane current creates a change in transmembrane potential (or action potential) which propagates along the fibre and initiates/co-ordinates its contraction [1]. The currents creating the action potentials of the activated fibres of recruited MUs summate to create dynamic electric fields in the volume conductor in and around muscles. Electrodes placed in these electric fields detect time changing voltage signals which are the electromyographic (EMG) signals discussed in this chapter. When a muscle is affected by a neuromuscular disorder, characteristics of its action potentials, and as a result of the EMG signals they create, change depending on whether the muscle is affected by a myopathic or neurogenic disorder and the extent to which the muscle is affected. Therefore, quantitative EMG signal analysis can be used to support the diagnosis of neuromuscular disorders. Clinical quantitative electromyography (QEMG) attempts to use the information contained in an EMG signal to characterize the muscle from which it was detected to support clinical decisions related to the diagnosis, treatment or management of neuromuscular disorders.

The main objective of this chapter is to provide an overview of different clinical EMG (detection, measurement and analysis) techniques and the information available in an EMG signal depending on how it was detected (i.e. what type of electrode was used and during what type of muscle activation protocol). How to extract and utilize information from EMG signals to clinically characterize the corresponding MUs and subsequently the whole muscle will also

be covered. Descriptions of muscle electrophysiology, EMG detection electrodes and information extraction techniques for surface and intramuscular electrodes are provided. A review and comparison of applications of EMG techniques for clinical decision support concludes the chapter.

2. Muscle morphology, physiology and electrophysiology

2.1. Morphological and physiological description of a muscle

2.1.1. MU structure and layout

Each muscle consists of muscle fibres. The muscle fibres of a muscle are grouped according to their innervating α-motor neuron. A MU refers to a single α-motor neuron and the muscle fibres it innervates [5]. A voluntary muscle contraction is initiated by the activation of motor neurons whose axons propagate action potentials to their terminal ends where they join with a muscle fibre via a NMJ as shown in Fig.1. More specifically, a NMJ is the area where the axon terminal of a motor neuron axon innervates a muscle fibre. In a normal muscle, when a motor neuron is activated (i.e. discharges an action potential) each of its innervated muscle fibres are also activated via their respective NMJ. At each NMJ, following the arrival of the action potential at its axon nerve terminal, a region of transmembrane current is produced across the sarcolemma membrane of its corresponding fibre which creates a change in muscle fibre transmembrane potential (or a muscle fibre action potential) which propagates along the fibre and initiates/co-ordinates its contraction. Therefore, in normal muscle, activation of a motor neuron causes all of its innervated muscle fibres to contract and contribute to the force generated by the muscle.

For each muscle, there is a pool (or group) of motor neurons which are activated during a voluntary muscle contraction. The number of muscle fibres in a certain motor unit and the diameter of these fibres determine the size of the motor unit or the magnitude of its contribution to the muscle force created. The number of muscle fibres within a motor unit is not constant. Most muscles have large numbers of smaller MUs and smaller numbers of larger MUs. The distribution of the MU sizes of a muscle determines how precisely its force can be controlled; the smaller the motor unit, the more precise its force and function.

A MU territory is the cross-sectional area of a muscle in which the fibres of a MU are randomly located. For a normal MU, its MU fibres are randomly positioned throughout its territory. MU territories can be conceived to be circular, with diameters taking values between 10 and 15 mm depending on the size of the MU. In addition, the MU territories of the MUs of a muscle are greatly overlapped. Therefore, in a normal muscle, adjacent muscle fibres rarely belong to the same MU. Instead, the muscle fibres of a MU are interdigitated with muscle fibres of many other motor units. The interdigitation and spatial distribution of the fibres of the MUs of a muscle, help evenly distribute the contributions of MUs to muscle force.

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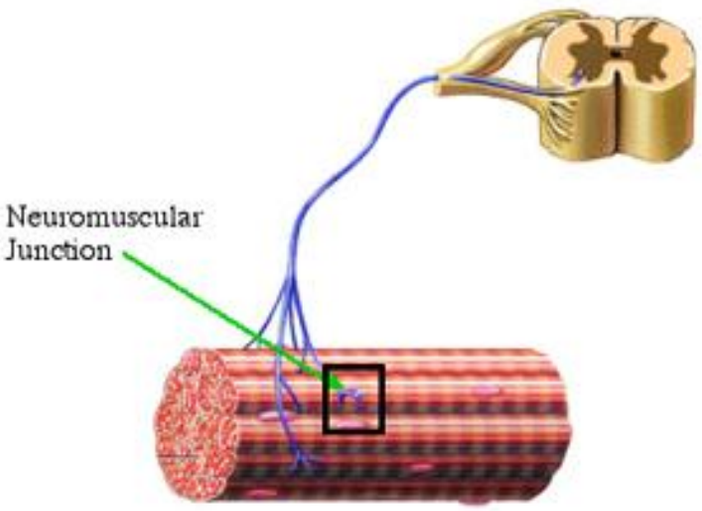

Figure 1. A motor unit [30]

2.1.2. MU activation (recruitment and rate coding)

When a MU is recruited, its motor neuron discharges a train of action potentials that propagate along its axon and, as described above, cause the muscle fibres of the MU to contract. The recruitment of only one MU leads to a weak muscle contraction. The recruitment of additional MUs leads to the activation of more muscle fibres and, as a result, muscle contraction becomes gradually stronger. Changing the rate at which a MU fires (i.e. the rate at which its motor neuron discharges an action potential) can also change the average force produced by a muscle. Therefore, muscle force is modulated by concurrent changes in the number of MUs recruited and their rates of firing.

Motor unit recruitment or derecruitment refers to the activation or deactivation of a MU or population of MUs and thus the subsequent addition or subtraction of the forces produced by its or their muscle fibres, respectively, to the overall muscle force. Motor unit recruitment strategies vary depending on the inherent properties of the specific motor neuron pools of a muscle. Smaller muscles with smaller pools or numbers of MUs tend to recruit all of their MUs earlier during an increasing force contraction and often have all of their MUs recruited at 30% of maximal voluntary contraction. Larger muscles with large numbers of MUs recruit MUs throughout the entire range of force generation.

In general, the firing times of a healthy MU can be modeled as a Gaussian renewal point process and the firing times of different MUs are usually independent of one another. Intervals between the firing times of a particular MU are referred to as inter-discharge intervals (IDIs) and the rate at which a MU fires is simply called its firing rate and often measured in pulses per second (pps)... MU rate coding refers to changing the firing rate of a MU (i.e. the inter-discharge intervals between motor neuron discharges). MUs are initially recruited with firing rates of

about 8 – 10 pps and can increase their firing rates up to 25 to 50 pps. In general, as the intended force of a contraction exceeds the recruitment threshold of a MU, its firing rate will increase.

In general, MUs are recruited in order of their size. When the muscle is initially activated, small MUs are recruited first. As the strength of a muscle contraction increases, MUs of progressively larger size are recruited [25]. The result of this process of adding sequentially larger MUs is a smooth increase in the created muscle force [32]. This orderly recruitment of sequentially larger MUs is referred to as the "Henneman size principle" or simply the "size principle" [32], [34], [35]. Henneman et al. noted that motor axon diameter, conduction velocity and, by further investigation, motor neuron size all increase with functional threshold [32]. There are exceptions to the size-ordered activation of MUs. For example, MU recruitment patterns can vary for different movement tasks, depending on muscle function, sensory feedback, and central control [34]. The force produced by a single MU is partly determined by the number and sizes of the muscle fibres in the motor unit (i.e. the MU size). Another important determinant of force is the frequency with which the muscle fibres are activated. Due to the Henneman size principle mentioned above, force increments due to recruitment are small, whereas during higher force contractions, force increments become much larger.

2.2. Muscle electrophysiology

An innervated muscle fibre is activated when the currents created by the activity of its NMJ create a transmembrane action potential that then propagates in both directions along the muscle fibre away from the NMJ initiating and coordinating contraction of the fibre. In other words, action potentials propagate along the axon of a motor neuron to activate the muscle fibres of a MU. The currents creating the action potentials of the activated muscle fibres linearly contribute to a spatially and temporally dynamic electric field created in the volume conductor in and around a muscle. The strength and spatial and temporal complexity of the created electric field is determined by the number of MUs active and their size and spatial extent. Electrodes placed in this electric field can be used to detect a time changing voltage signal (i.e. an EMG signal).

3. EMG signals

3.1. Volume conduction and detection of EMG signals

"Volume conduction is the spread of current from a potential source through a conducting medium, such as body tissues" [6]. Simulation models have been devised so that the effects of having different kinds of volume conductors and arrangements of detection electrodes on an EMG signal can be studied [67].

The voltage signal detected when measuring the dynamic electric field created in the volume conductor surrounding a muscle fibre by the currents that flow to create and propagate a muscle fibre action potential, is called a muscle fibre potential (MFP). In turn, the detected voltage signal associated with the firing of a MU is called a motor unit potential (MUP). A

MUP is actually the sum of the MFPs of it muscle fibres. The train of detected MUPs created by the repeated firing of the same MU is referred to as a motor unit potential train (MUPT). Thus, a MU can be represented by its MUPT or by a MUP template; which is an estimate of its typical or expected MUP shape. The detected MUPTs created by all of the active MUs during a muscle contraction summate to comprise a detected EMG signal. Thus, a detected EMG signal contains contributions from all of the muscle fibres active during a muscle contraction. The term "interference pattern" is also used to refer to the EMG signal detected during a muscle contraction.

Due to different distances between a detection electrode surface and the individual muscle fibres of a MU, the size and frequency content of the MFP contributions of the various fibres to the MUPs generated by a MU vary among the different fibres of the MU. There is an inverse relationship between both the amplitude and high frequency content of MFPs, and the distance between the contributing muscle fibre and the electrode detection surface such that muscle fibres that are closer to the detection surface [6] contribute larger and higher frequency content MFPs. In addition, the peaks of individual MFP contributions occur at different times, indicating that their associated muscle fibre action potentials are not synchronously propagating past or "arriving" at the electrode detection surface [6]. The difference in their arrival times is referred to as their temporal dispersion. Temporal dispersion is caused by the different conduction distances between the NMJs of the fibres of a MU and the electrode detection surface and the different muscle fibre action potential conduction velocities of the fibres of a MU. The number of muscle fibres contributing significant MFPs to a MUP and their respective temporal dispersions will determine the size and complexity of a detected MUP. The stability of the MUPs of a MU refers to how similar its detected MUPs are across multiple motor neuron discharges. MUP stability is primarily dependent on the consistency of the times required by the NMJs of a MU to initiate a muscle fibre action potential on their respective muscle fibre and the consistency of the propagation velocities of the initiated muscle fibre action potentials.

In addition to the concepts of MFPs, MUPs and MUPTs, there are additional extrinsic and intrinsic factors that impact the characteristics of a detected EMG signal. The extrinsic factors depend on the structure and placement of the electrode detection surface. Extrinsic factors include: the area, shape and distance between electrode detection surfaces; the location of the electrode detection surface with respect to the NMJs of the muscle; the location of the electrode detection surface with respect to the lateral edge of the muscle; and the orientation of the electrode detection surface with respect to the direction of muscle fibre action potential propagation [45]. Specific electrode configurations and their applications are described below. Intrinsic factors are related to inherent characteristics within the muscle itself. Intrinsic factors include: the number of active MUs, the fibre type composition of the muscle, the amount of blood capable of flowing through the muscle during the contraction, the diameters, depths and locations of the active fibres, and, for surface EMG signals, the amount of tissue between the surface of the muscle and the electrode detection surface [45].

3.2. Specific electrode configurations for detecting EMG signals

One way of envisaging an EMG electrode is to compare it to a receiving antenna. For telecommunications, dynamic electromagnetic signals propagate throughout air and an antenna detects these signals. Air in this case is analogous to the volume conductor throughout which currents spread. An EMG electrode acts as an antenna detecting, in this case, dynamic voltage signals generated by the activity of muscle fibres from which currents propagate throughout the volume conductor surrounding the muscle fibres and muscles [24].

Electrodes used to detect EMG signals are actually transducers that allow the electric fields created in the volume conductor surrounding muscle fibres by the ionic currents associated with muscle contraction to be detected and amplified using standard instrumentation amplifiers which are dependent on electronic currents. EMG signals can be detected using a bipolar electrode configuration; measuring the voltage difference using two, or more, active electrodes, or a monopolar electrode configuration; with one reference (passive) electrode and one active electrode. In general, an EMG signal can be detected using a surface or intramuscular electrode configuration. Accordingly, there are two classes or types of EMG signals, surface and intramuscular EMG signals, respectively.

3.2.1. Surface electrodes

Surface EMG electrodes are placed on the skin overlying a muscle. It is typical for surface EMG signals to be detected using a bipolar electrode configuration consisting of two electrodes with surface areas approximately equivalent to that of a 1 cm by 3 cm rectangle and with approximately 1 cm spacing. However, surface electrode arrays with more than 2 electrodes, smaller detection surfaces and electrode spacing have been developed. Huppertz et al. used two columns of electrodes [7] to detect surface EMG. In [13], a 2-dimensional array of electrodes, which consisted of 128 electrodes in total, was used.

3.2.2. Intramuscular electrodes

Intramuscular (or needle) electrode configurations are inserted through the skin and into a muscle. Intramuscular EMG signals can be detected using various needle electrode configurations. Below are some characteristics of clinically used needle electrodes. (Concentric and monopolar needle electrodes are the most commonly used needle electrodes.)

3.2.2.1. Needle electrodes

1. Concentric needle electrodes

A concentric needle electrode consists of a needle cannula in which an insulated core conductor is positioned. The cannula and core conductor are cut at a 15^{o} angle to expose the active detection surface. A concentric needle electrode usually has an elliptical active detection surface area of 0.07 to 0.08 mm^2 provided by its core conductor while its cannula serves as the reference electrode [6].

2. Monopolar needle electrodes

A monopolar needle electrode consists of a solid stainless steel needle coated with insulation except for its distal tip, which serves as the active detection surface. The reference detection surface consists of either another monopolar needle electrode or a surface electrode. Compared to a concentric needle electrode, a monopolar needle electrode has a larger active detection surface area of about 0.2 mm^2. [6].

3. Single fibre needle electrodes

A single-fibre EMG (SFEMG) needle electrode consists of a hollow cannula, which contains an insulated core exposed through a side port 7.5 mm from the tip of the cannula. The circular active detection surface has a diameter of 25 μm [6]. The surface of the cannula serves as the reference electrode.

3.3. Potential Information content

The electrode configuration and muscle activation protocol used to detected EMG signals depends on the objectives of the investigation being completed

3.3.1. Surface EMG signals

Because surface electrodes are placed on the skin overlying a muscle, whose muscle activation related electric fields they are detecting, the various distances between specific MUs and the muscle fibres of those MUs to the electrode detection surface(s) are large and relatively equal. As such, the MUPs of different MUs are composed of primarily of low frequency components (50 to 200Hz) and quite similar in shape and it is difficult to discriminate between the activities of different MUs. As the detection surface area increases more MUs become essentially equidistant from the electrode. This increases the number of MUs able to make significant contributions to a detected signal (or the uptake volume of the electrode) lowers there frequency content and reduces the ability to discriminate individual MU contributions. Reducing the inter-electrode spacing for bipolar electrode configurations can only somewhat counter the effects of increased detection surface area. Alternatively, as the detection surface area decreases, the uptake volume of the electrode reduces, the MUPs are composed of relatively higher frequency content components, and it is easier to discriminate individual MU contributions. Therefore, depending on the amount of detection surface area and the inter-electrode spacing, surface electrodes generally sample from a large number of MUs over a large portion of a muscle. Therefore, surface EMG signals primarily contain information regarding the overall activity of a muscle and are primarily used to assess muscle activation patterns and muscle fatigue [4].

Stalberg [19] was the first to introduce the idea of spike triggered averaging a macro detected EMG signal (i.e. an EMG signal detected using an electrode with a large detection surface) using individual motor unit firing times as triggers [18]. He used a macro electrode that had a cannula of length 15 mm centered on a single fibre needle (SFN) detection surface to acquire the signal triggering potentials. For each MUPT, the motor unit firing times are used as triggers

for locating 100 ms epochs in the macro detected signal. Each located interval is ensemble averaged to extract the macro MUP for the MU [18]. The size parameters of the macro MUPs, such as peak-to-peak voltage or area are related to the overall size of the contributing MU [15], [16]. When used with spike-triggered-averaging techniques surface EMG can be used to extract surface motor unit potentials (SMUPs) which are useful for assessing MU sizes [45] and can be used for estimating the number of motor units in a muscle [45].

An exception to conventional surface EMG signals are multi-channel signals simultaneously detected using arrays of surface electrodes with small detection surface areas and small inter-electrode spacing. These signals can be used for surface EMG signal decomposition [13] applications. Detecting surface EMG signals using multi-electrode arrays provides information about the spatial distributions of MU fibres under the electrode array, which in turn enhances the ability to discriminate individual MU activity relative to standard surface EMG electrode configurations.

One other application multi-channel surface EMG was to use a multi-channel electrode with four detection surfaces linearly positioned along the direction of the muscle fibres and with each detection surface aligned perpendicular to this direction [22]. Using a linear array of detection electrodes increases the possibility of interpreting EMG signal features compared to single-channel surface signals. Using a linear array of detection surfaces makes it possible to investigate in detail the processes of the generation, propagation, and extinction of muscle fibre action potentials.

3.3.2. Intramuscular EMG signals

Intramuscular or needle EMG electrodes are inserted through the skin and into the muscle and can be positioned at specific locations within a contracting muscle. As such, the various distances between specific MUs and the muscle fibres of those MUs to the electrode detection surface(s) can be significantly different. Therefore, intramuscular EMG electrodes can be positioned to preferentially detect the activity of MUs whose muscle fibres are closest to the detection surface(s) of the intramuscular electrode. This can result in the MUPs of different MUs being quite different in shape making it easier to discriminate between the activities of different MUs.

Intramuscular EMG signals can be acquired using selective electrodes with a small detection surface (e.g. concentric or monopolar needle electrodes) or using an electrode with a large detection surface (e.g. macro electrodes [19]) [17]. Generally, MUPTs detected using intramuscular electrodes provide local information about their respective MUs. The MUPs comprising intramuscular EMG signals can provide information related to MU size, MU muscle fibre distribution and the stability of time it takes for NMJs to depolarize their connected muscle fibre. In addition, MUPTs can provide information about MU recruitment and firing rates.

4. Neuromuscular disorders

Neuromuscular disorders change both the morphology and activation patterns of the MUs of the muscles affected. Therefore, the shapes of MUPs detected in muscles affected by neuromuscular disorders will differ from those detected in healthy or normal muscles. In addition, for a given level of muscle activation the number of MUPTs contributing to a detected signal, which reflects the level of MU recruitment, and the rates at which MUPs occur in detected MUPTs, which reflect MU firing rates, will differ.

A normal muscle at rest will have no electrophysiological activity (i.e. there will be no electric field created in its surrounding volume conductor). Muscles affected by a neuromuscular disorder can have spontaneous muscle fibre activity called fibrillations and/or spontaneous MU activity called fasiculations.

Myopathic disorders cause muscle fibre atrophy, splitting, hypertrophy and necrosis. Examples of atrophic and hypertrophic muscle fibres are diagrammed in Fig 2. Atrophic and split muscle fibres have smaller diameters and slower muscle fibre action potential propagation velocities. They therefore produce in general smaller and wider MFPs with later occurring peak vales. Hypertrophic muscle fibres have larger diameters and faster muscle fibre action potential propagation velocities. They therefore produce in general large and narrower MFPs with earlier occurring peak values. Necrotic fibres are not active and do not contribute to detected MUPs or muscle force. As such, myopathic MUPs, in general, are composed of fewer MFP contributions of varying size and with larger temporal dispersion than in MUPs detected in normal muscles. Myopathic MUPs are therefore generally smaller in size and more complex than normal MUPs. The variation in muscle fibre action potential propagation velocity in a muscle fibre affected by a myopathic process can be greater than normal. This in turn can increase the instability of myopathic MUPs across the MUPs of a MUPT.

Because the MUs of a myopathic muscle are generally smaller during equivalent muscle activations more of them must be recruited and they need to be activated at higher firing rates compared to a normal muscle [6]. Therefore, at equivalent levels of muscle activation, EMG signals detected in a myopathic muscle can become more complex than EMG signals detected in a normal muscle (see Fig 3).

In contrast, neurogenic disorders cause the loss of MUs and muscle fibre denervation. Subsequent to reinnervation of the denervated muscle fibres the surviving MUs have increased numbers of fibres with greater and clustered spatial fibre densities relative to normal muscle as seen in Fig.2. The increased number of MU fibres result in MUPs comprised of larger numbers of MFP contributions. The greater and clustered spatial fibre densities result in grouped MFP contributions. Consequently neurogenic MUPs tend to be larger and more complex than normal MUPs sometimes with distinct components or phases (e.g. satellite potentials). During the acute phase of reinnervation newly formed NMJs have larger variations in the time taken to initiate a muscle fibre action potential in their respective muscle fibres. This results in increased instability of neurogenic MUPs across the MUPs of a MUPT.

Because the MUs of a neurogenic muscle are generally larger and because they are fewer in number during equivalent muscle activations, fewer of them must be recruited but they need to be activated at higher firing rates compared to a normal muscle [6]. Therefore, at equivalent levels of muscle activation, EMG signals detected in a myopathic muscle can become more complex than EMG signals detected in a normal muscle. Therefore, at equivalent levels of muscle activation, EMG signals detected in a neurogenic muscle are generally less complex than (or sparse compared to) EMG signals detected in a normal muscle (See Fig 3).

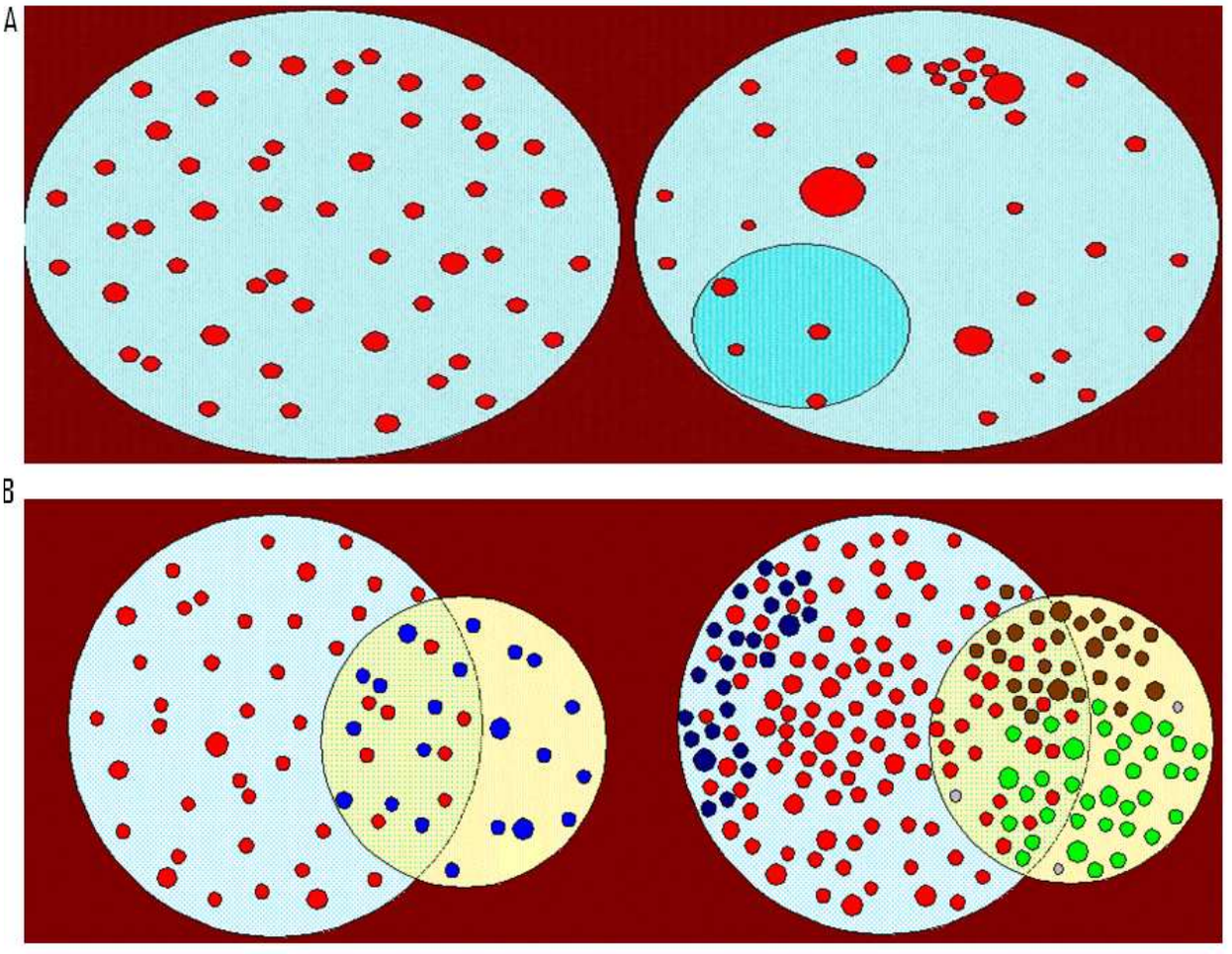

Figure 2. A. Normal MU vs. myopathic MU; B. Normal MU vs. neurogenic MU [43]

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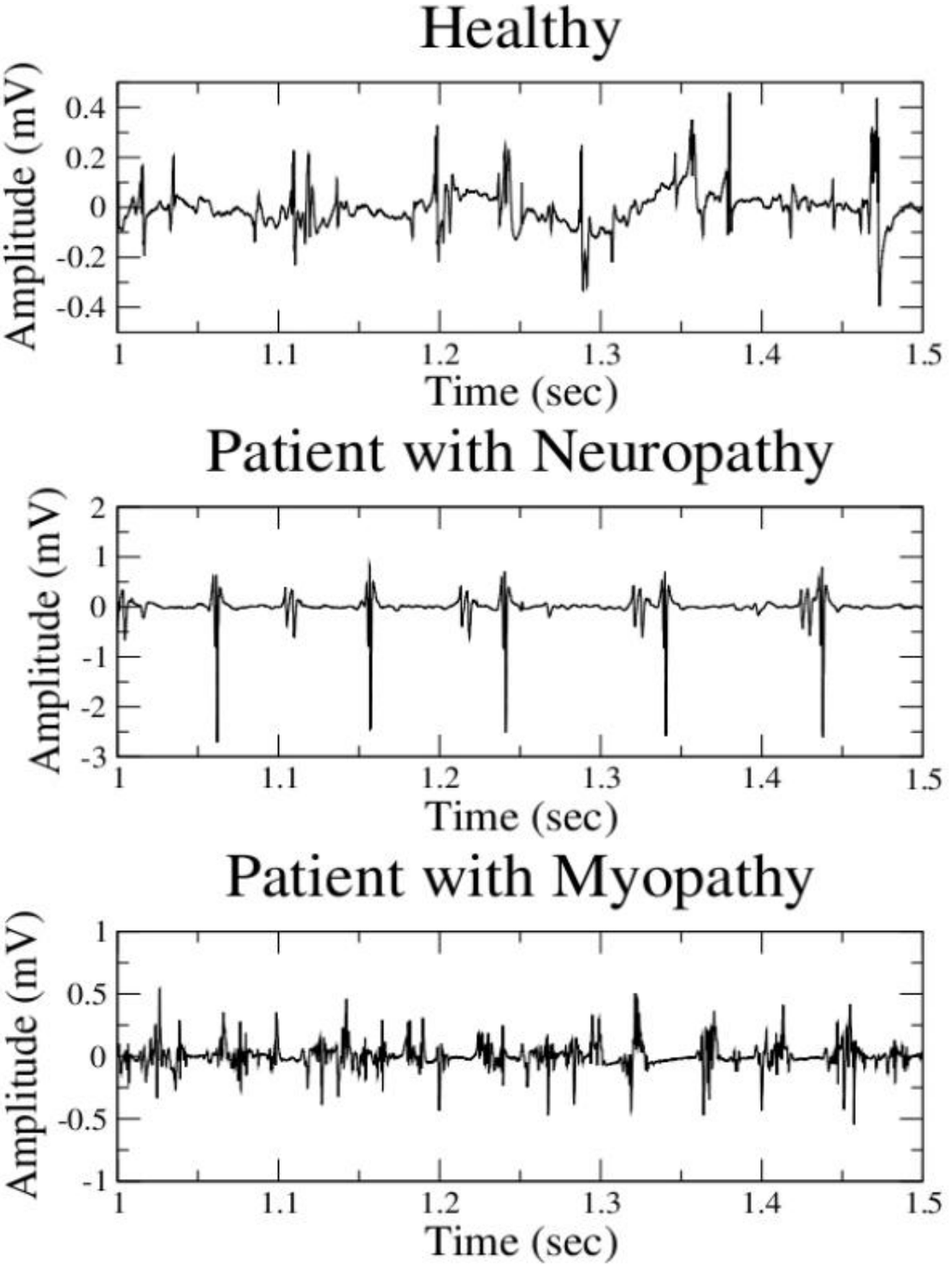

Figure 3. Examples of healthy, neurogenic and myopathic EMG signals [38]

5. How to extract clinically important information

Suitably detected EMG signals can contain information that can be used to assist with the diagnosis of neuromuscular disorders. Specific characteristics of a detected EMG signal can be related to the type of neuromuscular disorder present (i.e. myopathic or neurogenic) as well as the degree to which the muscle may be affected by a disorder. As described above, the changes in MU morphology and activation created by a disease process lead to expected changes in MUP shapes and stability as well as the level of EMG signal complexity. However, in order to use EMG signals to support clinical decisions, the EMG signals must be acquired from a contracting muscle during specific activation protocols and using specific detection electrode configurations. The activation protocol and detection electrode configuration used should provide EMG signals in which the effect of the changes in MU morphology and activation created by a disease process are emphasized. Specific aspects of the detected EMG signals can then be analyzed to determine if they were most likely detected in a myopathic, normal or neurogenic muscle. It this last step qualitative or quantitative analysis can be applied.

5.1. Qualitative electromyography

The current status quo for assessing the clinical state of a muscle is to qualitatively analyze EMG signals detected using needle electrodes following abrupt movement of the electrode, while the muscle is at rest and during low levels of muscle activation. Characteristics of the detected signals are subjectively compared to those expected to be detected in normal muscle. The signals detected following abrupt needle movement and while the muscle is at rest are grouped into what is classified as spontaneous activity. Following abrupt needle movement, if the muscle remains active (i.e. significant signals are detected) for a prolonged period of time this is a sign of abnormality. Likewise, if while the muscle is at rest, potentials related to muscle fibre fibrillation or MU fasciculation are detected the muscle is considered abnormal. The degree of spontaneous muscle activity is often subjectively graded using a discrete 4 or 5 level scale. MUPs contained in EMG signals detected during low levels of muscle activation are visually and aurally analyzed to assess their shape, size and stability either as they are presented in a free running or triggered raster display.

The firing rates of MUs and the number of recruited MUs are also estimated.

The advantage of analyzing an IP detected during minimal muscle activation is that individual MUPs can be recognized. Therefore information about their recruitment information and their firing rates can be obtained [21]. In order to estimate MU firing rates, a 500 ms epoch is displayed [6]. This technique depends on visual inspection to identify individual MUP discharges. The number of discharges of an MU in this 500 ms epoch is multiplied by 2 to get the firing rate [6]; to obtain the number of discharges in one second.

This is a semi-quantitative approach to implement IPA where an IP is detected during maximal force of contraction [14]. The IP is considered full when the signal baseline is completely obscured by MUP spikes [6]. If the baseline can be seen between MUP discharges, the IP is

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considered incomplete, while if individual MUPs can be recognized, the IP is considered discrete [6]. One border of the EMG envelope is defined by connecting the negative peaks while the other is defined by connecting the positive peaks. The voltage difference between these lines (borders) is the envelope amplitude [6]. The criteria are as follows [14]: if the IP is full and the envelope amplitude is small, this is a myopathic pattern, and if the IP is discrete and the envelope amplitude is larger than its normal value, this is a neurogenic pattern.

The objectives of this qualitative analysis and characterization of the needle-detected EMG signals is to extract information regarding the morphology of a representative sample of MUs of the muscle being examined. Experienced and skilled clinicians can use these qualitative analyses to assist with the diagnosis of an examined muscle with respect to which, if any, specific disease processes may be present and if present, to what extent.

One of the main disadvantages of qualitative EMG analysis is inter and intra-rater variability. Specific assessments made and the consistency with which they are made depend on the training, experience and skill of the examiner. In addition, no more than a few MUPs can be qualitatively analyzed at a time [4]. Therefore, qualitative analysis is restricted to low levels of muscle activation where only a few MUs are recruited and consequently the EMG signals detected are the aggregation of only a few MUPTs.

5.2. Clinical Quantitative EMG (QEMG)

Quantitative electromyography (QEMG) is an objective assessment of several aspects of detected EMG signals to assist with the diagnosis of a muscle under examination and also to assess the severity of an existing disorder if one is detected. QEMG is also sometimes used to assess the status of a detected disorder (active or not) and its time course (chronic or acute) [6]. Quantitative analysis is an automated process, unlike qualitative analysis, which typically requires comparing measured feature values of an EMG signal detected in a muscle under examination to standard or training set values from EMG signals detected in muscles of know clinical state (i.e. myopathic, normal or neurogenic). As a result, standardization or the collection of training data needs to be completed properly; for instance, data should be grouped based on age, gender, and specific muscle. In addition, the EMG signals need to be acquired using a standardized and consistent technique regarding the electrode used, the detection protocol, etc [4]. QEMG aims at increasing diagnostic sensitivity and specificity. Unlike qualitative analysis, quantitative analysis is not limited to studying just the first few recruited MUs and EMG signals detected at higher levels of muscle activation can be analyzed.

Accuracy and transparency are two important factors that must be taken into consideration when selecting or designing a QEMG technique for clinical use. Accuracy is a major issue for any supervised learning problem as the ultimate purpose is to correctly categorize, a muscle being examined so that its condition can be correctly weighted in determining the overall patient diagnosis. Transparency is essential here as well because a clinician should be able to clearly understand the rationale behind the characterization process. A clinician is expected to have moderate knowledge of statistics and if the complexity of a certain technique is beyond that, it is considered as a non-transparent characterization technique. Rule-based classifiers

usually provide this required transparency when they are used in QEMG but their accuracy levels are not as high as support vector machines or neural networks.

To perform QEMG, the complete EMG signal, or interference pattern, can be analyzed or individual MUP activity can be isolated from an EMG signal using level or window triggering or EMG signal decomposition methods. If EMG signal decomposition methods are used, individual MUPT can be analyzed which allow information about typical MUP shape, MUP shape stability and MU activation patterns to be used. The next sections discuss QEMG methods based on interference pattern and individual MUPT analysis, respectively.

5.2.1. Interference Pattern (IP) analysis

As mentioned earlier, the term "interference pattern" is used to refer to the complete EMG signal detected from a contracting muscle. The term "interference pattern" is sometimes used to describe the EMG signal detected during a maximal contraction only but the former definition is more common. The characteristics of an interference pattern (IP) depend on the level of muscle activation maintained during its detection and the type of electrode used. The level of activation determines the number of recruited MUs and their firing rates. The type of electrode used determines the shape characteristics of the MUPs (duration, area, amplitude, etc.) that are created by the active MUs and which in turn comprise the IP.

The term "interference pattern analysis" (IPA) refers to those techniques that analyze an IP. IPA is used when a global analysis of an EMG signal is desired. IPA is a quantitative analysis which can be completed using either a frequency or time domain representation of the IP [6]. Following are brief descriptions of common IPA techniques.

5.2.1.1. Frequency domain analysis

Any signal of time can be represented by a summation of sinusoidal functions of several frequency values, phase shifts and magnitudes. Therefore, a frequency domain representation of an IP can be obtained if these frequency values, phase shifts and magnitudes of the signal are identified. A frequency domain representation reveals information about MUP amplitudes, and durations as well MU firing patterns. For instance, high frequency components are representative of MUPs with short durations and short rise times, while low frequency components are representative of to MUPs with long durations and long rise times [8].

5.2.1.2. Time domain analysis

Time domain analysis basically depends on detecting the main characteristics of the time domain representation of an IP. Detecting changes in the sign and slope of an IP was how it was initially performed [8]. Later, more specific characteristics of the time domain signals were found to be important. For instance, the number of turns and their amplitude are important features for discriminating between IPs detected in myopathic, normal and neurogenic muscles. A peak is identified to be a turn if the change in amplitude between this peak and the previous peak exceeds a prespecified threshold, while the amplitude is the difference in voltage values between successive peaks of opposite polarity [8].

5.2.1.3. Clouds analysis

Clouds analysis uses the number of turns and the mean turn amplitude features of IPs detected during several contractions maintained at different levels of muscle activation ranging from slight effort to maximal. The number of turns and the mean turn amplitude for each IP define points in a two dimensional plot in which is overlaid a cloud or region [8]. The cloud defines the area in which 90% of data from IPs detected in normal muscle are expected to be. Accordingly, a muscle is considered diseased if more than 10% of its IPs provides data points which are outside of the cloud.

One of the limitations of IPA is that because of superpositions of MUPTs it is difficult to detect marginal levels of disorders. Small numbers of abnormal MUPTs may be lost in IPs generated by a majority of normal MUPTs.

5.2.2. MUP template / MUPT characterization

A MUPT is composed of the MUPs created by a single MU. The typical MUP shape of a MUPT is represented by its MUP template. The stability of the MUPs with in a MUPT can be estimated as can the firing behavior of the MU that created the MUPT. MUPT characterization refers to performing supervised learning to determine if a MUPT was created by a normal or abnormal (disordered) MU, if just two categories are considered or by a myopathic, normal or neurogenic MU if three categories are considered. This characterization is based on a training stage that is performed using training data suitably representing each category. MUPT features used for MUPT characterization often consist of MUP template morphological features; features extracted from the time domain representation of the MUP template [4] as well as spectral features; those extracted from its frequency domain representation [4]. MU firing pattern features have not yet be effectively used. Typically, a feature selection step is performed to select the best feature subset. As is the case with any supervised learning problem, feature selection can be filter-based (quality metric of the feature subset depends on information content like interclass distance or correlation) or wrapper-based (quality metric of the feature subset depends on the accuracy of the characterization process using such feature set). However, wrapper-based feature selection techniques are used more frequently [56].

In addition to the intrinsic MUP template features, like turns, duration, amplitude, etc, combinations of features can be used if they improve the characterization results. For instance, MUP template thickness (area/amplitude) can be added to the features used for characterization to improve classification performance as the discriminative power of the feature set would be higher.

5.2.2.1. Signal detection and preprocessing

1. Level and/or window triggering

Individual MUPTs can be extracted for quantitative analysis using level or window triggering methods. These methods allow the MUPs created by a single MU to be extracted, but only if their amplitudes are unique with respect to the amplitudes of MUPs created by other MUs.

These methods can be used with careful positioning of the needle and during low level of muscle activation. Only one MUPT can be extracted from the EMG signal detected during muscle contraction. Therefore, for each MUPT to be extracted a separate contraction must be performed.

2. EMG signal decomposition

EMG signals are the linear summation of the MUPTs created by the MUs active in a muscle. EMG signal decomposition extracts individual MUPTs from an EMG signal. Unlike level or window triggering, EMG signal decomposition allows several MUPTs created by MUs concurrently active during a single muscle contraction to be analyzed. The accuracy of the MUPTs extracted by an EMG signal decomposition algorithm determines the type of analyses that can be successfully applied to the extracted MUPTs. The MUPTs extracted during EMG signal decomposition can be further analyzed to assist in diagnosing neuromuscular disorders.

EMG signal decomposition involves three main steps, described in the following paragraphs.

The first step is to detect the MUPTs comprising an EMG signal. Some EMG signal decomposition algorithms attempt to detect all the MUPTs that existed in the EMG signal while others attempt to extract only MUPTs that had a major contribution to the EMG signal. The following step is to determine the shapes of the different MUPs. This can be done by categorizing the MUPs in the signal based on their shapes and sizes. This categorization, if implemented properly, reveals clusters of MUPs with similar shapes and sizes. As a result, MUPs with different shapes and sizes should belong to different clusters. MUPs with similar shapes and sizes were most probably created by different discharges of the same MU, while MUPs with unique shapes and sizes (i.e. not belonging to cluster or to a cluster with very few members) are most probably superpositions. The main outcome of this step is to identify the number of MUs that contributed significant MUPs to the EMG signal (i.e. to estimate the number of MUPTs with significant MUPs) and to estimate the MUP template of each discovered MUPT.

The second step is to determine the class of every template. Superpositions of MUPs are harder to deal with in the first step as well as in this step. If the overlap is only slight, the constituents might still be recognizable. But if the overlap is complete it might be necessary to try different alignments of the templates to see which gives the closest fit. The motor unit discharge patterns can also be used to help determine which MUs are involved in a superimposed MUP [36]. As discharge rates are assumed to be rather orderly (i.e. IDIs can be assumed to follow a Gaussian distribution), the time at which a particular discharge took place can be estimated from the time at which the preceding or following discharge took place.

The final step in decomposition is to validate the results to ensure they are consistent with the expected physiological behavior of MUs. If there are unexpected short IDI in any of the discharge patterns, or if there are detected MUPs that have not been assigned to a MUPT, then the decomposition is probably not correct or incomplete. On the other hand, if all the activity in the signal (i.e. the detected MUPs) has been adequately accounted for by the set of extracted MUPTs which in turn represent MUs with physiologically realistic discharge patterns, then there is a good chance that the decomposition is substantially complete and accurate [36].

5.2.2.2. Non-transparent classification techniques

MUPT characterization can be performed using probabilistic techniques. Probabilistic techniques provide a MUP characterization in terms of conditional probabilities that sum to 1 across all of the categories considered. For instance, a probabilistic technique can suggest that considering the features of a MUPT there is a 10% probability it was detected in a myopathic muscle, a 70% probability it was detected in a normal muscle and a 20% probability it was detected in a neurogenic muscle neurogenic if three categories are considered.

Various methods have been used in the literature to perform MUP template characterization, ranging from conventional to advanced classifiers. For example, linear discriminant analysis (LDA), decision trees and a standard Naive Bayes (NB) classifier were implemented and compared in [9]. LDA attempts to find a linear combination of features that maximizes the between class variance and minimizes the within class variance and it relies on this as a basis for optimal classification. Using these trivial classifiers has the advantage of being rather more transparent than using more advanced pattern recognition techniques like neural networks and support vector machines.

Artificial neural networks were first used for MUP template characterization in [10] and [11]. More progress in this direction was achieved in [12] as artificial neural networks were used along with radial basis functions and probabilistic neural networks in a two-phase classifier, which increased MUPT characterization accuracy. In the second phase of the classification, a C4.5 decision tree was used to determine whether the disorder was myopathic or neurogenic, if any. Another example of using neural networks in MUP analysis can be found in [63].

In [53] autoregressive (AR) modeling and cepstral analysis were applied to characterize MUP templates and the training dataset was built on normal MUP templates as well as MUP templates taken from myopathic muscles. It was concluded in [53] that using AR modeling and cepstral analysis along with time domain features (in particular duration) led to categorizations with high accuracy in the assessment of myopathic MUP templates (in this work two categories were used; normal and myopathic). In [54], MUP templates were classified into three categories; normal, myopathic and neurogenic using support vector machines (SVM).

Using artificial neural networks in classification could lead to over-fitting; a classifier that has difficulty in producing the same accuracy with new or more generalized data. As mentioned earlier, using a SVM and artificial neural networks does not provide enough transparency and renders it more difficult for clinicians to understand how a certain classification decision was made.

5.2.2.3. Transparent rule-based MUPT classification techniques

An example of a transparent rule-based classification technique is the two-stage classifier developed in [55]. This two-stage classifier is based on utilizing radial basis function artificial neural networks and decision trees. The combined use of an artificial neural network and a decision tree reduces the number of tuned parameters required and allows an interpretation of the classification decisions to be provided [55].

Techniques based on pattern discovery (PD) represent another example of transparent rule-based techniques used for MUPT characterization. Pattern discovery is an information theory based technique established to detect significant patterns in data and then to use these patterns for classification [5]. PD was first introduced by Wong and Wang [57]-[60]. PD is applied on discrete data and, as a result, a quantization step is required for each feature that has continuous values, which is the case with most MUPT features. The number of discretization bins can be identified according to the nature of the problem at hand and the dataset used. For instance, if the number of bins is three; low, medium and high for each feature, there might be some loss of accuracy resulting from placing "very high" and "slightly high" values in the same bin. On the other hand, using five bins; very low, low, medium, high and very high can solve such a problem but more training examples are needed to keep the same number of expected occurrences per bin. In the PD classification algorithm, the first step is to discover the "significant" patterns; patterns that are repeated more often than expected assuming a random occurrence [56]. Rules are composed of patterns that include a muscle category. The order of a rule is equal to the number of MUPT features plus the muscle category. For example, high amplitude values in neurogenic MUPTs are a 2nd order rule [5]. Each rule has an associated weight of evidence (WOE) that denotes how much evidence the rule holds in support of a certain category [9]. For rule selection during testing, the highest order rule for each category is selected first. WOEs of selected rules are added to be normalized and this process continues until there are no more rules or all features have already been included in the previously selected rules [56]. In addition to the well-known pros and cons of discretization, characterizations performed by PD are transparent as the technique is rule-based which makes it feasible to explain to a clinician the rationale behind the classification decisions. However, when PD is used, there is a decrease in accuracy due to the discretization performed on the continuous MUPT feature values.

In [61], a fuzzy inference system was introduced. This system is based on using PD in combination with fuzzy logic theory to yield a hybrid system. The idea was to reduce quantization error via assigning memberships for every MUPT feature value based on their position within their assigned bin. The fuzzy membership values allow the same MUPT feature value to be considered in more than one rule simultaneously. Using this technique for establishing rules is similar to the method by which humans manually interpret certain data values and then attempt to classify these values, which makes it very useful, at least in terms of transparency, in a clinical decision support system.

5.2.3. Muscle categorization

The ultimate purpose of characterizing MUPTs is to characterize the muscle from which they were detected. The statistical method for muscle characterization can be performed by calculating mean values for sampled MUPT features and comparing them to expected normative mean values (Note: comparisons should be standardized with respect to age, gender, muscle, EMG detection technique, etc.). Using the expected normative mean and outlier threshold values the overall category of a muscle is then determined based on the mean values of the sampled MUPT feature values with respect to these thresholds. For instance,

Stalberg identified the outlier range to be outside of the mean ± 2 × standard deviations range. This way, a categorization of the muscle being examined can be obtained. As an example for standard feature values, MUP template values documented in [62] are still considered standard values for MUP template duration, amplitude and shape.

The above muscle categorization techniques do not provide any measure of confidence. Probabilistic muscle categorization, on the other hand, addresses this weakness as it provides probabilities describing MUPT characterizations as well as the overall muscle characterization. More formally, a probabilistic MUPT characterization technique assigns a likelihood measure to each MUPT category under consideration. For each MUPT characterization, a set of n likelihood measures is obtained, where n is number of muscle categories under consideration (2 or 3) [4]. For each MUPT, this set of likelihood measures should sum to 1.

5.2.3.1. Aggregation of MUPT characterizations

Characterizations of MUPTs must be aggregated to obtain the overall muscle characterization of the muscle from which these MUPTs were detected. As with MUPTs, a set of n muscle likelihood measures is obtained, where n is the number of muscle categories and the muscle is considered to belong to the category that has the highest category likelihood value. Muscle likelihood values can be considered confidence measures in a particular characterization. In [64], [65], the idea of implementing probabilistic characterization and aggregating MUP template characterizations using Bayes' rule was first introduced. MUP template characterization was performed using Fisher's LDA. Other techniques used Bayes' rule to aggregate MUP template likelihood measures obtained from multiple classifiers like decision trees, LDA and Naive Bayes [56].

5.2.3.2. Measures of confidence and involvement

A muscle characterization likelihood value (measure) indicates the probability that the muscle, from which the characterized MUPTs were detected, actually belongs to the given category, conditioned on the evidence provided by the set of MUPT characterizations. Thus, a muscle characterization likelihood measure can be considered a measure of confidence in making a particular categorization based on the available evidence. For instance, a muscle confidence score of 75% for a given category means that, out of all the muscles that are assigned that score, 75% of such muscles actually belong to that category.

Another relevant concept in the context of muscle categorization is that of the level of involvement (LOI). When the values of the arithmetic mean of MUPT features are used to aggregate MUPT probabilities, the conditional probabilities resulting from a muscle characterization technique correlate well with the level of involvement (LOI) of a disease [66].

It is not easy to predict LOI due to the fact that confidence in making a correct muscle categorization decision at lower levels of disease involvement is low, which results in greater variability and lower accuracy in the LOI measurement [4].

6. Summary

An overview of the basis of EMG signals and the types of information they may contain depending on how they are detected was provided in addition to descriptions of various clinical QEMG techniques. The main objective was to emphasize the specific information targeted for extraction by clinical QEMG techniques and how this information can be extracted so that the sampled MUs, that created the MUPs comprising an EMG signal, can be accurately characterized and subsequently used to characterize and then categorize an examined muscle. Different clinical QEMG techniques were described. The bulk of the ongoing research in clinical QEMG is centered around improving muscle categorization accuracy using transparent clinical QEMG techniques so that characterization results can be explained to clinicians.

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References

[1] Campbell Biology, 6th edition

[2] Windhorst U, Johansson H. Modern techniques in neuroscience research. Springer; 1999

[3] H. Parsaei, D. W. Stashuk, S. Rasheed, C. Farkas, and A. Hamilton-Wright, "Intramuscular EMG Signal Decomposition," Crit Rev Biomed Eng, vol. 38, no. 5, pp. 435–465, 2010

[4] C. Farkas, A. Hamilton-Wright, H. Parsaei, and D. W. Stashuk, "A review of clinical quantitative electromyography," Crit Rev Biomed Eng, vol. 38, no. 5, pp. 467–485, 2010

[5] T. Adel, D. Stashuk, Muscle categorization using PDF estimation and Naïve Bayes classification," embc, 2012

[6] D. Dimitru, A. Amato, M. Zwarts, Electrodiagnostic Medicine, second edition.

[7] H. J. Huppertz et al., Muscle Nerve 20, 1360, 1997.

[8] William F. Brown, Charles F. Bolton, Michael J. Aminoff, Neuromuscular Function and Disease, Basic, Clinical, and Electrodiagnostic Aspects

[9] Pino L, Stashuk D, Boe S, Doherty T. Motor unit potential characterization using "pattern discovery". Medical Engineering & Physics. 2008 Jun;30(5):563-573.

[10] Christodoulou C, Pattichis C. Unsupervised pattern recognition for the classification of EMG signals. IEEE Trans. Biomed. Eng. 1999 Feb;46(2):169-178.

[11] Schizas CN, Middleton LT, Pattichis CS. Neural network models in EMG diagnosis. IEEE Transactions on Biomedical Engineering. 1995;42(5):486-496.

[12] Katsis CD, Exarchos TP, Papaloukas C, Goletsis Y, Fotiadis DI, Sarmas I. A two-stage method for MUAP classification based on EMG decomposition. Comput. Biol. Med. 2007;37(9):1232-1240.

[13] J. Blok, J. Van Dijk, G. Drost, M. Zwarts and D. Stegeman, A high-density multichannel surface electromyography system for the characterization of single motor units, Rev. Sci. Instrum. 73, 1887 (2002).

[14] Buchthal F, Kamieniecka Z, The diagnostic yield of quantified electromyography and quantified muscle biopsy in neuromuscular disorders. Muscle Nerve;2:265-280, 1982.

[15] Roeleveld K, Stegman DF, Falck B, Stalberg E. Motor unit size estimation: confrontation of surface EMG with macro EMG. EEG Clin Neurophysiol;105:181–8, 1997.

[16] Doherty TJ, Age-related changes in the numbers and physiological properties of human motor units. PhD Thesis, University of Western Ontario, 1993.

[17] Stashuk D. Decomposition and quantitative analysis of clinical electromyographic signals. Med Eng Phys; 21:389–404, 1999.

[18] Dan Stashuk, EMG signal decomposition: how can it be accomplished and used?, Journal of Electromyography and Kinesiology 11, 151–173, 2001.

[19] Stalberg EV. Macro EMG, a new recording technique. J Neurol Neurosurg Psychiat; 43:475–82, 1980.

[20] J.V. Basmajian, W. J. Forrest, G. Shine, A simple connector for fine-wire EMG electrodes. J Appl Physiol 21:1680, 1966.

[21] Petajan JH, AAEM Minimonograph # 3: Motor Unit Recruitment. Muscle Nerve; 14:489-502, 1991.

[22] Roberto Merletti, Dario Farina, Marco Gazzoni, The linear electrode array: a useful tool with many applications Journal of Electromyography and Kinesiology 13, 37–47, 2003.

[23] G. E. Loeb and C. Gans. Electromyography for Experimentalists, chapter 6, pages 60-70. The University of Chicago Press, Chicago, 1986

[24] Saksit, PhD Thesis, chapter 2: physiology of EMG

[25] American Association of Electrodiagnostic Medicine. Glossary of terms in electrodiagnostic medicine. Muscle Nerve. 2001;Suppl 10:S1-50.

[26] Ounjian, M., R.R. Roy, E. Eldred, A Garfinkel, J.R. Payne, A. Armstrong, A. Toga, and V.R. Edgerton Physiological and Developmental Implications of Motor Unit Anatomy. J. Neurobiol. 22:547-559, 1991. Motor unit territory.

[27] Bodine-Fowler, S., Garfinkel, A., Roy, Roland R., and Edgerton, V. Reggie. Spatial distribution of muscle fibres within the territory of a motor unit. Muscle and Nerve 13:1133-1145, 1990.

[28] Garnett, R. & Stephens, JA. The reflex responses of single motor units in human first dorsal interosseous muscle following cutaneous afferent stimulation. J. Physiol. Land. 303: 35l-364, 1980.

[29] Kanda, K., Burke, R. E., & Walmsley, B. Differential control of fast and slow twitch motor units in the decerebrate cat. Exp. Brain Res. 29:57-74, 1977.

[30] Jennifer Hill, Exercise Physiology Student, Spring 2010 [http://www.unm.edu/~lkravitz/Exercise%20Phys/motorunitrecruit.html]

[31] Carlo DeLuca. Control Properties of Motor Units. J. exp. Biol. 115, 125-136, 1985

[32] Henneman, E., Somjen, G. & Carpenter, D. O. (1965). Functional significance of cell size in spinal motoneurons. J. Neurophysiol. 28, 560-580.

[33] Adrian ED & Zotterman Y. (1926). "The impulses produced by sensory nerve endings: Part II: The response of a single end organ.". J Physiol (Lond.) 61: 151–171.

[34] Hodson-Tole EF, Wakeling JM. Motor unit recruitment for dynamic tasks: current understanding and future directions. J Comp Physiol B. Jan 2009;179(1):57-66

[35] Gordon T, Thomas CK, Munson JB, Stein RB. The resilience of the size principle in the organization of motor unit properties in normal and reinnervated adult skeletal muscles. Can J Physiol Pharmacol. Aug-Sep 2004;82(8-9):645-61

[36] Miki Nikolic, PhD Thesis, Univ. of Copenhagen, 2001.

[37] Yamada R, Ushiba J, Tomita Y, Masakado Y. Decomposition of Electromyographic Signal by Principal Component Analysis of Wavelet Coefficient. IEEE EMBS Asian-Pacific Conference on Biomedical Engineering; Keihanna, Japan. pp. 118-119, 2003

[38] Zennaro D, Welling P, Koch VM, Moschytz GS, Laubli T. A Software Package for the Decomposition of Long-Term Multichannel EMG Signal Using Wavelet Coefficients. IEEE Trans Biomed Eng, 50(1):58–69. doi: 10.1109/TBME.2002.807321, 2003

[39] K. Roeleveld, J. H. Blok, D. F. Stegeman, A. van Oosterom, Volume Conduction Models for Surface EMG; Confrontation with Measurements

[40] Plonsey R: Bioelectric Phenomena. McGraw Hill, New York, 1969.

[41] Stegeman DF, Dumitru D, King JC, Roeleveld K: Near and far-fields: source characteristics and the conducting medium in neurophysiology. J Clin Neurophysiol (In press).

[42] Fang J, Agarwal GC, Shahani BT, Decomposition of EMG signals by wavelet spectrum matching. Procedures of the 19th Annual International Conference of the IEEE Engineering in Medicine and Biology Society; Chicago, IL, USA. pp. 1253-1256, 1997.

[43] Barkhaus PE, Nandedkar SD: Recording characteristics of the surface EMG electrodes. Muscle Nerve 17:1317–1323, 1994.

[44] Walter, C.B. Temporal quantification of electromyography with reference to motor control research. Human Movement Science 3: 155-162, 1984.

[45] M. Raez, M. Hussain, F. Mohd-Yasin, Techniques of EMG signal analysis: detection, processing, classification and applications

[46] Stashuk DW, Kassam A, Doherty TJ, Brown WF. Motor Unit Estimates Based on the Automated Analysis of F-Waves. Proceedings of the Annual International Conference on Engineering in Medicine and Biology Society. 1992;14:1452–1453.

[47] Micera S, Vannozzi G, Sabatini AM, Dario P. Improving detection of muscle activation intervals. IEEE Engineering in Medicine and Biology Magazine. 2001;20(6):38–46.

[48] Thexton AJ. A randomization method for discriminating between signal and noise in recordings of rhythmic electromyographic activity. J Neurosci Meth. 1996;66:93–98.

[49] Bornato P, de Alessio T, Knaflitz M. A statistical method for the measurement of the muscle activation intervals from surface myoelectric signal gait. IEEE Trans Biomed Eng. 1998;45:287–299. doi: 10.1109/10.661154.

[50] Determination of an optimal threshold value for muscle activity detection in EMG analysis Kerem Tuncay Ozgunen, Umut Celik and Sanli Sadi Kurdak, Journal of Sports Science and Medicine (2010) 9, 620-628

[51] Di Fabio, R.P, Reliability of computerized surface electromyography for determining the onset of muscle activity. Physical Theraphy 67(1), 43-48, 1987.

[52] Gary Kamen, David A. Gabriel, Essentials of Electromyography

[53] Pattichis CS, Elia AG. Autoregressive and cepstral analyses of motor unit action potentials. Med Eng Phys. 1999 Sep; 21(6-7):405-419.

[54] Katsis C, Goletsis Y, Likas A, Fotiadis D, Sarmas I. A novel method for automated EMG decomposition and MUAP classification. Artificial Intelligence in Medicine. 2006 May;37(1):55-64.

[55] Katsis CD, Exarchos TP, Papaloukas C, Goletsis Y, Fotiadis DI, Sarmas I. A two-stage method for MUAP classification based on EMG decomposition. Comput. Biol. Med. 2007;37(9):1232-1240.

[56] Pino L. Neuromuscular clinical decision support using motor unit potentials characterized by 'pattern discovery'. Ph.D. dissertation, Dept. Syst. Des. Eng., Univ. Waterloo, Waterloo, ON, Canada, 2009.

[57] A. Wong, and Y. Wang, "Pattern discovery: a data driven approach to decision support," IEEE Trans Syst Man Cybern Part C: Appl Rev, vol. 33, pp. 114–124, 2003.

[58] A. Wong and Y. Wang, "High-order pattern discovery from discrete valued data," IEEE Trans Knowled Data Eng vol. 9, pp. 877–893, 1997.

[59] A. Wong and Y. Wang "Discovery of high order patterns," IEEE Trans Syst Man Cybern, vol. 2, pp. 1142–1147, 1995.

[60] Y. Wang, "High-order pattern discovery and analysis of discrete valued data sets," Ph.D. Thesis, Univ. of Waterloo, Waterloo, 1997.

[61] Hamilton-Wright A, Stashuk DW. Clinical characterization of electromyographic data using computational tools. (2006). 2006 IEEE Symposium on Computational Intelligence and Bioinformatics and Computational Biology, 1-7, 2006.

[62] Buchthal F, Pinell P, Rosenfalck P. Action potential parameters in normal human muscle and their physiological determinants. Acta Physiol. Scand. 32(2-3):219-229, 1954.

[63] Xie H, Huang H, Wang Z. Multiple Feature Domains Information Fusion for Computer-Aided Clinical Electromyography, Computer Analysis of Images and Patterns, 304-312, 2005.

[64] Pfeiffer G, Kunze K. Discriminant classification of motor unit potentials (MUPs) successfully separates neurogenic and myopathic conditions. A comparison of multi- and univariate diagnostical algorithms for MUP analysis. Electroencephalography and Clinical Neurophysiology/Electromyography and Motor Control, 97(5):191-207, 1995.

[65] Pfeiffer G. The diagnostic power of motor unit potential analysis: An objective Bayesian approach. Muscle & Nerve, 22(5):584-591, 1999.

[66] Pino LJ, Stashuk DW. Using motor unit potential characterizations to estimate neuromuscular disorder level of involvement. In: 2008 30th Annual International Conference of the IEEE Engineering in Medicine and Biology Society. Vancouver, BC: 4138-4141, 2008.

[67] J. Malmivuo, R. Plonsey, Bioelectromagnetism, 1995.