New technologies for active medical devices:
Evoked potentials in the spinal cord during stimulation for pain relief.

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Outline

• Active implants – Technology challenges.
• Epidural Spinal Cord stimulation.
• Novel ECAP recording system.
• Properties of dorsal column fibres.

= data from sheep
= data from humans
# Technology Challenges and Key Ideas

## CURRENT Process Capability

<table>
<thead>
<tr>
<th>Tissue Interface</th>
<th>Hand Assembly</th>
<th>10’s of channels</th>
<th>Automated µTechnology</th>
<th>100’s of channels</th>
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## Packaging

<table>
<thead>
<tr>
<th>Discrete components</th>
<th>5-10 year life</th>
<th>Single Distributed ASIC</th>
<th>Complex Scalable Systems.</th>
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## Electronics & Architectures

<table>
<thead>
<tr>
<th>Titanium/Laser Weld</th>
<th>All in one big box</th>
<th>µChip scale Biocompatible Package</th>
<th>Much smaller less invasive devices</th>
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### Medical

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<th>Automated µTechnology</th>
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### Educational

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<th>Automated µTechnology</th>
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Epidural Spinal Cord Stimulation

Electrode Position

Dural Mater

Epidural Space

Ligamentum Flavin

Electrode Position
Dermatome Selectivity

Orthodromic

Thalamus

Antidromic

Periphery

Sensory Nerve Endings

DRG

Dorsal Column

Physiological Midline

Periphery

1

2

1

Anterior

Posterior

C2

C3

C4

C5

C6

C7

C8

T1

T2

T3

T4

T5

T6

T7

T8

T9

T10

T11

T12

L1

L2

L3

L4

L5

S1

S2

S3

S4

S5

S6

NICTA

saluda Medical
Spinal Cord Stimulation for chronic Pain

- **Predictability**
  - Trial stimulation used to assess benefit.

- **Stability**
  - Patient movement produces uncomfortable stimulation
  - Long-term electrode migration

- **Invasiveness**
  - Procedure time.
  - Paraesthesia Generation.
  - Uncomfortable side effects.
Mechanism?

- SCS in use for 30 years
- 65% of patients get 50% pain relief
- Mechanism not understood.
- No direct measures of spinal cord electrophysiology in situ.

Measurement of Neural Potentials

Surface Potentials

- **Evoked response**
  - 10k
  - 0.7μV

- **Cellular Recordings**
  - 1k
  - 0.25μV
  - 1000k
  - 7.4 μV

**Spatial Resolution**

- 1-10cm
- mm
- μm

**Non Invasive**

- EEG
- ECOG
- Local FP

**Whole Nerve Activity**

- Compound potentials from Large numbers of fibres

**Highly Invasive**

- Single Unit Recording Patch Clamp
- Intra Cellular micro electrodes
Signal to noise – electrode impedance

**SFAP potential at various electrode fibre electrode separations**

**Noise Floor**
- Cellular Recordings: 5 µV
- Evoked response: 0.25 µV
- Surface Potentials: 0.7 µV

**Fibre Diameter (µm)**
- 100 µm
- 1000 µm
- 10000 µm

**SFAP Amplitude**
- 1x Noise
- 2x Noise
- 1/70xNoise
ECAP Measurements.

Major Problems

- Amplifier Saturation and recovery.
- Artifact increases with stimulation current

Novel ECAP recording system

24 Independent Channels
0.2 $\mu$V rms noise floor
104dB dynamic range
Arbitrary Waveform Stimulation
Full optical isolation IEC 60-601 compliant

MCS Bench-top system

Raw ECAP data.
No artifact treatment at all
Single ended measurement
Anatomical properties

Triphasic Potential, P1, N1, P2 peaks

Amplitude modulation corresponds to inter-vertebra spacing
Continuous recording

100 Gb data 24bit/24 channels
ECG measured and ECG frames discarded.
40 samples per average.
Early and Late Response

Low velocity activity appears at high stimulation currents.
Features – early response

- Amplitude Growth Curve
- N1 – Peak Latency

Two graphs show the relationship between current (mA) and voltage (V) for different pulse widths (PW) of 40µs and 120µs. The graphs are labeled with different symbols representing subjects E1 to E16.
Features – Late Response

Amplitude Growth - Rapid Onset at Threshold

N1 – Peak Latency – Response not propagating

40µs PW

120µs PW

\[ \text{Amplitude Growth - Rapid Onset at Threshold} \]

\[ \text{N1 – Peak Latency – Response not propagating} \]
Fibre properties

We know

- Recruitment characteristics and the thresholds

Because

- Threshold is related to fibre diameter.

- Stimulation recruits a relatively narrow range of fibre diameters in the dorsal column

- Conduction velocity is dependent on fibre diameter

- Observed velocity is not dependent on stimulation above a threshold
Fibre properties

- Velocity proportional to fibre diameter.
- Calculation of SFAP (single fibre action potential) and field models. The reverse problem.

![Velocity and Fibre Diameter Graph](image)

- Propagation delay
- Calculation of SFAP (SFAP)
- Field models (Field)
- Recruitment threshold
- V_peak-to-peak (P2-N1)
- Current level
- Fibre diameter
- Modelled fibre
- Current-threshold

![Franken-Haeuser - Huxley Measurement Graph](image)
Aβ potentials at best pain relief varied considerably. Conduction velocity from 49ms⁻¹ up to 65ms⁻¹

8.1 to 10.8μm diameter fibres.
Aβ Conduction Velocity

Small difference in Aβ conduction velocity orthodromic versus antidromic.

Very little change in conduction velocity with increasing stimulation current.
Paraesthesia coverage correlates with $A\beta$ potential

CAP amplitude corresponds to different dermatomes and coverage of painful area

Translates to Pain Relief
Variation with Posture

Measured Aβ response

- Lying on back
- Sitting
- Back
- Both Legs
- Leg

Extent of pain relief

Stimulus current

- 10mA
- 20mA
- 30mA
- 40mA
- 50mA

R² values:
- 0.9871
- 0.9948
- 0.991

Measured Aβ response in µV:
- 100µV
- 120µV
- 140µV
- 160µV

Response peak-to-peak variations with different postures.
Variation with Posture

Aβ responses and late responses vary with posture. Late responses generate discomfort and muscle stimulation. High Aβ recruitment is also uncomfortable.
Contributions to ECAP

Compound action potential is the sum of the contributing single fibre potentials

\[
ECAP = \sum_{n=1}^{T} SFAP(n)
\]

The difference in response between two currents is the contribution from the additionally recruited fibres
ECAP Subtraction Technique

A new population of slowly propagating fibres emerge at high stimulation currents.
Slower Fibres recruited at high currents Responses

The major contribution to ECAP, Aβ potentials demonstrate a narrow range of conduction velocities
Threshold Response

..averaged response
Signal to noise

Averaging Across time

Time slide response from single shot

\[ \Delta t \]
Low threshold wind-up

Averaged amplitude growth curve

Amplitude growth per stimulus
Response Curves

Adaptation varies from animal to animal

Dynamic properties

Wind up

Stimulation Current

Aβ Amplitude
Refractory Period Measurements

Conduction Velocity
60 – 100 ms\(^{-1}\)

40 µS pulse width

~20% of the response from fibres with long refractory periods

Electrode 13
Recruitment in SCS - Caution

Masker Probe

100 ms\(^{-1}\)
60 ms\(^{-1}\)

Fibre diameter

Current Level

10 µm  16 µm

N1 Latency Measures

\[ \Delta 10ms^{-1} \]

Do we only see a small distribution of fibre diameters because only the large fibres produce sufficient field?
Dorsal Column Recruitment

• Top surface of the dorsal columns Recruited by SCS.
• Increasing current selects a larger surface area

Human data indicates much smaller and many more fibres responding than predicted by Holshiemer

Conclusions

• SCS stimulates $\alpha\beta$ fibres in the dorsal column.
• Antidromic activation of $\alpha\beta$ fibres is responsible for pain relief for SCS.
• Recruitment favours geometric spread across the surface of the dorsal column rather than penetration.
• ECAP response measurements provide a means to optimize performance of SCS systems.
  – Both in design (electrode geometries).
  – Patient evaluation.
  – Patient device set up.
• Feed back control of stimulus.
• New algorithm design.
Acknowledgements

IS – Current
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Melanie Hotchkiss

Past
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Peter Ayre
Jutta Reif
Central Sensitisation is the origin of neuropathic pain

- There are changes in the spinal cord as a result of neural plasticity.
- In animals this manifest as changes in synaptic organisation.

Multiple applications

**APPROVED**

- Deep Brain Stimulation
  - Parkinson’s Disease
  - Essential Tremor
- Cochlear
  - Profound Deafness
- Vagal Nerve Stimulation
  - Epilepsy
  - Depression
- Peripheral Nerve Stimulation
  - Chronic Pain
- Spinal Cord Stimulation
  - Chronic Pain
  - Angina Pain
- Sacral Nerve Stimulation
  - Incontinence

**FUTURE**

- Deep Brain Stimulation
  - Epilepsy
  - Depression
  - Tinnitus
  - Obsessive Compulsive Disorder
  - Tourette’s Syndromes
- Vagal Nerve Stimulation
  - Congestive Heart Failure
  - Obsessive
- Occipital Nerve Stimulation
  - Headache
- Spinal Cord Stimulation
  - Peripheral Vascular Disease Pain
  - Diabetic Neuropathy
- Sacral Nerve Stimulation
  - Pelvic Pain
  - Sexual Dysfunction
- Gastric
  - Cholelithiasis
  - Irritable Bowel Syndrome
- Artificial Retina
  - Rod/Rhodopsin Pigmentosa