Optimisation of Nerve Cuff Electrode Recordings for Functional Electrical Stimulation Applications

By

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To my Sister
ABSTRACT

There are about 600 spinal cord injuries (SCI) in Britain every year. The effects are irreversible and devastating, leaving parts of the body permanently paralysed. Functional Electrical Stimulation (FES) is a method to restore some partial functionality to paralysed muscles. Typical FES applications include restoration of hand grasp for tetraplegics patients, restoration of standing and standing up for paraplegics and restoration of bladder function for people with incontinence.

Most of the early systems developed are open-loop systems with no feedback to regulate the stimulation. However, they are difficult to use because of their inability to cope with unexpected disturbances. Electroneurogram (ENG) activity recorded from peripheral nerves using cuff electrodes have been shown to be a reliable source of feedback in FES applications, eliminating most of the problems faced with externally-worn sensors. This thesis is dedicated to the optimisation of cuff electrodes in FES applications in terms of the suppression of EMG interference. The single fibre action potential is modelled using monopolar, bipolar and tripolar electrode structures using state of the art models. The effect of parameters such as cuff length, cuff radius, fibre diameter and electrode separation are investigated. It is found that in tripolar recordings the signal depends only on electrode separation and not on cuff lengths.

The relationship between cuff geometry and interference from surrounding muscles in cuff electrode recordings is addressed. It is found that moving the end electrodes away from the cuff ends improves immunity from interference.

A new cuff electrode configuration termed the screened tripole is proposed with higher inherent signal-to-interference ratio than current recording arrangements. Also in this thesis a closed-loop recording method is proposed, which allows the automatic nulling of residual Electromyogram (EMG) in tripolar electrode recordings. This method has the potential to reduce the high-order filters required in some FES applications. This will enable the development of mostly analogue systems, which are more suitable for implantation.
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<td>Absolute Refractory Period</td>
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<td>Compound Action Potential</td>
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<td>Common-mode Rejection Ratio</td>
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<td>SFAP</td>
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<td>SIR</td>
<td>Signal-to-Interference Ratio</td>
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<td>SNR</td>
<td>Signal-to-Noise Ratio</td>
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1.1 INTRODUCTION

Spinal cord injuries due to stroke or accidents can cause permanent loss of sensation and voluntary motor function. Currently, regeneration of affected central neurones and restoration of functionality is not possible. Partial restoration of mobility can be achieved by the use of functional neuromuscular stimulation (FNS) also called functional electrical stimulation (FES), which is widely successful as shown in many studies and experiments [1]-[7]. The stimulation is achieved by passing regulated electrical currents into the target muscle tissue or via motor nerves branching from the spinal cord, which innervate the target muscle. This can be carried out invasively through electrodes implanted around the motor branches or by the use of surface electrodes. However the latter technique suffers from a lack of selectivity and the need for large stimulating currents. Advances in FES have resulted in the use of various methods to restore, for example, hand grasp for tetraplegic patients [8]-[30], bladder function by stimulation of the sacral roots [31]-[53], and gait for paraplegic individuals [54]-[60].

Most of the early systems, which apply electrical stimulation to specified muscle groups or to a motor branch, are open-loop systems, which rely on the user's experience and on visual feedback. As a result, in most cases, this produces excessive forces to hold an object, for example in hand grasp. Also the system must be able to respond to sudden disturbances due to change in process parameters such as force, force orientation and muscle fatigue.

In order to obtain more refinement, researchers have turned to closed-loop systems, which require feedback signals carrying information resulting from e.g., contact force on the skin. One problem of implementing such systems is the need for reliable, stable sensors for chronic implantation. This sensory information can be provided by the use of external sensors in neuroprostheses [61]-[64]. These however suffer from major drawbacks, which restrict their use beyond the laboratory. These drawbacks include calibration drifts, sensitivity to temperature changes and untidy cosmetic appearance, which make them unsuitable for implantation purposes because they are difficult to care and maintain over long periods of time.
In order to overcome this difficulty, natural sensors in the glabrous skin have been shown by various experiments [65]-[69] to be a reliable source for sensory information to control prosthetic devices in FES systems. It seems that the recorded neural activity from mechanoreceptive units in the glabrous skin is closely related to the various components of contact force.

Sensory signals from single receptors are carried in neurons. However, for carefully chosen nerve sites, the compound signal although it originates from 1000s of neurons, can give an informative signal.

The compound action potential (CAP) is the sum of the single fibre action potentials (SFAPs). Therefore, the compound nature of the CAP is determined by the diversity of fibre types, their individual conduction velocities and distribution in the compound nerve. For more information see Appendix 1. Electrical recording of the CAP generated by excitation of a peripheral nerve has a wide range of applications in basic research and, in particular, in the assessment of neuromuscular disease. A nerve contains several tens of thousands of single afferent nerve fibres of different diameters typically between 2 and 20µm [70]-[71]. They can be classified into Aα, Aβ, Aδ and C fibres. The largest fibres in cutaneous nerves are Aα and Aβ, with conduction velocities between 30 and 72m/s and these conduct impulses from mechanoreceptive units in the glabrous skin [72]. A cross section of a nerve bundle is shown in Fig. 1.1. For more details see appendix 1.1.
1.2 CUTANEOUS MECHANORECEPTIVE AFFERENTS

There are four classes of mechanoreceptors present in the human hand [74], which are shown in Fig. 1.2. These mechanoreceptors differ by their rates of adaptation to mechanical stimulation (SA= slow adaptation, FA= fast adaptation) on the glabrous (hairless) skin and in their receptive fields (I=small, II=large). Very rapidly adapting (FAII) receptors sending out one or two impulses per pressure stimulus (Pacinian corpuscles). Fast adapting (FAI), with discharges that cease about 50-500 ms after the onset of the pressure stimulus (Meissner corpuscles) and slowly adapting continuing to discharge stimulus induced action potentials even when the pressure is maintained for a long time (Merkel’s cells, SAI), (Ruffini endings, SAII).
Fig. 1.3 Receptive fields and innervation densities for various mechanoreceptors. From Vallbo and Johansson, 1984 [74].

The receptive field of a mechanoreceptor is the area within which an applied stimulus of specified intensity can elicit a response of the receptor. The receptive fields of Merkel-cell units, which are shown in Fig. 1.3 are small ranging from 3 to 50mm², which corresponds to diameters of 2 to 8mm, whereas the receptive field of the Ruffini endings are relatively large. The receptive fields for the Meissner corpuscles are just as small as those of the Merkel’s cells, whereas those of the Pacinian corpuscles cover a broad area.

No studies have been performed on the receptors in the human foot sole, however it is a safe to assume that the rapidly adapting receptors make the largest contribution to the
total recorded Electroneurogram (ENG) signal [75]. In this study the ENG signal recorded from cats was modelled using a three part model representing the slow, medium and fast adapting receptors. Maximum correlation occurred between the modelled and the recorded signals when the contribution from the fast adapting receptors was made large. Therefore the ENG signal takes on the form of phasic bursts in response to mechanical stimuli on the glabrous skin.

1.3 INTRAFASCICULAR ELECTRODES

Some investigations into the recording of neural activity from peripheral nerves have used single unit intrafascicular electrodes [76]-[78] inserted into the nerve tissue during open surgery. Although this technique provides a highly selective recording of individual fascicles within the nerve trunk, the migration of the electrodes and the consequent nerve damage make this technique at least in its present form unsuitable for long term implantation. For long term chronic recordings in free-moving animals, cuff electrodes have emerged in the last two decades as a reliable method to record the neural activity of peripheral nerves [67].

1.4 CUFF ELECTRODES

Cuff electrodes have been used to record the ENG from peripheral nerves in various experiments [59,65,66,67,68,69,75,79]. Neural activity recorded from the cuff electrodes is used in FNS systems to provide feedback information to control the stimulation of paralysed muscles in paraplegic and tetraplegic subjects. A nerve cuff recording electrode consists of an insulting tube typically made of silicone rubber with circumferential metal electrodes placed along the inner cuff walls as shown in Fig. 1.4. Here a zipper closure method developed by Hoffer et al. [80] is used to seal the cuff, after surgical placement, to isolate a length of nerve from the external fluid and tissue. The cuff material must be biologically compatible, flexible and electrically insulating.
Fig. 1.4 Schematic diagram of a Cuff electrode using a zipper closure developed by Kallesoe et al. 1996 [80].

The electrodes are usually made from coated stainless steel or Pt/Ir sewn to the inside of the cuff walls. Cuff electrodes can also be fabricated using platinum foil electrodes fixed by rubber bands on a Teflon coated mandrel dip-coated with silicone [81]. The recording electrodes usually encircle more than 80% of the perimeter of the cuff. The internal diameter of the cuff must be at least 20% larger than the diameter of the nerve [82] to avoid compression of the nerve bundle and therefore obstruction of the blood supply. Stein [83] has shown that tight cuffs reduce slightly the number of large myelinated fibres. He also observed that there was an increase in the impedance of the electrodes in the first few weeks after implantation but this was attributed to tissue in growth inside the cuff. For more details see [84]. It was suggested by Hoffer et al. [82] that, using three electrode cuff structure with the recording carried out between the central electrode and the two shorted end electrodes which are placed at the ends of the cuff, the cuff length must at least equal to the wavelength of the neural signal and about ten times greater than the cuff inner diameter. The effect of cuff length on the actual amplitude and shape of the recorded extracellular action potential is shown in Fig. 1.5. According to Hoffer [82] the vertical distance at mid-cord between the travelling extracellular wave represents the instantaneous potential difference between the centre electrode and the tied end electrodes, which are at the same potential. It can been seen from fig. 1.5 that to obtain a maximal response for the extracellular action potential (maximal ΔV), the length of the cuff must be equal to the wavelength of the action potential.
EXTRA-AXONAL POTENTIAL WAVEFORM (mm)

Fig. 2. (A) Schematic representation of the extraaxonal potential waveform generated by a 64 m/s fiber (adapted from Marks and Loeb, 1976), shown traveling in space from left to right. A 5 mm long, tripolar cuff electrode is represented as a cord, with its isopotential ends touching the waveform at all times. The instantaneous potential difference \( \Delta V \), recorded by the center electrode with respect to the end electrodes, is given by the vertical distance from cuff midpoint to waveform. (B) Seven positions of the cuff (as cord) are shown as the wave travels through it. (C) The development of the triphasic signal (+, −, +) recorded by the tripolar cuff electrodes as the wave travels past them is shown. The times \( t_1 - t_7 \) correspond to the cuff positions shown in B (modified from Hoffer, 1975, Fig. 1).

Fig. 1.5 Schematic representation of the extraaxonal potential waveform and the effect of cuff length on the amplitude and shape of the triphasic extracellular action potential according to Hoffer. From [82].

1.5 CHARACTERISTICS OF SIGNAL AND NOISE SOURCES

The amplitude of the neural signal can range up to a few \( \mu \)V. The frequency spectrum extends from about 800Hz to 10kHz [85], with most power in the 800 to 2000Hz region [7]. In addition to the neural ENG signals, the electrodes tend to pick up stimulating artefacts from the stimulating electrodes in FES systems. These potentials can be several orders of magnitude higher than the potentials recorded in the ENG. When this situation occurs the ENG amplifier saturates and slowly drift back to its original mode with a time constant determined by the frequency response of the amplifier. The simplest way to
eliminate this artefact is to ground the input during stimulation. This avoids saturation of the input amplifier [86].

Also the recording electrodes pick up electromyogram (EMG) interference from stimulated and non-stimulated active muscles nearby. The amplitude of the EMG signal is on the order of few mV, three orders of magnitude larger than the ENG signal. The frequency range of the EMG interference during neural recording extends from about 1Hz to 3kHz with most of the power being concentrated in the 50-150 Hz range. Thus the EMG signal is a major source of interference in nerve cuff recordings.

Classically biopotential signals are obtained from bipolar electrodes [87]. These electrodes are often symmetrically located electrically with respect to ground. As a result the most appropriate amplifier in this case is a differential one. Because such electrodes usually have a common-mode voltage with respect to ground that is much larger that the signal amplitude, these differential amplifiers must have high common-mode rejection ratios (CMRR) to minimize artefacts due to the common mode signals. Ideally the CMRR should be infinite, but because of nonlinearities and because components can never be exactly matched, typical CMRR range from 60dB to 120dB. These differential amplifiers can be used to minimize the interference in biopotential recording from magnetic fields, electric fields and electromagnetic fields. For more details see [88].

Stein et al. [83] have shown that when one records with one or two electrodes (bipolar) in a cuff, the neural signal is swamped by the much larger signals from surrounding muscles. It was described that the lack of improvement when recording differentially between two electrodes within the cuff may seem surprising at first, since differential recording is a classical method of rejecting common-mode signals as mentioned above. However the cuff is open at both ends and EMG currents flow through the cuff and this causes a potential drop between the electrodes in the cuff. Therefore bipolar recording does not improve the rejection of muscle signals since the EMG signals are not identical at the two electrodes and are therefore not rejected by a differential amplifier.

To reject the EMG interference from cuff electrode recording, a tripolar electrode configuration is used. In the earliest version of this arrangement, the so-called the quasi­tripole arrangement [67,82], three electrodes are placed symmetrically along the cuff, with the two outer electrodes connected together as shown in Fig. 1.6. This ideally forces
the EMG potential at the central electrode to be equal to the potential at the two outer electrodes, so that when they are measured differentially and because of the high CMRR of the differential amplifier, they cancel each other.

In a modified version of this arrangement termed the true tripole arrangement, the cuff outer electrodes are not connected together and the three electrodes are connected in pairs to two first stage differential amplifiers. The outputs from the differential amplifiers are added together using a third amplifier as shown in figure 1.7. Ideally the EMG signals at the outputs of the two differential amplifiers are equal and opposite and therefore are cancelled by the third amplifier.

Since the conductive medium for the EMG signal is the surrounding fluid, which can be treated as a resistive element, it is safe to assume that the EMG signal is picked up simultaneously by the recording electrodes. Therefore the EMG signal at the two end electrodes will exhibit an amplitude variation, but negligible phase difference [89].
Direction of flow of EMG Current

Fig. 1.6 The Quasi-tripole arrangement. Hypothetical signals for the ENG and the EMG signals are shown. In the ideal case the EMG signals at the centre electrode and the shorted end electrodes are identical. Without the connection between the end electrodes the EMG signals at the three recording electrodes are not identical. The suppression of the EMG in this arrangement relies on the high CMRR of the differential amplifier.

Direction of flow of EMG Current

Fig. 1.7 The true-tripole arrangement. Hypothetical signals for the ENG and the EMG are shown. Note that the EMG signals at the three recording electrodes are not identical. Also it can be concluded that the use of differential recording between two electrodes in the cuff will not reject the EMG. Only by using the three electrode configuration rejection of the EMG is possible. The rejection in this case relies on the fact that the EMG signals from the outputs of the differential amplifiers are equal and opposite.

The frequency spectrum of the ENG signal recorded from cuff electrode depends on various parameters such as cuff length, electrode separation and on the electrode configuration used, i.e., monopolar, bipolar or tripolar [89], see also chapter 2. In other words, the cuff electrode structure behaves as a spatial filter for the neural activity
recorded from a nerve bundle. Also, given that the ENG is the superposition of all the single fibre action potentials (SFAPs), the cuff electrode parameters should be chosen so that the frequency response of the spatial filter should match the frequency response of the largest fibres within the nerve bundle, which contribute the most to the neural signal [67].

Noise sources also originate from the intrinsic noise of the amplifier, which is in the μV range and the thermal noise from the cuff itself (i.e., from the electrode-tissue interface), about 0.7μV [85]. As a result the signal to noise ratio (SNR) is low, even sometimes below 0dB. To remedy the problem, significant work has focused on three main fronts to improve the signal to noise ratio [90]:

- Improvements in the electrode configurations to obtain a better performance at the front end of the system, [84,91].
- Improvements in the electrode/amplifier configurations, [92,93].
- Improvements in the post-processing of ENG signals through the use of high-order digital filters and high-order algorithms to obtain better threshold detection for use in foot-drop applications [7].

With signal levels on the order of a few μV maximum, amplifier noise is very significant compared to thermal noise from the cuff [85]. The problem is that existing low-noise amplifiers achieve their noise specifications when the noise input impedance of the amplifier is matched to the impedance of the electrodes, which is roughly in the 1-2 kΩ range. In order to solve this problem [67], [82], the use of step-up transformers with turn ratio of 20 was suggested. It was found that even with transformer coupled amplifiers like the MicroProbe amplifier (MicroProbe, Inc.) that the noise contribution from the amplifier accounted for at least 65% of the total noise power [90].

With direct-coupled designs such as the one implemented by [75], the total noise contribution from the amplifier might be as high as 85% of the total noise power. In another study by Pflaum et al. [93], using AMP01s (Analog Devices) in the first stage of a true tripole configuration, shown in Fig. 1.7, performed as well as the transformer type MicroProbe amplifier in a quasi tripolar configuration in terms of SNR. Unfortunately, at the moment, such low noise amplifiers require a lot of power, which is not inconvenient

---

1 Ratio of voltage noise to current noise
for implantable applications, which need low power circuits. It seems that there is a great need for research into low-power low-noise preamplifiers for ENG signal detection.

As an example of state-of-the-art ENG recording using nerve cuffs, Fig. 1.8 shows a cuff electrode recording from a cervical level 5 (C5) tetraplegic man using a quasi tripole configuration. A 2 cm cuff with inner diameter of 2.6 mm was implanted around the digital nerve, which innervates the index finger. Three multistranded stainless steel electrodes had been placed symmetrically inside the cuff, (for more detail see [69]). The width of the stimulation pulses was increased beyond the threshold for muscle activation as shown in Fig. 1.8A, which is achieved after 0.5 s. Also shown are the forces applied on the surface of the index finger during electrical stimulation of surrounding muscles, see Fig. 1.8C. Fig. 1.8D shows the contamination of the raw ENG signal with stimulation and EMG artefacts. Useful ENG signal was obtained when the raw signal was passed through fourth-order band-pass filter (1000-4000 Hz). So the ENG signal is correlated to the forces applied externally. However, the recorded signal is contaminated with stimulation and EMG artefacts.
Fig. 1.8 Recording from a tetraplegia patient using a quasi-tripole arrangement. A) Width of stimulation pulses. B) Perpendicular force applied on the radial index finger. C) Shear force applied. D) Raw ENG data. E) Filtered ENG data.

1.6 SUMMARY OF QUESTIONS TO BE ANSWERED

If practical FNS systems are to be implemented beyond the laboratory, complete implantable sensors have to be realised. They must be reliable, stable for long periods of time, and consume little power.

This thesis is dedicated to finding an optimal system for recording of ENG activity using nerve cuffs. The following investigations have been carried out.

1. The extent to which a cuff linearises the internal field, when exposed to a non-linear external field, and how the cuff geometry affects linearity.

2. Determination of the best electrode configuration.

3. The best method to reduce the mismatches of the electrode impedances within the cuff.

4. The best method to cancel automatically any dynamic interference due to manufacturing tolerances in the cuff.

These points are addressed in the following chapters:

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Data provided from Dr Andreas Lickel, SMI, Denmark
Chapter 2. In this chapter a comparison between the various cuff electrode configurations in the detection of the single fibre action potential is made. The effect of cuff parameters, i.e., cuff length, radius, electrode position, electrode separation, and fibre diameter on the amplitude and the frequency content of the single fibre action potential is presented.

Chapter 3. Here the effect of cuff geometry on interference reduction is investigated. The interference was generated by an external current source placed outside the cuff. The main question was how the linearity is affected by the cuff geometry.

Chapter 4. In this chapter the traditional quasi-tripole with the true-tripole configuration are compared. Also a new configuration that combines the advantages of both is introduced.

Chapter 5. A method that reduces EMG interference in ENG cuff electrode recordings is introduced. It is based on the true-tripole with closed-loop feedback.

Chapter 6. Conclusions and future directions are presented.

Throughout this thesis a key consideration has been, to develop cuff electrode configurations and systems for ENG detection applicable for low power implantable solutions.

Chapter 3 has been published in the IEEE Transactions on Biomedical Engineering, whereas chapter 4 has been accepted for publication in the same journal. Chapters 2 & 5 will be submitted to the IEEE Transactions on biomedical engineering at a later date. As a result there is some amount of overlap between the chapters, especially in the introduction sections.
1.7 APPENDIX 1.1: ELEMENTS OF NEUROPHYSIOLOGY

1.7.1 NERVE FIBRES

In peripheral nerves, individual axons are enveloped in a loose connective tissue, the endoneurium (figure A1.1, from [94]). Small groups of axons are closely associated with a bundle called a nerve fascicle.

![Diagram of peripheral nerves](image)

*Fig. A1.1 Structure of the peripheral nerves. From [94].*
The fascicle is defined by a sheath of connective tissue, the perineurium, which varies in thickness from 1μm to 60μm [95]. In surgical procedures it can hold structures without tearing. In addition to its mechanical strength, the perineurium is a diffusion barrier, isolating the endoneural space around the axons from the surrounding tissue. Several fascicles together form fascicular bundles within and extensive multi-laminated perineurium. The fascicular bundles in turn collectively form the peripheral nerve that is embedded in loose connective tissue called the epineurium.

A large nerve trunk may contain anything from one to over a hundred funiculi, with diameters ranging from about 0.4 to 3.5 mm. The unmyelinated axons are protected throughout their course by a chain of overlapping Schwann cells, whereas the myelinated axons are each surrounded by a myelin sheath derived from the membranes of the Schwann cells. Each Schwann cell manufactures a segment of the myelin sheath, and the nodes of Ranvier are the points where one Schwann cell succeeds another. The distance between the nodes of Ranvier varies directly with the size of the fibre; in a small one they may be as little as 0.1 mm apart, but in large fibre perhaps as much as 1.0mm.

Each funiculus of the cutaneous nerve trunk contains large and small myelinated fibres to a density of about 10000-13000 per square millimetre of cross-section. These fibres are outnumbered three or four to one by unmyelinated fibres. The diameters of the unmyelinated axons in a typical cutaneous nerve range from approximately 0.4μm to 1.1 μm; the largest myelinated ones, which range from approximately 1μm to 16 μm, with a peak between 1 and 5μm and another between 6 and 12μm. The larger myelinated fibres characteristics of motor nerves are almost completely absent, so that the myelinated spectra of cutaneous and motor nerves are very different (Fig. A1.2).
Conduction velocities of myelinated nerve fibres vary from a few m/s, to more than 100 m/s. In the invertebrate nervous system, the peripheral nerves have been classified into groups according to conduction velocity and function. In general, the greater the nerve fibre diameter, the greater its speed of conduction. Large axons are primarily concerned with proprioceptive sensation and somatic motor function (α group), and conscious touch and pressure (β group). Smaller fibres are concerned with pain and temperature sensations (δ group), as well as autonomic function (B group). Table A1.1 lists the various fibre types, along with their electrical characteristics and diameter [96].

At the peripheral end the fibres branch and terminate either as naked endings or in terminal encapsulations of many varieties such as the Pacinian corpuscle, other include Meissner's corpuscle, Merkel's discs, and the Ruffini endings. These encapsulated endings are found mainly in hairless or glabrous skin: the palms of the hands and soles of the feet, the lips, and parts of the external genitalia. The fibres from encapsulated endings are mainly of group Aβ (Table A1.1).
Table A1.1 The electrical characteristics and diameters of various fibre types [96].

<table>
<thead>
<tr>
<th>Fibre Type</th>
<th>Function <em>(examples)</em></th>
<th>Fibre diameter <em>(µm)</em></th>
<th>Conduction velocity <em>(m/s)</em></th>
<th>Spike duration <em>(ms)</em></th>
<th>Absolute refractory period <em>(ms)</em></th>
</tr>
</thead>
<tbody>
<tr>
<td>Aα*</td>
<td>Afferents- muscle spindle, tendon Efferents</td>
<td>12-20</td>
<td>70-120</td>
<td>0.4-0.5</td>
<td>0.4-1</td>
</tr>
<tr>
<td>Aβ*</td>
<td>Afferents- touch</td>
<td>5-12</td>
<td>30-70</td>
<td>0.4-0.5</td>
<td>0.4-1</td>
</tr>
<tr>
<td>Aγ*</td>
<td>Efferents- muscle spindle</td>
<td>3-6</td>
<td>15-30</td>
<td>0.4-0.5</td>
<td>0.4-1</td>
</tr>
<tr>
<td>Aδ*</td>
<td>Afferents- temperature fast pain</td>
<td>2-5</td>
<td>12-30</td>
<td>0.4-0.5</td>
<td>0.4-1</td>
</tr>
<tr>
<td>B*</td>
<td>Sympathetic, preganglionic</td>
<td>&lt;3</td>
<td>3-15</td>
<td>1.2</td>
<td>1.2</td>
</tr>
<tr>
<td>C**</td>
<td>Sympathetic Postganglionic afferents slow pain</td>
<td>0.4-1.2</td>
<td>0.5-2</td>
<td>2</td>
<td>2</td>
</tr>
</tbody>
</table>

*myelinated ** unmyelinated
1.7.2 SPREAD OF THE ACTION POTENTIAL TO THE AXON [97]

The peripheral axon terminals of the primary afferent serve as sensory receptors. Stimulus-gated ion channels, not voltage-gated ones, predominate in the membrane of these sensory receptors and they produce receptor or generator potentials. If the generator potentials are large enough then action potentials will be generated the axon hillock. As the action potential develops at the trigger zone, the potential difference between the axon hillock and adjacent parts of the neurone causes currents to flow down the axon (orthograde) and back into the soma (retrograde). These local circuit currents produce, in these adjacent parts of the cell, a depolarising electrotonic potential that is an attenuated version of the action potential. The depolarisation produced by the electrotonic potentials in the neighbouring membrane causes voltage-gated Na⁺ channels to open and this leads to action potential generation, at least in those areas where the depolarisation due to the electrotonic potential is above threshold (see Fig. A1.3).

In myelinated axons, the next action potential is initiated at the next node of Ranvier where voltage-gated Na⁺ channels are very dense. In the internode, which may be quite long (1-2 mm), there are few voltage-gated Na⁺ channels and the threshold for the action potential is infinite. In cells with unmyelinated axons, the membrane of the axon immediately adjacent to the axon hillock is excited by the depolarisation. The spread of the action potential to nearby membrane is passive, i.e., electrotonic, and occurs with decrement. The important point is that each action potential at the trigger zone is the stimulus, via local circuit currents and electrotonic spread, for producing an action potential in the axon.
1.7.3 THE CONDUCTION CYCLE: CONDUCTION OF THE ACTION POTENTIAL IN THE AXON

Conduction of the action potential down the axon occurs because local circuit currents generated by the action potential at one site depolarise the neighbouring axonal membrane to threshold, causing it to generate an action potential, which starts the whole process over again (see Fig. A1.4). Backward going (antidromic) action potentials are not generated in the axon during conduction because the membrane immediately behind the action potential is still in its absolute refractory period.

In myelinated fibres, which in the vertebrate brain tend to be relatively large diameter (5 to 20 μm), the action potential at one node of Ranvier is, because of the insulating properties of the myelin, effective as a stimulus via electrotonic spread over distances of up to 1-2 mm. Thus, conduction velocity is much more rapid than in unmyelinated fibres because of each cycle of AP generation - electrotonic spread - AP generation covers a much greater distance. This mode of conduction is called saltatory conduction. Saltatory conduction is a very robust process. The amplitude of the electrotonic potential that reaches the next node of Ranvier is 4 to 6 times the threshold (10 mV). Thus, the safety factor (SF) for conduction, the ratio of the stimulus amplitude to the threshold, is 4 to 6.

In unmyelinated nerve fibres, which are small diameter in the vertebrate nervous system, the process is spatially restricted such that only the membrane immediately
adjacent (within 50 - 100 mm) to the action potential is depolarised to threshold by the local circuit currents. This means that the conduction velocity of the action potential is low since each cycle of AP generation - electrotonic spread - AP generation covers relatively little distance.

The process of saltatory conduction is not as simple as outlined above. In fact, the wavelength of the action potential is a centimetre or more in large-diameter myelinated axons. Thus, while the basic process of AP generation - electronic spread - AP generation is correct, it takes place over a much greater spatial extent than indicated.

1.7.4 IMPORTANCE OF MYELINATION

The addition of many wraps of glial cell membrane (Schwann cells in the periphery, oligodendroglial cells in the CNS) around the axon is the key factor in the role of myelination in increasing the conduction velocity of axon. This myelin sheath acts as an insulator, greatly increasing the effective transverse resistance of the membrane \( r^\perp \). This reduces leakage currents and prevents the local circuit current from leaking out of the axoplasm except at the nodes of Ranvier. This greatly increases the distance over which electronic spread is effective. Technically this is described as an increase in the length constant. The length constant is equal to the distance over which an electrotonic potential will spread before declining to 37% of its original value. It is calculated from the equation \( \lambda = (r^\perp /r_a)^{1/2} \), where \( r_a \) is the longitudinal resistance of the axoplasm. Myelination increases from a few hundred \( \mu \)m or less in unmyelinated fibres to a few thousand \( \mu \)m in myelinated fibres. This is the main factor accounting for the increased conduction velocity (CV) of myelinated nerve fibres. An additional positive influence of myelination is that, by increasing the thickness of the layer of insulation around the axon, it decreases the effective capacitance \( (c_m) \) of the axon membrane. This decreases the charge storage capability of the internodes and contributes to more effective spread of local circuit currents (see Fig.A1.5).
1.7.5 THE COMPOUND ACTION POTENTIAL

Most peripheral nerves contain a variety of fibres of different diameters, some myelinated and some not, so if we use a pair of external electrodes to record the response to a single shock delivered to the whole nerve, we usually obtain a very complex waveform [98]. If we insert a microelectrode in an axon we record the classic monophasic action potential as shown in Fig. A1.6(a). But if we record using a pair of external electrodes some way apart, we register the action potential twice over as shown in figure A1.6(b) and c). This is a biphasic recording with a swing of potential first in one direction and then in the other about a resting value of zero. If the electrodes are brought closer together, the two individual responses will begin to overlap producing a smaller biphasic response as shown in Fig. A1.6(c). One way to get around this problem (not possible in real situations) apart from using intracellular electrodes is to arrange that the travelling action potential never gets to the second electrode, by crushing the nerve between the two recording electrodes. However the monophasic recording obtained in this case is considerably smaller compared to the intracellular recording case (Fig. A1.6a).
In real preparations, the recording electrodes are not only recording from a single axon but from all the active fibres in the nerve bundles. The biphasic potential waveform from the whole nerve is likely to be lopsided one, with some of the fibres contributing biphasically and others monophasically as shown in Fig. A1.7. If the nerve is crushed between the recording electrodes the pattern of peaks in the compound action potential gives a spectrum of the conduction velocities of the fibres in the nerve. In such a spectrum from a large peripheral nerve, it is often possible to distinguish groups of fibres according to the classification outlined in Table A1.1.
Fig. A1.7 The compound action potential recorded using two external electrodes. a) Biphasic recording. b) Monophasic recording with the nerve crushed between the recording electrodes. The differences between the conduction velocities give rise to a dispersed compound action potential. Below actual recording from frog sciatic nerve with the A groups shown on an expanded time scale in the inset. From [98].
1.8 REFERENCES


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CHAPTER TWO

A COMPARISON BETWEEN CUFF ELECTRODE CONFIGURATIONS FOR THE RECORDING OF SINGLE FIBRE ACTION POTENTIALS

2.1 ABSTRACT

The recording of single fibre action potential (SFAP) was modelled in monopolar, bipolar and tripolar electrode structures using a finite difference method and a one-dimensional model of the cuff electrode structure. The effect of parameters such as cuff length, cuff radius, fibre diameter, and electrode separation on the extracellular SFAP recordings were investigated. In monopolar and bipolar recordings the SFAP amplitude depends on cuff length and on electrode position/separation whereas in tripolar recording it only depends on electrode separation. The frequency responses of the monopolar and tripolar configurations are shown to be band-pass responses, whereas the bipolar gives a non-uniform spatial frequency response.
2.2 INTRODUCTION

Nerve cuff electrodes have been used to record the Electroneurogram (ENG) from peripheral nerves in various experiments [1,2]. Information such as slippage in hand grasp [3] or foot-to-ground contact [4] has been extracted from the recorded ENG signal. This signal is the summed activity of the single fibre action potentials (SFAPs) generated by the afferent fibres within the nerve bundle. These active fibres innervate the mechanoreceptive units, which are still intact after spinal cord injury. These units fire in response to mechanical stimulation on the glabrous skin. Most of the contributions to the ENG signal are provided by type FAX and FAII receptors [5] in the glabrous skin. These receptors exhibit no tonic (steady state) activity and only fire in response to abrupt changes in the applied force. The main reason for using a cuff electrode, to record the activity of these receptors, is that it provides a good restriction to the flow of extrafascicular currents from the nerve bundle, thus allowing the potential difference to be picked up by electrodes embedded in the cuff.

Many analytical tools have been developed to model the SFAP recorded in nerve cuffs. For example, Stein and Pearson’s (1971) [6] one-dimensional analysis of nerve signals, recorded in a locally-restricted extracellular space such as paraffin oil, is applicable to nerve cuffs. However many assumptions were made regarding the minimum length and the minimum aspect ratio for which the analysis holds. In addition, the extracellular potentials at the cuff ends were considered to be negligible or zero to simplify the analysis. In order to model more complicated structures with inhomogeneity, anisotropy and finite dimensions, numerical models [7,8,9] are used. However, these models require much computational effort even for a single fibre in a fascicle [9,10].
In this chapter a 2-D numerical finite difference model [8] is used to show how the geometry of the cuff affects the recorded nerve signal in monopolar, mobipolar, bipolar and tripolar electrode structures, shown in Fig. 2.1.

2.3 METHOD

To calculate the potentials recorded from cuff electrodes due to activity at the Nodes of Ranvier of nerve fibres within the nerve bundle, a two-part numerical model is used. The first part is a fibre model, where the membrane currents at the Nodes of Ranvier of myelinated nerve fibres, are treated as current sources within a volume conductor model. The membrane currents can be calculated using the Hodgkin-Huxley equations (for more detail see appendix 2.1), whereas distributed cable models represent the inter-nodes. In the second part, a finite difference method is used to calculate the potential distributions by solving Poisson’s equation in a 2-D grid, rather than a 3-D grid, due to the cylindrical symmetry.
2.3.1 FIBRE MODEL

The fibre model has been adopted from McNeal (1976) [11] and as modified by Struijk (1997) [8]. All equations used to describe the membrane kinetics at the Nodes of Ranvier are listed in [8]. In Fig. 2.2, the membrane action current (AC) is obtained from Node 11 of a 10μm-diameter fibre with 21 Nodes of Ranvier. This current template is used as a current source in the volume conductor model [9]. The amplitude of the action current is scaled for different fibre diameters but its duration is kept the same for all fibre diameters [8].

2.3.2 INHOMOGENEOUS MODEL

A Red-black Gauss-Seidel finite difference method with an over-relaxation factor of 1.9 was used to calculate the potential field in the 2-D grid (see appendix 2.2). The physical model of a nerve with a single cylindrical fascicle consists of five compartments whose conductivities are given in Table 2.1 [8]. The fascicle radius was 0.5mm enclosed by a perineurium with a thickness of 50μm. The thickness of the cuff material was always 0.5mm. The model is symmetrical around the lower axis where the myelinated fibre was positioned. A Neumann boundary condition was applied at this boundary to reflect the symmetry, while, at the other three boundaries, a Dirichlet boundary was applied. The number of grid points used in the model was 260 × 163 (z, r), with small grid sizes.
near the cuff and nerve bundle (non-uniform mesh). The number of iterations required so that the relative change in the potential at the lower axes is no more than $10^{-7}$, was different for different cuff lengths.

<table>
<thead>
<tr>
<th></th>
<th>$\sigma_z (1/\Omega m)$</th>
<th>$\sigma_r (1/\Omega m)$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fascicle</td>
<td>0.6</td>
<td>0.083</td>
</tr>
<tr>
<td>Perineurium</td>
<td>0.0034</td>
<td>0.0034</td>
</tr>
<tr>
<td>Cuff</td>
<td>$10^{-6}$</td>
<td>$10^{-6}$</td>
</tr>
<tr>
<td>Electrode</td>
<td>6.0</td>
<td>6.0</td>
</tr>
<tr>
<td>Surrounding Fluid</td>
<td>1.0</td>
<td>1.0</td>
</tr>
</tbody>
</table>

We have adopted a similar approach to that used in [8] for monopolar simulations to calculate the recorded signal in nerve cuffs using multi-pole electrodes, by using the reciprocal theorem and the lead field concept [12]. Instead of calculating the potential impressed on the recording electrodes due to the activity at the Nodes of Ranvier, within a nerve bundle, reciprocal currents of specific coefficients are impressed on the recording electrodes in symmetrical monopolar, bipolar or tripolar configuration in the following manner:

1. A unit current (+1) for monopolar recording
2. A dipole (+1, -1) for bipolar recording
3. A tripole (+1, -2, +1) for tripolar recording

The lead field generated by these current poles is computed using the finite difference method at the lower axis of the model where the active fibre is placed. Then, the action current at each node of Ranvier is multiplied by the lead field at each node to obtain the contribution from this node. After that, the contributions from all the nodes are added to obtain the total recorded signal. This method has the advantage that the finite difference method has only to be solved once for a specific electrode configuration, regardless of fibre parameters. It has been shown by Struijk [8] that modelling the membrane currents as current sources in a volume conductor is a better way to calculate the extrafascicular action potential than using classical methods [13]. The main advantage of the
numerical method is that modelling finite cuffs without any boundary conditions at the cuff ends with complex nerve and cuff geometries can be easily implemented. Also ignoring the leaking of currents in the internodes is justified given that the field potential at the recording electrode is not influenced by this omission at large distances from the nerve fibre (> fibre diameter).

2.3.3 ONE-DIMENSIONAL ANALYSIS

As action potentials travel along a nerve fibre they generate action currents which in general are dissipated in the extrafascicular medium. However, if the nerve is placed within a restricted extrafascicular space, e.g., an insulating cuff, these action currents produce extrafascicular potentials which can be measured, e.g. by electrodes embedded within the cuff. The potential, \( V_e(z, t) \), measured at a single electrode embedded in an insulating cuff of length \( L \) can be approximated by the following 1-D expression due to Stein [6] and modified by Struijk [8]¹:

\[
V_e(z, t) = \frac{R_e}{R_e + R_a} \left[ \left( 1 - \frac{z}{L} \right) V_m(0, t) - V_m(z, t) + \left( \frac{z}{L} \right) V_m(L, t) \right]
\]  

(2.1)

Where \( R_a \) and \( R_e \) are the resistances of the intrafascicular and extrafascicular space respectively, \( L \) is the length of the cuff and \( z \) is the distance from the proximal end of the cuff to the electrode and \( V_m(t) \) is the transmembrane action potential. A typical form of \( V_m(t) \) for a 10\( \mu \)m diameter fibre is shown in Fig. 2.3.

¹ Struijk [8] discusses the limitations of the one-dimensional analysis compared to homogeneous and inhomogeneous models of the nerve. In the one-dimensional analysis the extrafascicular potentials outside the cuff are assumed to be negligible.
Equation (2.1) and the template transmembrane action potential are used to calculate the extrafascicular potential at a position $z$ ($0 \leq z \leq L$) within the cuff as a function of time. Note that although the transmembrane potential $V_m(t)$ is monophasic, the recorded extrafascicular potential $V_e(z,t)$ is in general triphasic resulting from volume conduction effects. In the 1-D model given in equation (2.1), this effect is represented by the presence of three terms with a sequence of signs (+,-,+). For bipolar recording (see Fig. 2.1), the potential recorded is:

$$V_{\text{bipo}} = V_{e1}(z_1,t) - V_{e2}(z_2,t) = \frac{R_e}{R_e + R_n} \left[ \frac{z_2 - z_1}{L} V_m(0,t) + V_m(z_2,t) - V_m(z_1,t) + \frac{z_1 - z_2}{L} V_m(L,t) \right]$$

(2.2)

Whereas for tripolar recording the extrafascicular potential is:
\[ V_{\text{tripo}} = V_{e1}(z_1, t) - 2V_{e2}(z_2, t) - V_{e3}(z_2, t) = \]
\[ \frac{R_e}{R_e + R_a} \left[ 2V_m(z_2, t) - V_m(z_1, t) - V_m(z_3, t) \right] \]

(2.3)

In most cases, \( R_a \gg R_e \) and both are proportional to \( L \). Therefore in tripolar recording
the signal amplitude does not depend on cuff length but on inter-electrode separation.

The frequency response for the different cuff configurations can be obtained by taking
the Fourier transform of the above equations. The frequency response of the recorded
signal can be expressed as:

\[ G(f) = H(f)V_m(f) \]

(2.4)

Where \( G(f) \) is the spectrum of recorded signal, \( V_m(f) \) is the spectrum of the
transmembrane action potential and \( H(f) \) is the frequency response of the cuff electrode.

By evaluating the above equation for the three different configurations, the frequency
response \( H(f) \) can be obtained (the scaling factor \( \frac{R_e}{R_e + R_a} \) is not included):

\[ H_{\text{mono}}(f) = \frac{1}{L} \exp(-2j\pi f z / V) + \left( \frac{z}{L} \right) \exp(-2j\pi f L / V) \]

(2.5)

\[ H_{\text{bipo}}(f) = \frac{z - z_j}{L} \exp(-2j\pi f z_2 / V) - \exp(-2j\pi f z_1 / V) + \]
\[ \left( \frac{z_j - z_2}{L} \right) \exp(-2j\pi f L / V) \]

(2.6)

\[ H_{\text{tripo}}(f) = 2 \exp(-2j\pi f z_2 / V) - \exp(-2j\pi f z_1 / V) - \exp(-2j\pi f z_3 / V) \]

(2.7)

Where \( V \) is the speed of the action potential, which is proportional to fibre diameter:

\[ V = 5.58 \times D \]

Where \( V \) is in m/s and \( D \) in \( \mu \text{m} \) [14].
2.4 RESULTS

2.4.1 MONOPOLAR RECORDING (INHOMOGENEOUS MODEL)

Fig. 2.4 The peak-to-peak SFAP amplitude (10μm fibre) against the position of the electrode inside the cuff, for various cuff lengths. The cuff radius was set to 1mm.
Fig. 2.5 The peak-to-peak SFAP amplitude against fibre diameter for various cuff lengths. The cuff radius was set to 1mm.

Fig. 2.6 The SFAP amplitude against cuff radius for various cuff lengths. The fibre diameter was set to 10μm.

Fig. 2.4 shows the effect of electrode position on the amplitude of the recorded signal.
for a 10μm fibre at the axis of the nerve bundle. The maximum peak-to-peak amplitude occurs at half cuff length for cuff lengths below 30mm. Above cuff length of 30mm the peak-to-peak amplitude is not at its maximum at the middle of the cuff. The reason for this is that the first peak of the triphasic waveform increases and then decreases in favour of the third peak [8], whereas the second peak remains constant. The amplitude at the middle of the cuff for cuff lengths above 30mm is ~1.75μV, whereas at the ends of the cuff the peak-to-peak amplitude is around 0.45μV.

The variation of the SFAP amplitude with fibre diameter is shown in Fig. 2.5. The amplitude increases with fibre diameter from 0.1μV for a 4μm fibre up to 7.5μV for a 20μm fibre. The response is similar for cuff lengths above 25mm. Fig. 2.6 shows the effect of cuff radius on the SFAP amplitude. The amplitude is inversely proportional to the square of the radius.

2.4.2 MOBIPOLAR RECORDING (INHOMOGENEOUS MODEL)

![Graph showing the peak-to-peak SFAP amplitude against cuff length.](image)

Fig. 2.7 The peak-to peak SFAP amplitude against cuff length. The inner cuff radius is 1mm and the outer cuff radius is 1.525mm.

In Fig. 2.7, the SFAP amplitude for the Mobipolar arrangement [15] is shown against cuff length for a 10μm fibre. The inner cuff has a radius of 1mm and the outer cuff has a
radius of 1.525 mm. The response has a similar behaviour to the monopolar response with a peak amplitude of 1.71 μV. The mobipolar arrangement was introduced to reduce the length of the cuff in applications where space is a problem such as in hand grasp. However, like the monopole (Fig. 2.4), the signal decreases rapidly with cuff length below 30 mm.
Fig. 2.8 The peak-to-peak SFAP amplitude against (d/L) for various cuff lengths where d is the distance between the electrodes and L is cuff length. The fibre diameter is 10μm.

Fig. 2.8 shows the variation of the SFAP with electrode separation for various cuff lengths. The maximum peak-to-peak amplitude is ~2.35μV, whereas near the ends of the cuff, the amplitude varies between 0.35 and 0.65μV. The point at which the amplitude reaches its maximum is different for different cuff lengths, being close to 50% for small and medium size cuffs (5-20mm) but, for long cuffs (25-50mm), the maximum occurs at ~35%.
2.4.4 TRIPOLAR RECORDING (INHOMOGENEOUS MODEL)

Fig. 2.9 The effect of end electrode separation on SFAP amplitude recorded for a 10μm fibre with a cuff radius of 1mm. A) SFAP amplitude against end electrode separation in mm. B) SFAP amplitude against (d/L) where d is the end electrode separation and L is cuff length.

In Fig. 2.9 the SFAP is shown against end electrode separation for a 10μm fibre. In Fig. 2.9A, the amplitude variation is plotted for various cuff lengths. However the responses are the same irrespective of cuff length which confirms equation (2.3).
In tripolar recordings the SFAP depends only on inter-electrode separation. For the same inter-electrode separation, different cuff lengths will give the same amplitude. The amplitude recorded is asymptotic to 3.5μV.

2.4.5 FREQUENCY RESPONSE (ONE-DIMENSIONAL MODEL)

Fig. 2.10 The frequency response of the three configurations: Monopolar (solid line), bipolar (heavy line) and tripolar (dotted). A) $Z_i = 0.01xL$, $V=55m/s$, $L=30mm$. B) $Z_i = 0.2xL$, $V=30m/s$, $L=30mm$. C) $Z_i = 0.4xL$, $V=30m/s$, $L=30mm$. D) $Z_i = 0.2xL$, $V=30m/s$, $L=10mm$. 
Fig. 2.11 SFAP templates for the three configurations. For various electrode positions in monopolar recording, and for various electrode separations in bipolar and tripolar recordings.
Using the one-dimensional equations (2.4), (2.5) and (2.6) the frequency responses of the three configurations are shown in Fig. 2.10. The tripolar and the monopolar arrangements show similar responses when the end electrode in the tripolar arrangement are at the ends of the cuff (Fig. 2.10A). Both show a periodic band-pass response, with the first peak at \( f = L/V \) for monopolar recording and \( f = (Z_3-Z_1)/V \) for tripolar recording. In bipolar recording the response is complicated. As a result a cuff electrode can be treated as a spatial filter for nerve recordings with the transmembrane action potential as the input signal. The response of the filter depends on fibre diameter (conduction velocity), electrode separation, cuff length and electrode configuration. For example different fibre diameters would give different first peaks in the frequency response for the same cuff length and electrode configuration. For completeness Fig. 2.11 shows the SFAP templates for the three configurations.

2.5 DISCUSSION AND CONCLUSIONS

The electrode position in monopolar recording is quite important. The amplitude of the recorded neural signal at the end of the cuff is about 25% of the amplitude recorded at the middle of the cuff. For example for a 50mm cuff, 12mm either side of the central electrode the signal amplitude drops significantly (see Fig. 2.4). The peak-to-peak amplitude of the SFAP increases with fibre diameter because the SFAP amplitude increases with conduction velocity, which has a linear relationship with fibre diameter. Also, the SFAP amplitude decreases with cuff radius because this reduces the constrictive properties of the cuff.

In bipolar recording the amplitude of the recorded signal depends on the electrode separation. On one hand, near the ends of the cuff, the electrodes pick up very small signals because they are influenced by the low resistance region outside the cuff. On the other hand, in the middle of the cuff, both electrodes pick up almost the same signal (the extrafascicular voltage drop is small), so cancellations occur.

For tripolar recording the maximum amplitude occurs when the end electrodes are at the ends of the cuff, though the amplitude is less sensitive to end electrode separation in this region. An interesting result in tripolar recording is that the signal depends only on electrode separation not on cuff lengths and positions (distance between the central
electrode and either end of the cuff) of the electrodes in the cuff. This result has not been reported before. The reason for this is that in most studies the end electrodes were placed at the ends of the cuff and the cuff length was varied so the dependency on electrode separation only was overlooked. The optimal length for an action potential travelling at 60 m/s was in the region of the 30 mm as reported by Stein et al., 1977 [16] on his experimental work on the cat hind limb. However, Hoffer et al. 1990 [17] has suggested that the cuff length must be at least equal to the wavelength of the transmembrane action potential, which in turn depends on the conduction velocity. However, we believe that Hoffer’s proposition should relate more specifically to electrode separation rather to cuff length. In our simulations we have found an optimum end electrode separation of ~30mm for 99% of maximum amplitude for a 10μm fibre (55.8 m/s, [8]). The one-dimensional analysis will give a higher optimal length than the inhomogeneous model. The reason is that the signals at the ends of the cuff are assumed to be zero (boundary conditions) whereas in the inhomogeneous model these signals are small but not zero.

We have used equations (2.4), (2.5) and (2.6) to obtain the frequency response of each configuration. The monopolar and tripolar recordings are similar in their frequency response only when the tripolar end electrodes are at the ends of the cuff. The length and the electrode separation should be optimised so the maximum spatial frequency of the signal of interest (ENG) matches the spatial filter characteristic of the cuff electrodes. The reason for this is that the cuff electrode behaves as a spatial filter with different frequency responses for different fibre diameters. So given a specific fibre group in the nerve bundle, cuff parameters such as cuff length, electrode separation and electrode configuration should be optimised for maximal signal. In principal selective recording by fibre diameter populations is possible if high order band-pass spatial filters can be devised as in multi-cuff electrode techniques.

The monopolar results have been published elsewhere in [8], however the other results, to the best of our knowledge, have not been published. In our simulations, except for Fig. 2.10, we have used a numerical model to obtain the potentials recorded from a cuff electrode due to the activity at the Nodes of Ranvier. No assumptions were made regarding boundary conditions at the ends of the cuff as in the one-dimensional analysis. The results obtained from these simulations of the SFAP are in general applicable to ENG
signals where thousands of fibres are distributed randomly within the nerve bundle but not concentrated at the centre of the bundle. With natural excitation only a fraction of the fibre population is activated and we can safely assume that the ENG signal is the sum of the SFAPs. The reason for this is that the position of the fibre inside the nerve bundle is not very important in cases where circumferential electrodes are used, which is the case in our 2-D simulations (hence the symmetry).
2.6 APPENDIX 2.1: NERVE FIBRE MODEL

A myelinated nerve fibre can be approximated by the equivalent electrical network shown as described by McNeal’s model [11] below:

\[
\begin{align*}
V_{e,n-1} & \quad I_{n-1} \\
V_r & \quad G_m \\
V_{i,n} & \quad C_m \\
V_{e,n} & \quad I_n \\
V_{i,n+1} & \quad G_m \\
V_{e,n+1} & \quad I_{n+1}
\end{align*}
\]

Fig. A2.1 Electrical network representation of a myelinated nerve fibre using McNeal’s model [11].

- \( G_a \) – axial internodal conductance
- \( V_r \) – resting potential
- \( G_m \) – nodal membrane conductance
- \( V_{e,n} \) – external potential at node \( n \)
- \( V_{i,n} \) – internal potential at node \( n \)
- \( I_n \) – membrane current at node \( n \)

McNeal assumed the myelin to be a perfect insulator and the potential on the surface of each node to be equipotential by assuming the axon diameter to be small enough so as not to influence the electric fields generated by external stimulating electrodes. This therefore enables external voltages by stimulating electrodes, of any geometry, placed near the nerve axon to be incorporated into the model. The model incorporates the voltage sensitive ion channel kinetics.

The membrane capacitance, \( C_m \) is given by:
and the axial conductivity, \( G_a \), is given by:

\[
G_a = \frac{\pi d^2}{4\sigma_a L}
\]

Where the constants are given as:

- \( C_m \) membrane capacity
- \( \rho_a \) axial internodal resistivity
- \( l \) nodal gap length
- \( L \) internodal distance
- \( d \) \( \mu \text{m} \) diameter of axon

The parallel combination of \( C_m \) and \( G_m \) represents the nerve cell membrane impedance.

Referring to the network shown in figure A2.1, the ionic currents passing through the \( n \)th node is a function of the difference between the internal and external voltages.

Therefore summing the membrane ionic currents at node \( n \):

\[
C_m \frac{d}{dt} (V_{i,n} - V_{e,n}) + I_{i,n} + G_a (V_{i,n} - V_{i,n-1}) + G_a (V_{i,n} - V_{i,n+1}) = 0
\]

(A2.1)

Collecting terms and rearranging:

\[
C_m \frac{d}{dt} (V_{i,n} - V_{e,n}) + I_{i,n} = G_a (V_{i,n-1} - 2V_{i,n} + V_{i,n+1})
\]

(A2.2)

Now the potential at node \( n \) is given by:

\[
V_n = V_{i,n} - V_{e,n} + V_r
\]

(A2.3)

Substituting for \( V_n \) from (A2.3) in (A2.2) gives:

\[
C_m \frac{d}{dt} (V_n - V_r) + I_{i,n} = G_a \left( V_{n-1} + V_{e,n-1} + V_r - 2(V_n + V_{e,n} + V_r) \right) + V_{n+1} + V_{e,n+1} + V_r
\]

(A2.4)
this gives:

\[ C_m \frac{d}{dt} (V_n + V_r) + I_{i,n} = G_e \left( V_{n-1} + V_{e,n-1} - 2V_n + V_{n+1} - 2V_{e,n} + V_{e,n+1} \right) \]  

(A2.5)

where \( n = \ldots, -2, -1, 0, 1, 2, \ldots \)

The initial condition at time \( t=0 \) is given by \( V_n(0) = 0 \) for all \( n \).

Near threshold, the nerve cell membrane behaviour becomes non-linear. For the ionic currents at the excitation node, McNeal used the equations of Frankenhaeuser and Huxley, which were based on frog myelinated nerve fibres. However the work done by Chiu [18] suggests that there is no significant non-linear voltage dependant potassium channels at the nodes of Ranvier in myelinated rabbit nerve fibres. In these axons the repolarisation current has been demonstrated to be mainly due to leakage current which contains potassium and chloride ions. Consequently, the equations for the ionic currents are based on the results of Chiu et al [18] and adapted to a temperature of 37°C.

The equations for the ionic equations as described by Struijk [8] are as follows:

\[ I_{ion} = \pi d l (I_{Na} + I_L) \]  

(A2.6)

\[ I_{Na} = \bar{g}_{Na} h m^2 (E - E_{Na}) \]  

(A2.7)

\[ I_L = \bar{g}_L (E - E_L) \]  

(A2.8)

where

\[ E = V + V_r \]  

(A2.9)

\[ \frac{dm}{dt} = \alpha_m (1 - m) - \beta_m m \]  

(A2.10)

\[ \frac{dh}{dt} = \alpha_h (1 - h) - \beta_h h \]  

(A2.11)

and

\[ \alpha_m = \frac{(0.363 E + 126) / (1 + \exp(-49 - E) / 5.3)}{1} \]  

(A2.12)
\[ \beta_m = \frac{\alpha_m}{\exp\left(\frac{E + 56.2}{4.17}\right)} \]  \hspace{1cm} (A2.13) \\
\[ \alpha_h = \frac{\beta_h}{\exp\left(\frac{E + 74.5}{5}\right)} \]  \hspace{1cm} (A2.14) \\
\[ \beta_h = \frac{15.6}{\left[1 + \exp\left(\frac{-56 - E}{10}\right)\right]} \]  \hspace{1cm} (A2.15)

The parameters are:

- \( \varepsilon_{\text{Na}} \) maximum sodium conductivity \((15.45 \times 10^3 \ \text{l/(Qm)}^2)\)
- \( g_L \) leakage conductivity \((1.28 \times 10^3 \ \text{l/(Qm)}^2)\)
- \( E_{\text{Na}} \) sodium equilibrium potential \((35.64 \text{ mV})\)
- \( E_L \) leakage equilibrium potential \((-80.11 \text{ mV})\)
- \( V_r \) membrane resting potential \((-80.0 \text{ mV})\)
- \( c_m \) membrane capacity \(0.02 \text{F/m}^2\)
- \( \rho_a \) axial internodal resistivity \(0.7 \Omega\text{m}\)
- \( l \) nodal gap length \(1.5 \mu\text{m}\)
- \( L = 100D \) internodal distance
- \( d/D \) ratio of axon to fibre diameter
- \( D \) diameter of fibre \(\mu\text{m}\)
2.7 APPENDIX 2.2: VOLUME CONDUCTOR MODEL

Maxwell's equation states that the curl of the magnetic field strength is the sum of the conduction, source and displacement currents [19]. The equations as described in [19] are:

\[ \nabla \times H = \sigma E + J_s + \varepsilon \frac{\partial E}{\partial t} \]  \hspace{1cm} (A2.16)

where

- \( H \) is the magnetic field strength
- \( E \) is the electric field
- \( \sigma E \) is the conduction current
- \( \varepsilon \) is the conductivity tensor
- \( \varepsilon \frac{\partial E}{\partial t} \) is the displacement current
- \( \varepsilon \) is the electric permitivity

In a quasistatic conditions the last term is zero. In this application the conductivity of the medium is inhomogeneous and anisotropic [21].

Therefore equation (A2.16) can be written as:

\[ \nabla \times H = \sigma E + J_s \]  \hspace{1cm} (A2.17)

taking the divergence of A2.17 gives:

\[ \nabla.(\nabla \times H ) = \nabla.(\sigma E + J_s ) \]  \hspace{1cm} (A2.18)

the left hand side is zero, therefore:

\[ - \nabla.(\sigma E) = \nabla J_s \]  \hspace{1cm} (A2.19)

the electric field can be written as:

\[ E = -\nabla \phi \]  \hspace{1cm} (A2.20)
substituting for \( \bar{E} \) in A2.19 gives:

\[
\nabla \cdot (\sigma \nabla u) = \nabla \cdot \bar{J}, \quad \text{(A2.21)}
\]

Now taking the current source as a point source at \((x_0, y_0, z_0)\)

The right hand side of A2.21 can be written as:

\[
\nabla \cdot (\sigma \nabla u) = -I_o \delta \quad \text{(A2.22)}
\]

where \( \delta = \delta(x-x_0, y-y_0, z-z_0) \) is a delta function

Expanding equation A2.22 in the Cartesian co-ordinate system gives:

\[
\frac{\partial}{\partial x} \left( \sigma_x \frac{\partial u}{\partial x} \right) + \frac{\partial}{\partial y} \left( \sigma_y \frac{\partial u}{\partial y} \right) + \frac{\partial}{\partial z} \left( \sigma_z \frac{\partial u}{\partial z} \right) = -I_o \delta \quad \text{(A2.23)}
\]

which is Poisson’s equation.

However the cuff and the nerve tissue structure can be regarded as cylindrically symmetrical. Therefore, equation A2.23 can be transformed into cylindrical co-ordinates as shown below:

\[
\frac{1}{r} \frac{\partial}{\partial r} \left( r \sigma_r \frac{\partial u}{\partial r} \right) + \frac{1}{r} \frac{\partial}{\partial \theta} \left( \sigma_\theta \frac{\partial u}{\partial \theta} \right) + \frac{1}{r^2} \frac{\partial}{\partial \theta} \left( \sigma_\theta \frac{\partial u}{\partial \theta} \right) = -I_o \delta \quad \text{(A2.24)}
\]

Because of the cylindrical symmetry the term with \( \theta \) is zero, therefore, equation A2.24 can be written as:

\[
\frac{1}{r} \frac{\partial}{\partial r} \left( r \sigma_r \frac{\partial u}{\partial r} \right) = -I_o \delta \quad \text{(A2.25)}
\]

The right hand side resembles \( N \) infinitely thin rings with current \( I_i \) and radius \( R_i \). Therefore equation A2.25 can be written as described in [19]:

\[
\frac{1}{r} \frac{\partial}{\partial r} \left( r \sigma_r \frac{\partial u}{\partial r} \right) = -\sum_{i=1}^{N} \frac{I_i}{2\pi R_i} \delta(r - R_i, z - z_i) \quad \text{(A2.26)}
\]

The discretization of equation A2.25 was adopted from Struijk [8], which is slightly different from the one described by Rijkhoff, et al, 1994 [20].
The discretization of equation A2.26 as described by Struijk [8] is carried as follows:

Define:

\[
\tau_{ij}^r = \frac{h_{i-1} \sigma_{ij}^r + h_i \sigma_{ij}^r}{h_{i-1} + h_i} \quad (A2.27)
\]

\[
\tau_{ij}^z = \frac{k_{j-1} \sigma_{ij}^z + k_j \sigma_{ij}^z}{k_{j-1} + k_j} \quad (A2.28)
\]

where these conductivities are shown in figure A2.2.

\[
\begin{align*}
\tau_{ij}^r &= \frac{h_{i-1} \sigma_{ij}^r + h_i \sigma_{ij}^r}{h_{i-1} + h_i} \\
\tau_{ij}^z &= \frac{k_{j-1} \sigma_{ij}^z + k_j \sigma_{ij}^z}{k_{j-1} + k_j}
\end{align*}
\]

Fig. A2.2 Definition of grid and conductivities.

The derivatives of equation A2.26 can be approximated as:

\[
\left[ \frac{\partial}{\partial r} \left( \sigma_r \frac{\partial}{\partial r} \right) + \frac{1}{r} \sigma_r \frac{\partial}{\partial r} \right] u_{ij} = a_{ij} u_{ij-1} + b_{ij} u_{ij+1} - \left( a_{ij} + b_{ij} \right) u_{jj} \quad (A2.28)
\]

where

\[
a_{ij} = \frac{\tau_{ij}^r}{k_{j-1}} \left( \frac{2}{k_{j-1} + k_j} - \frac{1}{2r_j} \right) \quad (A2.29)
\]

and

\[
b_{ij} = \frac{\tau_{ij}^z}{k_j} \left( \frac{2}{k_{j-1} + k_j} + \frac{1}{2r_j} \right) \quad (A2.30)
\]
\[
\left[ \frac{\partial}{\partial z} \left( \sigma_z \frac{\partial}{\partial z} \right) \right]_{ij} = c_y u_{i-1,j} + d_y u_{i+1,j} - (c_y + d_y) u_{ij}
\] (A2.31)

\[
c_y = \frac{2\tau_{i-1j}^z}{h_{i-1}(h_{i-1} + h_i)}
\] (A2.32)

\[
d_y = \frac{2\tau_{ij}^z}{h_i(h_{i-1} + h_i)}
\] (A2.33)

\[
\left[ \frac{I_n(t)}{2\pi r_n} \delta(r - r_n, z - z_n) \right]_{ij} = e_y I_{ij}
\] (A2.34)

\[
e_y = \frac{2}{(h_{i-1} + h_i)(k_{j-1} + k_j)\sigma_j}
\] (A2.35)

Combining equations A2.27-A2.35, we obtain:

\[
u_y = \frac{a_y u_{y-1} + b_y u_{y+1} + c_y u_{i-1,j} + d_y u_{i+1,j} - e_y I_{ij}}{a_y + b_y + c_y + d_y}
\] (A2.36)
2.8 REFERENCES


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CHAPTER THREE

THE EFFECT OF NERVE CUFF GEOMETRY ON INTERFERENCE REDUCTION: A STUDY BY COMPUTER MODELING*

3.1 ABSTRACT

The effect of non-linearity in the extrafascicular field in tripolar electrode cuffs on interference pick-up was investigated. It was concluded that the interference is sensitive to electrode separation especially in short cuffs. This suggests that significant improvements can be obtained by placing the end electrodes a few mm from the cuff ends.

Index Terms- Electromyogram (EMG), electroneurogram (ENG), end effects, linearisation, nerve cuffs.

3.2 INTRODUCTION

INSULATING cylindrical nerve cuffs incorporating metal electrodes [1,2,3] have been used in various experiments to record the Electroneurogram (ENG) [4,5]. Recording of neural activity has many applications in rehabilitation [6]. Although there is only a weak correlation between the applied sensory excitation (e.g. force between foot and floor) and the recorded ENG signal [4], it nevertheless enables ENG information to be used in closed-loop functional electrical stimulation (FES) systems. The amplitude of ENG activity is the order of a few μV [4], [7]. However, in addition to the neural signal, the measuring electrodes are exposed to various externally generated sources of noise of which the Electromyogram (EMG) signal is the most important. Since the magnitude of the EMG potential is the order of a few millivolts (mV), i.e., three orders of magnitude larger than the ENG signal [7], EMG signal pickup is a major problem in the reliable recording of ENG signals.

The earliest multi-electrode technique proposed to reject the EMG signal was the *pseudo-tripole* arrangement [8]. In this scheme, three electrodes are mounted symmetrically on the inside of an insulating cuff of length L and diameter D. The outer electrodes were connected together by wire. It was argued by Stein et al. [8] that because there can be no voltage drop in the longitudinal direction due to the short circuit connection between the two end electrodes, the currents generated by external fields flow through the short circuit connection rather than through the cuff. However, because of the electrode-tissue interface impedance [9], the potentials within the outer electrodes are not, in fact, equal [10], and any external sources will force some ionic current to flow through the cuff (probably more than 50% of the total current, depending on the ratio of the access resistance to the longitudinal resistance) with a corresponding interference potential between the electrodes. However, in spite of this, use of the pseudotripole arrangement results in a significant reduction of the recorded EMG signal, suggesting the influence of an additional suppression mechanism.

Assuming that the fluid inside the cuff is a homogeneous conductor and hence, to a first order of approximation, behaves like an ideal one-dimensional distributed resistor, it follows that the potential varies approximately linearly with distance along the length of the cuff. The interfering voltages recorded from a symmetrical tripolar electrode structure placed in a linearised field of this type are equal and opposite and can be
Fig. 3.1 Electrode cuff structure. Three recording electrodes are symmetrically placed along the cuff. Also the ideal (linear) behaviour of the EMG field inside the cuff is shown. The linearisation of the field allows the use of symmetrical tripolar electrodes to reduce the interference. Note that ideally the interference signals at the outputs of the differential amplifiers are equal and opposite.

cancelled by connection to a suitably designed differential amplifier arrangement. This linearisation of the extrafascicular field appears to be the main mechanism causing the rejection of the EMG signal and other sources of interference in tripolar electrode structures [11]. In the case where the aspect ratio (L/D) is not so large that the cuff can be assumed to behave like an ideal distributed resistance, departures from linearity occur near the ends of the cuff. In this paper, the effects of cuff length and electrode separation on interference pick-up are investigated.

3.3 THE EXTRAFASCICULAR FIELD

If $V_e(z)$, the extrafascicular field inside the cuff as a function of distance along the cuff, was perfectly linear irrespective of the topology of the external field, $V_e(z)$ could be represented as follows:

$$V_e(z) = \gamma z + V_e(0)$$  \hspace{1cm} (3.1)

where the gradient $\gamma$ is defined by the potentials at the ends of the cuff and the cuff length:
\[ \gamma = \frac{V_e(L) - V_e(0)}{L} \]  

(3.2)

However, due to the presence of end effects, linearity is degraded near the ends of the cuff. This effect can be modelled by adding an additional, non-linear term \( C(z) \) to (3.1):

\[ V_e(z) = \gamma z + V_e(0) + C(z) \]  

(3.3)

There are two main reasons for the presence of end effects. Firstly, the finite length of the cuff distorts the isopotential lines generated by current sources in the muscle surrounding the cuff due to the requirement that the isopotential lines must be normal to the insulating cuff. Second, the nerve fascicle is not a perfect insulator and therefore current redistribution occurs between the extrafascicular region and the nerve [12]. Consider the interference voltage \( V_i \) measured with the true-tripole arrangement [11], which is shown in Fig. 3.1:

\[ V_i = V_{e1} + V_{e3} - 2V_{e2} \]  

(3.4)

Substituting for \( V_e \) from equation (3.3) we obtain:

\[ V_i = (z_1 + z_3 - 2z_2)\gamma + [C(z_1) + C(z_3) - 2C(z_2)] \]  

(3.5)

For a symmetrical tripolar arrangement, the first term in equation (3.5) is zero and the interference recorded is dependant only on the non-linear terms. This demonstrates that the non-linear term in equation (3.5) has a major influence on the residual interference recorded in a symmetrical tripolar configuration.

### 3.4 MATERIALS AND METHODS

In order to study the effect of the electrode cuff structure on the interference pick up, an inhomogeneous anisotropic, two-dimensional model similar to that described in [13] was used. The problem is three dimensional, but by assuming cylindrical symmetry, it can be solved in a 2-D grid. The potential field in this 2-D grid is solved by applying Poisson’s equation in cylindrical co-ordinates \((z; r)\). We have chosen the centre of the cuff as the centre of the model.

The model used is shown in Fig. 3.2. There are four compartments. Compartment 1 represents the nerve with a radius of 0.5 mm, while compartment 2 represents the perineurium with a thickness of 50 \( \mu m \). Compartment 3 represents the insulating cuff, which has a thickness of 1 mm and a radius of 1 mm in all cases. Compartment 4, surrounding cuff and nerve, represents the fluid. The model dimensions are 240x54
mm. The conductivity of each compartment is given in Table 3.1 [13]. A simple monopolar

![Isopotential lines generated by a monopolar source.](image)

The conductivity of each compartment is given in Table 3.1 [13]. A simple monopolar

source was used to simulate the interference from external sources. The source was placed in the same position for all cuff lengths and the amplitude of the current source was set to 1mA so the potential variation around the cuff is on the order of a few mV, which is unfavourable for ENG recording. The field we have used in the following sections is shown in Fig. 3.2.
Dirichlet boundary conditions were set on the top left and right boundaries. On the lower boundary a Neumann condition was applied to reflect the symmetry of the model. For more detail regarding boundary conditions see [14]. The field potentials in an inhomogeneous volume conductor model were calculated using a Red-Black Gauss-Seidel [15] finite difference method with an over-relaxation of 1.9. The number of points chosen is a compromise between the speed of convergence of the solution and the required resolution of the potential variation near the cuff [16]. The number of nodes used in the model was set to 340×169. The final mesh was graded to give higher density of cells near the cuff and the nerve for better resolution. The spacing of grid cells was set to 0.1×0.05 mm near the cuff, whereas near the upper left and right boundaries, which is outside the region of interest, the grid cell spacing was set to 2×1 mm. The number of iterations needed for adequate convergence was set by the condition that the relative change in the sum of the potentials from each iteration to the next, at the lower axis, was less than $10^{-6}$.

### Table 3.1 The Conductivity of each compartment [13].

<table>
<thead>
<tr>
<th>Compartment</th>
<th>$\sigma_1 (1/\Omega m)$</th>
<th>$\sigma_2 (1/\Omega m)$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluid</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Nerve Fascicle</td>
<td>0.083</td>
<td>0.6</td>
</tr>
<tr>
<td>Perineurium</td>
<td>0.0034</td>
<td>0.0034</td>
</tr>
<tr>
<td>Cuff</td>
<td>10E-6</td>
<td>10E-6</td>
</tr>
</tbody>
</table>

3.5 RESULTS

The extrafascicular field gradient depends on the difference between the potentials at the two ends of the cuff, which in turn depends on the external field generated outside the cuff. Fig. 3.3 shows the external field generated by the monopolar source outside the cuff and the extrafascicular field in the cuff. Although the external field is highly non-linear, the extra fascicular field approaches ideal (linear) behaviour. How, therefore, does the EMG interference depend on the positions of the end electrodes?
Potential (mV)

Fig. 3.3 The External (dotted) and the internal field (solid) for a cuff length of 20 mm as a function of distance along the cuff (z).

Fig. 3.4 shows the dependence of the interference on electrode separation for various cuff lengths. For short cuffs (about 5-10mm), the interference varies rapidly with end electrode separation (d) with maximum interference occurring when the end electrodes are near the ends of the cuff. Whereas for medium (10-20mm) and long cuffs (30-40 mm), the interference is less sensitive to electrode separation and the maximum interference is significantly less than the case for short cuffs. In all cases, the interference is more sensitive to end electrode separation when the end electrodes are near the ends of the cuff, suggesting that reductions in the interference pick up can be made by placing the end electrodes a few mm from the cuff ends. With the electrodes placed at the ends of the cuff, a 10mm cuff shows a 40% improvement in interference reduction from a 5mm cuff. For longer cuffs (30-40mm), the improvement reaches up to 90%.
3.6 DISCUSSION

The cuff/electrode geometry has a major influence on the reduction of EMG and other sources of interference such as electromagnetic fields and displacement currents induced into the body and the cuff from power lines. In this study the interfering source was modelled by a current source placed 1 mm from the cuff walls. For short cuffs, the linear region within the cuff is quite small and the interference level is very sensitive to electrode separation. For medium and long cuffs, the linear region occupies a larger portion of the total length of the cuff, and, therefore, the interference pick-up is less sensitive to electrode separation. This is illustrated schematically in Fig. 3.5. Bearing in mind that to maximise the ENG signal, the end electrode spacing must be at least equal to the wavelength of the transmembrane action potential [1]. This result shows that there is more freedom in setting the electrode spacing to maximise the ENG signal to noise ratio in long cuffs. For example, for a 10μm fibre in a nerve bundle the minimum cuff length was found to be 28mm with monopolar recording [13]. For tripolar recording, in paraffin oil, a 30mm constriction was found to be optimal for tripolar recording [8]. For all cuff
lengths, interference pick up is very sensitive to electrode separation in the case when the end electrodes are near the ends of the cuff. If the cuff is longer than the wavelength of the neural signal, the ENG signal saturates when the electrodes are near the ends of the cuff. As a result, placing the electrodes few mm away from the cuff ends reduces the EMG signal without altering the amplitude of the ENG signal and hence improves the signal to interference ratio.

![Diagram](image)

**Fig. 3.5** The effect of the extent ($l$) of the non-linear region on interference suppression in short ($L'$) and long cuffs ($L$).

There is a difference between short and long cuffs in terms of their ability to reject interference. Up to 81% interference reduction can be achieved when long cuffs (40mm) are employed compared with short cuffs (10mm). In this case, part of the reason for this is the high resistance to current flow provided by a long restriction, i.e., less current flows into a long cuff than into a short one. On one hand, the finite length errors would be more prominent in short cuffs than in long cuffs, because the distorted region occupies a relatively large fraction of the cuff length (see figure 3.5). On the other hand, for long cuffs, current redistribution between the extrafascicular and the intrafascicular regions is more prominent due to the long distance available for current flow between the extrafascicular and the intrafascicular regions. However, finite length effects produce larger distortions from linearity than current redistribution effects [12] due to the small currents involved in the latter, i.e., low extrafascicular resistance compared to the intrafascicular resistance. Therefore, in general, long cuffs are inherently more immune to interference than short cuffs and by moving the end electrodes inwards in short cuffs it is possible to achieve the same performance in terms of interference reduction as is the case.
In general, for a cuff constrained by surgical considerations, to be of a particular length, the position of the outer electrodes is a compromise between the signal amplitude [1], [13] and the EMG interference level.

3.7 REFERENCES


4.1 ABSTRACT

A theoretical investigation of different ENG recording techniques using electrode cuffs is presented. A new screened tripole arrangement is proposed with a higher inherent signal to interference ratio than the true tripole, which also allows the nulling of the residual EMG signal. The reduction in interference is small because the electrode impedance is large compared to the source resistance.

*Keywords*— Nerve cuff electrodes, ENG recording, Residual EMG, Tripolar electrodes, Screened tripole.

4.2 INTRODUCTION

Insulating Cuffs incorporating metal electrodes are established as a safe and reliable method of chronically recording the Electroneurogram (ENG) from peripheral nerves [1,2]. Such ENG can be used as feedback signals in functional electrical stimulation (FES) applications [3,4]. Within the insulating cuff are a number of circumferential electrodes, which enclose the nerve. Typically, the voltage between these electrodes, due to the natural electrical activity of the nerve, is only microvolts and, given the source resistance of the electrodes, the signal-to-noise ratio is low [5]. Furthermore, active muscles produce electromyographic (EMG) potentials of millivolts and these tend to interfere with the recorded ENG.

Differential amplifiers finds wide use in measuring biopotential signals due to their high common-mode rejection ratio (CMRR), which helps in rejecting unwanted interference from electric, magnetic and electromagnetic sources outside the body. Most biopotential signals are recorded using bipolar electrodes. Usually, the interfering signals at both electrodes are identical and therefore are rejected by the CMRR of the differential amplifier. Stein et al. [2] recorded ENG signals in the presence of EMG interference using monopolar, bipolar and tripolar electrode structures in the cuff. It was concluded that bipolar recording between two electrodes in the cuff did not improve the rejection of EMG interference compared to monopolar recording. The reason given for this was that the cuff is open at both ends and EMG currents flow through the cuff, and this current flow causes a potential drop between the two recording electrodes. As a result the EMG interference at the two electrodes are not identical and therefore cannot be rejected by CMRR of the differential amplifier.

The first tripolar technique used to reduce this interference, which was later termed the quasi-tripole (QT) by Riso et al. [6] was introduced by Stein et al. [7] and Hoffer [8] and is shown in Fig. 1. Three equally-spaced ring electrodes are enclosed in an insulating cuff with the two end electrodes shorted together. Recording is carried out between the central electrode and the shorted outer electrodes, as indicated. Significant reduction in the EMG signal is obtained, and it was originally suggested by Stein et al. that there could be no voltage drop in the tissue between the two end electrodes due to the short circuit between the electrodes. However this explanation is incomplete. The main reason for the success of the QT was postulated by Struijk et al. [9]. His explanation was that the cuff
(insulating tube) linearises the internal field generated by external sources (i.e., EMG), and because of the symmetrical placement of the electrodes, cancellation is achieved. Thus the tripolar cuff is more immune to EMG due to both screening and linearisation. For more details see [11].

![Fig. 4.1 The Quasi-tripole arrangement.](image)

Since the introduction of the QT, which is still widely used in research, other configurations have emerged with the promise of further reduction in interference. The best known is the true-tripole (TT) [6]. Most of these techniques have originated from surface spatial filters in the detection of the EMG [12,13]. In this chapter we investigate the advantages and the disadvantages of these two arrangements and introduce the Screened-tripole (ST). This new arrangement combines the advantages of both the QT and the TT.

### 4.3 THEORY

#### 4.3.1 QUASI-TRIPOLE (QT)

The QT [7,8] is shown in Fig. 4.1 with lumped impedances representing the impedance to ionic current in the volume conductor of the tissue and the non-ohmic electrode-tissue interface. $Z_{i1}$ and $Z_{i2}$ represent the tissue impedances inside the cuff, $Z_t = Z_{i1} + Z_{i2}$, $Z_0$ is the tissue impedance outside the cuff, and $Z_{e1}$, $Z_{e2}$ and $Z_{e3}$ are the electrode-tissue impedances. If the EMG field is linearised within the cuff (i.e., ignoring any end effects as shown in chapter 3, [11]) and assuming that $Z_{e1} = Z_{e3} = Z_a$ and $G = 1$, it is easy to show that the residual EMG voltage at the amplifier output is given by the following expression:
where $I_{EMG}$ is the interfering EMG current that flows in the cuff. $V_q$ is zero in this case if $Z_{41} = Z_{42}$. In general, however, due to manufacturing tolerances in the placement of the electrodes and tissue inhomogeneities within the cuff, perfect balance will not occur. Since there is no externally variable parameter in (4.1), which allows the effect of the asymmetry to be removed, complete elimination of the EMG signal is not achieved using the QT approach.
4.3.2 TRUE-TRIPOLE (TT)

An alternative structure, known as the true-tripole (TT) is shown in Fig. 4.2 [6]. In the TT, the electrodes are connected in pairs to two differential voltage amplifiers, gains $G_1$ and $G_2$. The outputs of these amplifiers are then summed by a third amplifier, which we will assume to have unity gain. For a linearised EMG field\footnote{The EMG current flowing in the cuff is the result of all the EMG potentials generated outside the cuff and because of the linearisation effect, the direction of the EMG field would only change the polarity of this current.}, the residual EMG voltage appearing at the output is given by (see figure 4.2A):

\[ V_{tt} = G_1 Z_e 1 V_{1} + G_2 Z_e 2 V_{2} + G_3 \]

Fig. 4.2 The True-tripole arrangement. A) Tissue and electrode impedances associated with the true-tripole arrangement, B) The rejection of EMG interference.
For comparison, from (4.1) and (4.2), assuming that \( G_1 = G_2 = 1 \) in the TT case, it is readily apparent that \( V_{qt} < V_{tt} \). However, the crucial difference between the QT and the TT is that in the case of the TT, the amplifier gains can be employed to remove the residual EMG voltage. Also, the magnitude of the ENG signal picked up using the TT is about twice that in the QT (see figure 4.2B) and the TT has a better signal to noise ratio [6]. The reason for this is that the signal output of the true-tripolar arrangement is double that of the quasi-tripole arrangement as stated before, while the noise added by the extra amplifier is only increased by the square root of 2.

### 4.3.3 SCREENED-TRIPOLE (ST)

In this new arrangement, two additional electrodes placed at the ends of the cuff are connected by a wire as shown in Fig. 4.3. This has the effect of reducing the amount of current flowing in the cuff. The interference resulting from this arrangement is given by:

\[
V_{st} = I_{\text{EMG}} \frac{Z_0}{Z_0 + Z_t} [G_1 Z_{1,t1} - G_2 Z_{1,t2}] \tag{4.3}
\]

where the impedance \( Z_{cp} \) is the parallel combination of the electrode-tissue impedance \( Z_c \) between the outer end electrodes and \( Z_0 \). \( Z_c = Z_{c1b} + Z_{c1a} + Z_{c2a} + Z_{c2b} \). The ENG pickup is the same as for the TT, i.e., about twice that for the QT.

The sensitivities of the three electrode cuff arrangements to interference depend on the impedance quotients in equations (4.1), (4.2) and (4.3) assuming that the imbalance is due to \( Z_{t1a} \) and \( Z_{t2a} \). In the case of the QT, the electrode impedances are also a factor (equation (1)) but to allow a comparison, these have been ignored. Assume also that \( G_1 = G_2 = 1 \).

Using typical values for the impedances\(^2\) and assuming that \( Z_{t1} = Z_{c1a} + Z_{c1b} \) and \( Z_{t2} = Z_{c2a} + Z_{c2b} \), then the voltage quotients are:

\[
|V_{qt}| = 5.7 \mu V \\
|V_{tt}| = 12.5 \mu V
\]

\(^2\) \( Z_c = 2 \text{K}\Omega, Z_0 = 2000 \text{\Omega}, Z_t = 1 \text{K}\Omega, I_{\text{EMG}} = 1 \mu A, Z_{c1a} = 1.1 \text{K}\Omega, Z_{c2a} = 1.3 \text{K}\Omega, Z_{c1b} = Z_{c2b} = 300 \text{\Omega}, \)
\[ |V_{st}| = 11.4 \mu V \]

The ST will always be better (smaller) than the TT because \( Z_{cp} < Z_c \). The QT will also be better than the TT but the relative advantage depends on \( Z_t, Z_0, \) and \( Z_a \). However, unlike the QT, the ST shares the advantage of the TT that the interference can be nulled by trimming the ratio of \( G_1 \) and \( G_2 \).

![Screened-tripole arrangement](image)

**Fig. 4.3** The Screened-tripole arrangement.

### 4.4 METHODS

In addition to the above calculations using a lumped impedance model, we have simulated the effect of connecting the end electrodes on the field inside the cuff due to external sources, i.e., EMG, using an inhomogeneous volume conductor model similar to that in [10,11]. Here, a wire in the cuff walls connects the end electrodes. The cuff radius was set to 1mm and the cuff thickness to 1mm. The cuff is wrapped around a nerve bundle with radius of 0.55mm. These values are representative of typical cuff dimensions used in the recording and simulation of the ENG from peripheral nerves [1,2,10]. The field was generated by a point source placed outside the cuff. For more details on methods see chapter 3.

### 4.5 SIMULATION RESULTS

The connection between the end electrodes affects the gradient of the field inside the cuff. Fig. 4.4 shows the gradient of the field inside the cuff between the connected end electrodes for various cuff lengths. The gradient when the end electrodes are connected is smaller than the gradient with no connection, but never by more than two-fold. Furthermore, the gradient when the end electrode are at the ends of the cuff is almost the same in both cases. This result shows that if the end electrodes are placed at the ends
of the cuff, the connection has little effect on the gradient. The reason for this is that while the impedance $Z_0$ is only a few hundred ohms, $Z_c$, the electrode-tissue impedance, is in general an order of magnitude larger. Since $Z_c$ connects the two end electrodes, when they are placed at the ends of the cuff, the impedance between the end electrodes is dominated by $Z_0$. However, when the end electrodes are moved towards the centre of the cuff, the impedance is dominated by $Z_c$. Placing the end electrodes further inside the cuff therefore reduces the local field gradient and therefore reduces interference pickup. In addition, moving the end electrodes away from the ends of the cuff improves linearity by reducing non-linear end-effects, further improving interference suppression [11].
Fig. 4.4 The effect of the wire between the end electrodes on the field in the cuff due to interference sources outside the cuff for various cuff lengths. (+) Gradient between the connected end electrodes. (o) Gradient between the electrodes without the wire connection.
4.6 DISCUSSION

A primary requirement of an ENG recording system is to reduce the residual EMG, removing it completely, if possible. The TT offers this possibility by adjusting the gains of the first stage amplifiers, possibly using an automatic feedback control system. This approach has the potential to eliminate the high-order filters conventionally used to reduce interference such as EMG and improve the signal to noise ratio [4]. The new arrangement (the screened tripole), while still allowing adjustment, as in the TT, also features a higher inherent signal-to-interference ratio. The ST arrangement therefore allows a feedback control system that rejects EMG artefacts to converge more rapidly than if employed with a TT. This is convenient since the rejection of the EMG must occur within the time window of adjacent stimulation pulses, typically 50ms [1] in FES applications.

The amplitude of the ENG signal recorded from a ST will be less if the two recording (active) end electrodes are positioned away from the ends of the cuff. However, this is only critical when the cuff length is less than the wavelength of the action potentials determined by the largest fibres within the nerve bundle. Simulation results show that for a cuff length equal to the wavelength of the action potential, the single fibre action potential amplitude maximises when the outer electrodes in a tripolar configuration are near the ends of the cuff [10].

Connecting the end electrodes by a wire is useful even if the end electrodes are placed at the ends of the cuff. Although currently this connection has been implemented outside the cuff in the QT, future cuff developments will allow the wire connection to be included in the cuff walls so full advantage can be taken from the reduction in the field gradient. Also multiple electrodes, i.e., any tripolar electrode configuration can be positioned inside the active region, which can be defined as the region between the connected end electrodes.

It has been demonstrated that an increase in cuff length effectively decreases the gradient of the interfering field within the cuff, increasing the S/I ratio [11]. The use of a screen, as demonstrated in the ST, has the same effect as increasing the overall cuff length as shown in Fig. 4.4. The main reason for the significant improvements between short and long cuffs is that there is high resistance to current flow in long cuffs.
compared to short cuffs. As a result a larger fraction of the interfering current flows outside the cuff in long cuffs compared to short cuffs. Also the ends of the cuff are further away for the interfering source in long cuffs resulting in smaller potential differences at the two ends.

In this paper a simple one-dimensional lumped impedance model was used as in [5]. However because of end effects and non-linearity in the field [11], in particular for small cuffs, this is only an approximation of the field inside the cuff. However the analysis and general conclusions are still valid as demonstrated by the inhomogeneous model.

4.7 REFERENCES


CHAPTER FIVE

AN ADAPTIVE METHOD FOR EMG ARTEFACT REDUCTION IN NERVE CUFF ELECTRODE RECORDINGS

5.1 ABSTRACT

A method is presented for the reduction of EMG breakthrough in ENG recording systems. The method is based on the automatic equalisation of the interference in the two channels of a true-tripole recording arrangement by the implementation of a closed-loop feedback system. Experimental results show that the control system gives on average a 19.3dB improvement in SIR compared to a traditional open-loop true-tripole. The level of interference after adaptation is –50dB compared to –31dB before adaptation. This method has the potential to enable the development of a fully implantable recording technique without the need for high-order filters, which currently present a major problem in the development of a low-power implantable solution.
5.2 INTRODUCTION

ENG signals recorded from nerve cuff electrodes have the potential to replace artificial sensors as feedback signals in functional electrical stimulation (FES) applications. Typical applications include correction of foot-drop [1,2], hand grasp in tetraplegic patients [3], and bladder voiding [4]. Unfortunately, the neural signal recorded using this method is of the order of a few μV [5] and exhibits a low signal-to-interference ratio (SIR). The main reason for this is pick-up of large (mV range) electromyographic (EMG) potentials generated by excited muscles near the cuff. Also, the FES stimulation pulses produce artefacts that usually swamp the ENG signal to the preamplifier. Therefore, in order to improve recorded ENG signals, several methods have been suggested.

The earliest multi-electrode technique proposed to reject the EMG signal and other sources of interference was the quasi-tripole arrangement [6]. Other structures, including the true-tripole [7], and more recently the mobipolar arrangement [8] have been proposed. The main idea behind each of these methods is essentially the same i.e., to utilise the linearisation effect by the nerve cuff on the internal field [9,10]. Ideally in each configuration the electrodes are arranged in such a way that the EMG is cancelled, so that only the ENG signal is recorded.

However, despite the use of these methods, significant artefacts are still present in the recorded signal for three main reasons:

1) As shown by experiment [8], there is a significant correlation between changes in the amplitude of the ENG signal and changes in the nerve cuff impedances. This was attributed to tissue growth inside the cuff, which occurs after a period of implantation. It was concluded that the initial decrease in ENG amplitude was due to the decrease in the tissue impedance inside the cuff.

2) Tripolar electrode structures (see figure 5.1) require a high degree of symmetry. Manufacturing tolerances of perhaps ±0.5mm in the electrode positions will destroy the symmetry required, and result in large artefacts.
Fig. 5.1 The True-tripole arrangement.

Fig. 5.2 The power spectral densities of the raw ENG+noise, voluntary EMG+noise and the background noise. The EMG and the ENG spectrums overlap at 880Hz. Data obtained from a cuff implanted around the digital nerve in the hand.

3) The linearisation of the EMG field inside the cuff is not ideal due to the finite dimensions of the cuff (see chapters 3 & 4).

Examination of the power spectral density (PSD), shown in Fig. 5.2, of nerve cuff-recorded signals shows that the ENG signal spectrum peaks between 1 and 2 kHz, while the EMG peaks in the range between 100 and 200 Hz, with some energy still present up

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1 Provided by Dr Morten Haugland, SMI Denmark
to 2 kHz [11,2]. High-pass filtering the recorded ENG signal therefore attenuates the residual EMG artefacts since the frequency distributions of the ENG and the EMG are largely (but not completely) non-overlapping [2]. The order of filtering required is dependent on the FES application, and the anatomical position of the nerve cuff, with typical filters ranging from fourth-order for hand grasp [3], up to very high order (>90) digital filters for foot-drop correction [2].

Removing the stimulation artefacts is readily achievable by blanking the recording amplifiers during stimulation periods. The \textit{rectified-bin-integration} (RBI) algorithm [2,3] employs this method but its success has been limited due to the low \textit{signal to noise ratio} (SNR). As a result, second and third order algorithms have recently been demonstrated as methods to improve the results obtained by the RBI method, using \textit{digital signal processing} (DSP) techniques [2].

Unfortunately very high order filtering and high order algorithms require significant processing power and floating point computational accuracy, which is a major problem when low power implantable solutions are to be considered. Therefore in this chapter we introduce a method that significantly reduce EMG artefacts due to tissue inhomogeneities, and manufacturing tolerances. The method [12,13] is based on the true-tripole arrangement. The method takes advantage of the fact that the EMG activities from the two differential amplifiers are ideally equal and opposite. The feedback loop allows the automatic adjustment of the gains in opposite directions in practical situations so the residual EMG is removed. This method can be implemented using low power analogue techniques without the need for extensive high-order digital filtering. After introducing the fundamental theory in Section 5.3, methods are presented in section 5.4. In Section 5.5 simulations and experimental results are illustrated. Discussions are presented in section 5.6.

5.3 THEORY

Fig. 5.3 shows, in very schematic form typical variations of the EMG and ENG along the length of the cuff. However, manufacturing tolerances, tissue inhomogeneity and non-linearity in the field because of the finite dimension of the cuff, causes EMG breakthrough in ENG recordings. The breakthrough is caused by three types of errors:
Fig. 5.3 The true-tripole arrangement. Also the ENG and the EMG fields are ideally shown.

1) Static errors, which are generated by manufacturing tolerances in the placement of the electrodes in the cuff.

2) Slow changing errors, which are generated by the changes in impedances that occur after the implantation of the cuff due to tissue growth in the cuff.

3) Fast changing errors, which are generated by the changes in magnitude and orientation of the EMG field generated by excited muscles near the cuff.

If there are no mismatches in the cuff due to manufacturing tolerances or tissue inhomogeneities, the outputs from $G_1$ and $G_2$ in a true-tripole will be equal and opposite as far as the EMG signal is concerned. However any mismatches will produce large contamination due to the relative amplitude difference between the EMG and the ENG signals.

A block diagram of the control system is shown in Fig. 5.4 with hypothetical signals. It consists of a true-tripole recording structure in which the gains of the input differential amplifiers $G_1$ and $G_2$ have been made variable. The system operates by obtaining first the moduli of the outputs of the differential amplifiers $G_1$ and $G_2$ and comparing them to determine which is the largest. So for example as illustrated in Fig. 5.4 if the output $y_1(t)$ is larger than $y_2(t)$ (time $t_1$), the output of the comparator is high. This is integrated by the differential output integrator block and the gains $G_1$ and $G_2$ are changed by equal and opposite amounts to compensate for the error. As a result at time $t_2$, the outputs $y_1(t)$ and $y_2(t)$ are equal and opposite and the output from the comparator changes between the positive and the negative levels in such a way that the overall average change in $G_1$ and
\( G_2 \) is zero.

The outputs \( y_1(t) \) and \( y_2(t) \) from the differential blocks as shown in Fig. 5.4 can be expressed analytically as:

\[
y_1(t) = G_1(t) \times [x_{11}(t) + x_{21}(t)] \\
y_2(t) = G_2(t) \times [x_{12}(t) + x_{22}(t)]
\]

(5.1)

Where \( x_{11} \) is the ENG signal recorded by amplifier 1 and \( x_{12} \) is the ENG signal recorded by amplifier 2. \( x_{21} \) is the EMG signal from amplifier 1 and \( x_{22} \) is EMG signal from amplifier 2. The normalised adaptive gain blocks can be expressed as:

\[
G_1(t) = I \pm \Delta G \\
G_2(t) = I \mp \Delta G
\]

(5.2)

Where \( \Delta G \) is the feedback gain coefficient. For an ideal integrator, we obtain the following expression:

\[
\Delta G = \mu \varphi(t)
\]

(5.3)

where \( 1/\mu \) is the time constant of the integrator and \( \varphi(t) = \{+1, -1\} \) is the output of the comparator.

The two outputs are then summed to obtain the output signal \( s(t) \):
Fig. 5.4 Block diagram of the control system used for the removal of the EMG signal. The function of the control system is illustrated with hypothetical signals. For more details see text.

\[ s(t) = y_1(t) + y_2(t) \]  \hspace{1cm} (5.4)

However, most of the ENG activity is picked up by middle electrodes\(^2\) [8,14] and because of the linearistion effect on the EMG field:

\[ x_{ii} = x_{i2} = x_i \]  \hspace{1cm} (5.5)

and ideally:

\[ x_{ii} = -x_{i2} \]  \hspace{1cm} (5.6)

However, in practice symmetry will not occur. Assuming:
\[ x_{21} = E_1 \sin \omega t \quad \text{(5.7)} \]

and

\[ x_{22} = -E_2 \sin \omega t \quad \text{(5.8)} \]

If \( E_1 > E_2 \) then:

\[ G_1(t) = 1 - \Delta G \]
\[ G_2(t) = 1 + \Delta G \quad \text{(5.9)} \]

Combining equations 5.4-5.9 we obtain:

\[ s(t) = 2x + [(1 - \mu t)E_1 - (1 + \mu t)E_2] \sin \omega t \quad \text{(5.10)} \]

The second term in equation 5.10 is zero when:

\[ t = \frac{E_1 - E_2}{\mu(E_1 + E_2)} \quad \text{(5.11)} \]

Equation 5.11 shows that the control system is stable. However, the value of the time constant affects the speed of the system. The time constant can not be very long, because every time a muscle is stimulated, the system must be able to adjust \( G_1 \) and \( G_2 \) in a short time i.e., within the inter-stimulation pulse interval, which is typically 50ms [3]. Also the time constant cannot be very short because the comparator’s decision is affected by the ENG signal. By setting the time constant of the integrator longer than the time constant of the ENG signal, the control system has no effect on the ENG signal.

5.4 METHODS

5.4.1 SIMULATION METHODS

The behaviour of the methods using test signals representing the EMG and ENG signals was simulated. The asymmetry was simulated by making the EMG signal component of \( y_1(t) \) different than the EMG signal component of \( y_2(t) \).

5.4.2 EXPERIMENTAL METHODS

To test the two methods, ENG data\(^\text{3}\) was recorded from a 20mm cuff with 2.6mm inner diameter implanted in the hand of a tetraplegic subject, whilst the experimenter stroked the radial side of the index finger. At the same time reflex EMG was elicited from

\(^2\) The axial position of the electrode in the cuff is very important as shown in chapter 2. Near the ends of the cuff the electrode is exposed to the low resistive region outside the cuff.

\(^3\) Data obtained from Dr Morten Haugland, SMI, Denmark
surrounding muscles. The recording was done using two amplifiers (see Fig. 5.4), i.e., recording from the three electrodes in the cuff pair-wise, centre versus distal in channel 1 and proximal versus centre in channel 2. The ENG was used to regulate the stimulation of the paralysed muscles in the subject’s hand. For more detail see [3]. Signals from the two channels were amplified (x1000) sampled (12-bit) and stored. The control system was implemented off-line in MATLAB/SIMULINK. The recordings were low-pass filtered at 5000Hz off line to remove high frequency noise. To get a SIR measure from the ENG recordings, the power spectrum magnitude at 1500Hz representing the peak of the ENG activity was subtracted from the EMG peak, which is about 150Hz.
5.5 RESULTS

5.5.1 SIMULATION RESULTS

Fig. 5.5 A) The reduction of interference using control system when the asymmetry was 10%. $x_1(t)$ is a sine wave with amplitude of 10μV and frequency of 1200Hz and $x_2(t)$ is a square wave with amplitude of 1mV and frequency of 100Hz. B) The gain coefficients are $G_1$ and $G_2$.

Fig. 5.5A shows the reduction in interference using the control system. The asymmetry was 10% and the time constant was set arbitrarily to 0.2s. The variations of $G_1$ and $G_2$ are shown in Fig. 5.5B. $G_1$ increased linearly in the convergence period from 1 to 1.05, whereas $G_2$ decreased from 1 to 0.95. The overall gain change was 0.1, which is the value needed to remove the 10% asymmetry. The method converged to a steady state value within 10ms. The recovery time of the control system when interference stops is determined by the time constant of the control system and the difference between the previous and the new interference level.

Fig. 5.6A shows the successful reduction of interference using the control system in the case where the signals were separated by 200Hz. However in this case the time
constant was increased to 0.5s. The convergence time is about 25ms as shown in Fig. 5.6B.

Fig. 5.6 A) The reduction of interference in the case where the two signals are very close in the frequency domain. \( x_1(t) \) is a sine wave with amplitude of 10\( \mu \)V and frequency of 1200Hz. The interfering signal \( x_2(t) \) has an amplitude of 1mV and a frequency of 1000Hz. The reduction is achieved in about 25ms. B) The coefficients \( G_1 \) and \( G_2 \) during the learning process.
5.5.2 EXPERIMENTAL RESULTS

Fig. 5.7 Ten recordings in a true-tripole mode show the EMG break-through. No ENG activity was generated. The peak of the EMG activity is between 100-150Hz. Refer back to figure 5.1 for noise only data.

Reflex EMG signals were recorded in the absence of ENG activity. Ten recordings are shown in Fig. 5.7. The peak of the EMG, recorded in true-tripole mode, was around 150Hz, whereas the peak of the ENG activity, which is shown in Fig. 5.8, was around 1500Hz. The ENG spectrum is wider than the EMG spectrum; the reason is that the ENG spectrum is the weighted average of different single action potential spectra [15].
Fig. 5.8 Ten Recordings from the cuff electrode when the experimenter was stroking the index finger. The peak of the ENG activity was around 1500Hz.
Fig. 5.9 Recording in true-tripole mode during EMG reflex contractions. No ENG activity was generated.

Fig. 5.9 shows the time domain variation of EMG reflex contractions recorded in true-tripole mode. The average peak-to-peak variation of the EMG contractions of ten recordings was 0.0998 V.

ENG activity is shown in Fig. 5.10 when the experimenter was stroking the radial side of the index finger. The standard deviation (SD) of ten recordings of ENG activity was 0.0027 V whereas the SD of noise-only recordings was 0.0011 V giving a SNR of about 7dB.
Fig. 5.10 True-tripole recording. ENG activity only when the experimenter was stroking the index finger.
We have investigated the behaviour of the SIR as a function of the time constant (see 5.4.2). The result is shown in Fig. 5.11. For a small value of the time constant the SIR is very sensitive to variation in the time constant and increases rapidly towards an optimum value, which is between 1.5 and 2ms. The average SIR obtained using the true-tripole configuration was -16.65dB, whereas the average SIR at the optimal time constant was 2.74dB giving an average improvement of 19.3dB. Table 5.1 shows the SIR of the true-tripole and of the control system at the optimal time constant. In table 5.2 the comparison between the filtered output of the control system using a second-order filter, with the filtered open-loop true-tripole using a 4\textsuperscript{th} order band-pass filter (800-5000Hz) is made. This result shows that the order of the filter can be reduced if implemented with the control system.

**Fig. 5.11** The variation of the SIR as a function of the time constant. Ten recordings are shown when the experimenter was stroking the index finger in the presence of EMG contractions. The solid line represents the average value (mean ± SD) obtained from the control system. The dotted line represents the average from the open-loop true-tripole.
Table 5.1 Performance of the true-tripole arrangement and the control system at the optimal value of the time constant of 1.5ms.

<table>
<thead>
<tr>
<th>Recording</th>
<th>10*log10(SIR) [dB] true-tripole</th>
<th>10*log10(SIR) [dB] control system</th>
<th>Improvement SIR Ratio [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>-18.12</td>
<td>0.49</td>
<td>7159</td>
</tr>
<tr>
<td>2</td>
<td>-17.00</td>
<td>1.49</td>
<td>6966</td>
</tr>
<tr>
<td>3</td>
<td>-18.13</td>
<td>1.77</td>
<td>9686</td>
</tr>
<tr>
<td>4</td>
<td>-18.34</td>
<td>3.82</td>
<td>16326</td>
</tr>
<tr>
<td>5</td>
<td>-16.31</td>
<td>4.60</td>
<td>12243</td>
</tr>
<tr>
<td>6</td>
<td>-16.29</td>
<td>3.14</td>
<td>8672</td>
</tr>
<tr>
<td>7</td>
<td>-15.11</td>
<td>4.14</td>
<td>8314</td>
</tr>
<tr>
<td>8</td>
<td>-13.48</td>
<td>4.66</td>
<td>6412</td>
</tr>
<tr>
<td>9</td>
<td>-17.23</td>
<td>1.07</td>
<td>5668</td>
</tr>
<tr>
<td>10</td>
<td>-16.52</td>
<td>1.75</td>
<td>6617</td>
</tr>
</tbody>
</table>

Table 5.2 Comparison of the control system (filtered using a 2nd order band-pass filter between 800-5000Hz) with the open-loop true-tripole (filtered using 4th order filter with the same bandwidth) at the optimal value of the time constant of 1.5ms.

<table>
<thead>
<tr>
<th>Recording</th>
<th>10*log10(SIR) [dB] true-tripole filtered 4th order 800-5000Hz</th>
<th>10*log10(SIR) [dB] control system filtered 2nd order 800-5000Hz</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>43.71</td>
<td>60.51</td>
</tr>
<tr>
<td>2</td>
<td>45.16</td>
<td>62.77</td>
</tr>
<tr>
<td>3</td>
<td>44.24</td>
<td>63.95</td>
</tr>
<tr>
<td>4</td>
<td>43.98</td>
<td>65.21</td>
</tr>
<tr>
<td>5</td>
<td>45.83</td>
<td>66.52</td>
</tr>
<tr>
<td>6</td>
<td>46.08</td>
<td>65.07</td>
</tr>
<tr>
<td>7</td>
<td>46.83</td>
<td>65.46</td>
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<tr>
<td>8</td>
<td>47.74</td>
<td>65.97</td>
</tr>
<tr>
<td>9</td>
<td>43.74</td>
<td>62.09</td>
</tr>
<tr>
<td>10</td>
<td>44.35</td>
<td>62.61</td>
</tr>
</tbody>
</table>
In Fig. 5.12 recording from the true-tripole and the control system are shown. The time constant was set to the optimal value of 1.5ms. The EMG artefacts have been suppressed by the control system. The feedback coefficients $G_1$ and $G_2$ are shown in Fig. 5.13. They change in opposite directions to nullify the residual EMG artefacts. The amount of reduction achieved using the control system compared to the true-tripole configuration is illustrated in more detail in Fig. 5.14.
Fig. 5.13 The smoothed feedback coefficients for the recording shown in Fig. 5.12.
Fig. 5.14 Top: Comparison between the true-tripole and the control system. Bottom: the feedback coefficients.
5.6 DISCUSSION

In this chapter an adaptive method that significantly reduces residual EMG pickup is introduced. The method is based on the adaptive equalisation of EMG signals from the two channels of a true-tripole system. In the control system, we have taken advantage of the fact that the signal recorded from each pair in a true-tripole system are ideally equal and opposite. Similar techniques are employed in active noise control applications. Such applications include cancellation of noise in MR imaging [16]. The cancellation in that case is achieved by generating an internal inverted secondary interference source and then adding it to the main interference source to cancel it.

The true-tripole has been chosen as the input arrangement of the control system because it provides two channels, which are then used for EMG reduction. The quasi-tripole [6] and the mobipolar [8] were not considered suitable because they only offer one channel for signal processing. Although electrode impedance balancing has been suggested as a method of reducing artefacts [10] using a potentiometer in the quasi-tripole, it is less attractive compared to the true-tripole when combined with a closed-loop control system. In addition, the true-tripole gives improvements in the SNR compared to the quasi-tripole recording method [10]. Also it was shown in [8] that the open-loop tripolar electrode structure gives 1% higher compound action potential (CAP) to muscle artefact than mobipolar recording. In this chapter in a hand grasp application, it was shown using ENG signals contaminated with reflex EMG that the true-tripole employing a closed-loop feedback method gives on average a 19.3dB improvement in the SIR compared with the open-loop approach for an arbitrary level of asymmetry. An open-loop approach using an instrumentation amplifier with a high CMRR at the front end will not reject the EMG interference. The reason for this is that the rejection in this case relies on the matching of electrodes and tissue impedances in the cuff and because good matching cannot be obtained in real cuffs, only a closed loop solution is capable of suppressing the EMG interference.

1.5ms was the optimum setting for the time constant in the control system for ENG recordings during activation of voluntary EMG. However this might be different when ENG signals are contaminated with stimulation artefacts. One major difference, between the simulation and experimental results, is that in the simulations the interfering
signal was a continuous test signal whereas in the experimental results the EMG reflex activity only lasted for 20-30ms.

The sensitivity of the control system to EMG interference is determined by the comparator's ability to discriminate between the EMG signal outputs of $G_1$ and $G_2$ (see Fig. 5.4). In this study the control system was simulated using a computer model implemented in Matlab/Simulink. The sensitivity of the control system improved the SIR by 20dB. In a hardware realisation of the control system, careful attention should be given to the comparator's sensitivity, however voltage or current comparators with high sensitivity are available on the market today. Furthermore, an integrated silicon solution of the control system would allow even better resolving power compared to a discrete solution.

A major benefit of the control system is that it can separate signals very closely spaced in the frequency domain as shown by the test simulations. The overlap in the spectra of the ENG and the EMG signals is shown in Fig. 5.2. Also this problem has been encountered in cuff recordings for drop-foot correction [2], where a 91-pole band-pass filter with cut-off frequencies of 1.6-1.9kHz has been employed. The main reason suggested is that the EMG signal has energy content as high as 1kHz and the need to improve the SNR by rejecting out-of-band noise from the recording amplifier and the cuff.

The control system can be implemented using analogue integrated circuit technology. The analogue implementation can offer considerable advantage in the efforts of building fully implantable recording channels for FES applications. This suggests that the use of high-order filters (probably FIR filters) can be eliminated, and opens the way for analogue implementations using the control system and minimal filtering, which is more suitable for real implanted devices.
5.7 REFERENCES


CHAPTER SIX

CONCLUSIONS AND FUTURE DIRECTIONS
6.1 CONCLUSIONS

The main purpose of this project was to determine an optimum system for ENG recording using nerve cuff electrodes. Three main questions were addressed in this thesis:

a) Does the cuff linearise the internal field and to what extent does this help in rejecting interference from external sources?

b) Which cuff/electrode recording arrangement is the best?

c) How can the effects of manufacturing tolerances and tissue inhomogeneity be reduced?

6.1.1 LINEARISATION OF THE INTERNAL FIELD IN THE CUFF

Chapter 3 shows the linearisation of the internal field to be an important factor in the rejection of interference from external sources. The extent of the linearisation depends on the length of the cuff. In short cuffs, the linear region of the field is smaller than that for long cuffs. It was also shown that long cuffs (40mm) could achieve up to about 80% reduction in interference compared with short cuffs (10mm). In addition to cuff length, the interference was also found to be sensitive to end electrode separation. Short cuffs are extremely sensitive to end electrode separation, whereas, less sensitivity was observed in long cuffs. However, for all cuff lengths the highest sensitivity was obtained when the end electrodes are near the ends of the cuff. Furthermore, it was also shown in chapter 2 that the ENG signal peaked when the end electrodes were placed at the ends of the cuff and it was almost constant in this region. As a result, significant improvements can be achieved by increasing the cuff length beyond the end electrodes optimally spaced for ENG recording.

6.1.2 THE CHOICE OF THE CUFF/ELECTRODE CONFIGURATION

Several recording configurations have been considered to form the basic input unit of the recording system. These configurations include:


b) The true-tripole arrangement developed by Riso et al. 1995.
c) The recently devised mobipolar arrangement by Thomsen et al. 1998.

Most of these electrode arrangements can be regarded as open-loop recording channels with no facility to remove the residual EMG interference. Ideally, the suppression of EMG interference in the quasi-tripole arrangement relies on high CMRR at the input of the differential amplifier, but because of the mismatches in the electrode and tissue impedances the EMG signals at the inputs of the differential amplifier are not identical and therefore cannot be rejected by the high CMRR. The true-tripole arrangement offers advantages compared to the quasi-tripole and the mobipolar arrangement. The true-tripole arrangement offers two outputs from the differential amplifier stages. Information provided by these outputs can be used to adjust the gain of both amplifiers to reduce EMG contamination. In addition, the true tripole has a higher SNR compared to the quasi-tripole. However, the quasi-tripole has a lower EMG gradient along the cuff compared to the true-tripole. Therefore in chapter 4 a new arrangement termed the screened-tripole that combines the advantages of both was introduced. It was shown that by placing two additional shorted end electrodes in a true-tripole configuration, the gradient between these two electrodes and the interference are reduced. This screening effect can be used in any tripolar or multi-polar electrode structure by placing the remaining electrodes between the connected end electrodes. In addition, this screening effect becomes more significant when the connected end electrodes are not placed exactly at the ends of the cuff. The screened tripole approach has also been suggested by Andreasen et al. 1999. However in this case it was used with a quasi-tripole between the two shorted end electrodes. We believe that the screened-tripole should be used, as part of a true-tripole so the nulling of residual EMG would be possible.

6.1.3 REMOVAL OF RESIDUAL EMG DUE TO MANUFACTURING TOLERANCES AND TISSUE INHOMOGENEITY

In chapter 5 a method to reduce the residual EMG recorded in open-loop tripole electrode structures, based on the true-tripole was introduced. The method uses a closed-loop feedback system to change automatically the gains of the differential amplifier blocks to compensate for the interference mismatch. Experimental results were recorded from a cuff implanted around the digital nerve of a tetraplegic patient during activation of surrounding muscles.
It was possible to show that the control system gave on average, (over ten trials), a 19.3dB improvement in the SIR compared to the open-loop tripole. The level of interference after adaptation was −50dB compared to −31dB before adaptation. The optimum time constant was found to be about 1.5ms, which might be different for different cuff lengths. The reason for this is that the peaks of the ENG and the EMG spectra tend to change with cuff length. As a result, more detailed experimental testing is required with different cuff geometries. Possible applications of the control system range from the removal of EMG artefacts in foot-drop applications where voluntary EMG artefacts are large, to the reduction of voluntary EMG generated in standing up applications in paraplegia.

6.2 FUTURE DIRECTIONS

Our attention in this thesis has been focused on the reduction of the interference mainly EMG in ENG recording systems. Using the control system, the immunity from interference compared to current open-loop recording techniques, such as the quasi-tripole, the mobipolar and the true-tripole was improved. As a result the need for high-order filtering in many FES applications can be eliminated, thus enabling the development of fully analogue systems for implantable devices. One immediate step would be to build the control system as a discrete version so it can be implanted and tested in real time applications. Subsequently, an integrated solution can be realised for implantable purposes.

To optimise the usefulness of the ENG as a feedback signal capable of replacing external sensors, the signal to noise ratio needs to be increased. One way to achieve this is to use multiple tripoles in the cuff. It was shown in chapter 2 that the signal recorded from a tripolar electrode structure depends only on electrode separation, not on cuff length or tripole position within the cuff. The signals from these tripoles are delayed versions of each other. This delay can be eliminated by the use of correlation between the various channels. The signals from all the tripoles can be summed to improve the signal to noise ratio, because the noise sources from the tripoles are not correlated. The improvement is limited by the number of electrodes and the length of the cuff. Preliminary results with acute animal experiments indicate the validity of such a technique. It can be applied in most FES applications where
the S/N ratio is small. Also given that each channel in this multielectrode cuff is recorded in a true tripole mode, EMG reduction using the control system can still be employed.

A possible method for the removal of stimulation artefacts and provoked EMG responses is to use a mobipolar arrangement. In this arrangement an electrode is placed at the inner wall in the centre of the cuff. Directly at the outside of the cuff another electrode is placed. A second cuff is placed around the first cuff. Recording is made between the inner electrode and the outer electrode (see Fig. 2.1 in chapter 2). The idea behind this arrangement is that the ENG activity is recorded monopolarly by the inner electrode whereas the EMG artefacts are recorded bipolarly by the two electrodes. By using a differential recording, and because theoretically the EMG artefacts are the same at both electrodes, the EMG artefacts will be cancelled. This arrangement has not seen extensive use, but it has the potential to be used as an input to an adaptive filter utilising the least mean square (LMS) algorithm to cancel the artefacts.

Since 1975 most of the clinical and experimental trials in the use of the ENG signal as a source of feedback have used the quasi-tripole arrangement. A slightly different arrangement termed the true-tripole was introduced by Riso et al. that showed some advantages compared with the quasi tripole. In addition, the mobipolar arrangement was introduced and tested in acute and chronic animal experiments. However, in principle by using quadrupole and multipole configurations the amplitude of the ENG signal can be increased. Modelling these structures is realisable through the use of the inhomogeneous model developed by Struijk. Preliminary results from these modelling studies show a huge increase in the amplitude of the SFAP compared with the traditional quasi-tripole configuration. The signal recorded using the quasi-tripole configuration is proportional to the second difference of the transmembrane action potential as described by Stein. By using more electrodes, higher order differences of the transmembrane action potential, and hence larger amplitude signals can be obtained. Although this increase in the amplitude of the SFAP and ultimately in the ENG signal is based on modelling studies, it should also hold in practice. However, difficulties such as increase in noise and component count would need to be solved by optimised design.

At the moment there are various FES systems available for commercial use in the world.
One of these systems is the Brindley stimulator, which is dedicated to the successful treatment of neurogenic incontinence in patients with complete spinal cord injuries. To date, about 1500 patients have been treated with this implant. It relies on the prevention of the hyperreflexia (which causes the incontinence) by cutting the sacral posterior roots. The bladder is emptied by stimulation of the sacral anterior roots. In January 1999, the VOCARE bladder system marketed by the NeuroControl Corp. USA, which is produced by Finetech (UK), was approved for commercial use by the U.S. Food and Drug Administration (FDA). However, it is suitable only for complete spinal cord injury patients. The rhizotomy causes patients with incomplete injuries to lose valuable sensation. So for this group of patients, the system is required to detect the hyperreflexia, suppress it, and stimulate unidirectionally to prevent pain. Researchers in Denmark have investigated the use of the ENG signal from the sacral roots to detect bladder volume and the hyperreflexia in an animal model. So far they have concluded that it is very unlikely that bladder volume can be determined from the amplitude of the ENG signal because of the small and slow afferent activity during physiological bladder filling. However they were able to detect the hyperreflexia by detecting increases in variance of the ENG. These contractions were inhibited by stimulation of the dorsal roots. The investigators claim the ability to classify afferent activity from cutaneous, bladder and rectal receptors using their auto-correlation functions. However these experiments were performed under general anaesthesia with most of the noise sources absent. The presence of these noise sources such as the EMG will alter the performance of the system and contaminate the small-recorded ENG signal. The use of the control system to eliminate the EMG artefacts as demonstrated in chapter 5 in a human subject would be useful for this application. Also the system used in these animal experiments might not apply to humans in real time applications. To address this problem, researchers at University College London (UK) are looking to develop a novel implant for incontinence suitable for both complete and incomplete spinal cord injury patients. The aim is to develop an integrated circuit for both stimulation and recording of the sacral nerve roots. Ultimately in the future it is feasible to integrate the electronics on the cuff itself. This should solve some of the problem associated with the noise picked by the wires connecting the cuff to the implant and to the reduction of the common mode rejection ratio due to the cable capacitance. Also,
significant research is needed to reduce amplifier noise, which constitutes a large proportion of the total noise in ENG recording systems given that the ENG amplitude is in the μV range.