Multichannel on-scalp MEG based on high-$T_c$ SQUID magnetometers

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Invited presentation ED1-1-INV was given at ISS 2017, December 13-15, 2017, Tokyo, Japan.
Göteborg at the West Coast of Sweden
The gateway to Scandinavia
Outline

- Introduction
  - Magnetoencephalography (MEG) and focal MEG
  - High-$T_c$ SQUIDs
  - Why high-$T_c$ MEG
- MEG – Benchmarking a single channel high-$T_c$ MEG against a low-$T_c$ ELEKTA MEG
  - Benchmarking experiments with phantoms
  - Benchmarking and protocol for focal MEG on human subjects
- 7-channel high-$T_c$ MEG system (KAW NeuroSQUID project)
  - Direct feedback injection to minimize crosstalk
  - Preliminary measurements
  - Flux transformers
  - High-$T_c$ nanoSQUIDs
    - Single-layer device
    - Flip-chip device
- Conclusion
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- Conclusion
The human brain

- Most complex organ known
  - $\sim 10^{11}$ neurons and $\sim 10^{15}$ synapses
  - The number of combinations exceeds the number of particles in the universe!

- Cognition and consciousness
  - Understanding the brain
  - Philosophical questions

- Brain disorders a major burden for the society
  - In Europe, direct and indirect expenses of brain disorders about 800 billion euros per year*
  - Human suffering

*) Olesen et al., 2012
How to interrogate the brain

Benefits of MEG:

- Passive and safe, especially important for infants
- High temporal resolution of ~ms
- Reasonable spatial resolution of ~mm
- Spectral content of the signals
- Access to mechanisms and physiological interpretation

- EEG: high spatial resolution but poor temporal resolution
- PET: radioactive tracers
- EEG: electrical contact

EEG: Electro-encephalography
IEEG: Invasive Electroencephalography
MEG: Magnetoencephalography
MRS: Magnetic Resonance Spectroscopy
fMRI: functional MRI
SPECT: Single Photon Emission Cranial Tomography
PET: Positron Emission Tomography
The Brain
Magneto- and electroencephalography (MEG/EEG) – measuring electric brain activity

A single neuron: \( B \approx 0.01 \text{ fT} \)

10 000 synchronous and parallel neurons: \( B \approx 100 \text{ fT} \)

Currents in active neurons...

... give rise to small electric voltages and weak magnetic fields on the surface of the head

EEG = measuring the voltages on the scalp

MEG = measuring the magnetic fields

Courtesy by Lauri Parkkonen  
Parkkonen, 2009
Applications of MEG

- Clinical use
  - Epilepsy diagnostics
  - Localization of eloquent brain regions before resections
- Clinical research (e.g.)
  - Predictive diagnostics of Alzheimer’s disease
  - Personalized stroke rehabilitation
  - Assessing brain trauma
- Neuroscientific research

Mäkelä, Paetau & Parkkonen, SUST 2016

Courtesy by Lauri Parkkonen
Current MEG system’s issue: Sensors are far from the brain!

MEG with superconducting LTS-SQUID sensors – LHe cooling:

- non-adaptable sensor helmet
- large distance from brain to sensors
- limited spatial resolution

Distance to brain (cm)

Sensor count

Courtesy by Lauri Parkkonen

Iivanainen, Stenroos, Parkkonen (HBM 2013)
If the sensors could be on the scalp...

Distance to brain surface would reduce to less than half in adults. Even larger change in children.

On-scalp sensors

SQUIDs

"Iivanainen, Stenroos, Parkkonen (HBM 2013)"

Courtesy by Lauri Parkkonen
Why on-scalp MEG?

- Closer to the source
  - Larger signals
  - Can possibly get the same SNR with less sensitive sensors
  - Higher spatial resolution
  - Higher information capacity
  - Resolve more complicated sources?
- Avoid LHe (finite resource, ~500 kSEK/yr)
  - Can use
    - High-\(T_c\) SQUIDs at LN2 or
    - (OPMs heated above RT)
  - Simpler cryogenics for high-\(T_c\)
    - Flexible arrays
    - Cheaper systems
Focal MEG sensors in our case: HTS dc-SQUIDS based on bicrystal junctions

Weak links: bicrystal substrate $\rightarrow$ grain boundary $\rightarrow$ epitaxial YBCO film $\rightarrow$ microbridges crossing the grain boundary

High-$T_c$ SQUID magnetometers for MEG in an ILK dewar
Graduate student & SQUID & FFT

Berger waves/phenomena

Hans Berger and early EEG recordings from the 1930s
Graduate student & SQUID & FFT

a) Amplitude (fT)

Amplitude (fT)

Eyes closed, Eyes open

b) Frequency (Hz)

Frequency (Hz)

10
11
12
700
500
300
100

Time (s)

10 20 30 40 50 60

Time (s)

10 20 30 40 50 60
EEG recordings from 1930s

Hans Berger and early EEG recordings from the 1930s

Berger waves/phenomena
Our first high-$T_c$ SQUID-based MEG recordings

- Alpha modulation as expected
- Something strange in the theta band
  - Atypical of visual system
  - Higher power than alpha
2-channel high-\(T_c\) MEG system
Two-channel recordings: visual (O2) and sensorimotor (C4) alpha

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  - Benchmarking and protocol for focal MEG on human subjects

- Single-layer device
  - Flip-chip devices

- Conclusion
Work done in collaboration with NatMEG @ KI

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8) NatMEG, KI & Aalto University
9) NatMEG, KI & Radboud University
Benchmarking on phantoms (courtesy of Elekta)

Glass-fiber reinforced plastic (GFRP)

High-\(T_c\) SQUID

Plastic cylinder

77 K \(\text{Al}_2\text{O}_3\)

Vacuum

200 µm \(\text{Al}_2\text{O}_3\) window


Benchmarking on phantoms (courtesy of Elekta)

- High-$T_c$ SQUID
- Plastic cylinder
- Glass-fiber reinforced plastic (GFRP)
- 200 µm $\text{Al}_2\text{O}_3$ window


Results

Standoff distance: 3 mm for high-$T_c$ and 20 mm for low-$T_c$
Dipole 1 depth under the phantom shell: 24 mm
Expected signal amplitude gain: $\sim$3 times
Benchmarking on human subjects

Challenges:

- The limited number of channels for new sensor technology
- Time consuming to map the full field topography
- Habituation and changes in the subject’s alertness during measurement
- The location of sources is unknown - inverse problem needs to be computed!
- To locate the source, full-head field distribution required

A new benchmarking protocol is needed!
State-of-the-art vs. bicrystal grain boundary high-$T_c$ MEG system

Elekta Neuromag® TRIUX

102 low-$T_c$ SQUID magnetometers and 204 gradiometers

Capable of full head mapping

Sensor-to-subject distance $\sim 20$ mm

Sensitivity 1–5 fT/√Hz


High-$T_c$ MEG system

One or two channels

Single-layer bicrystal high-$T_c$ SQUID magnetometer

Sensor-to-subject distance $\sim 3$ mm

Sensitivity $\sim 40$ fT/√Hz

Magnetically shielded room at KI, Stockholm

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Benchmarking protocol

Brain signal

Somatosensory Evoked Field (SEF)

Auditory Evoked Field (SEF)
Benchmarking protocol

Brain signal

Elekta system

EEG cap

Somatosensory Evoked Field (SEF)

Auditory Evoked Field (SEF)
Benchmarking protocol

Brain signal
Equivalent current dipole (ECD) source
EEG cap

Elekta system

Somatosensory Evoked Field (SEF)
Auditory Evoked Field (SEF)
Benchmarking protocol

Brain signal

EEG cap

Somatosensory Evoked Field (SEF)

Auditory Evoked Field (SEF)
Benchmarking protocol

Brain signal

EEG cap

Somatosensory Evoked Field (SEF)

Auditory Evoked Field (SEF)
Results on AEF & SEF

Auditory evoked field after ~479 averages and 1–60 Hz band pass filtering

Somatosensory evoked field after ~616 averages and 1–500 Hz band pass filtering

More features due to close proximity? Worth further investigation with on-scalp MEG

Benchmarking: one high-Tc SQUID vs KI NatMEG Elekta System

- Auditory evoked fields: deep sources, results as expected
- Somatosensory evoked fields: shallow sources, strange results
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NeuroSQUID
Nanoscale superconducting devices for a closer look at brain activity

Vision: To make the most sensitive magnetometer capable of operation above 77 K by employing superconducting quantum effects at the nanoscale. Sensors based on this technology will lead to a paradigm shift in neuroimaging. World-leading competences and facilities will come together to explore the fundamental possibilities of this new approach.

34 397 000 kronor (~ 4 M$ / ~460 000 000 JPY)
NeuroSQUID

Cryostat and sensors

Crosstalk

Head phantom measurements

Preliminary alpha

Next step: Flux transformers

Next step: Nanowire-based SQUIDs
**NeuroSQUID**

**Cryostat**
- 0.9 L liquid nitrogen reservoir
- Vacuum + superinsulation
- Thin, concave plastic window
- Option to pump on nitrogen
- Minimum sensor-to-room temperature distance $\approx 1$ mm
- $T_{\text{base}} = 80$ K (70 K with pumping)
- $\Delta T < 100$ mK
- $t_{\text{hold}} = 19$ h (22 h with pumping)
Cryostat – outer part and inner guts

- Sapphire window on inner LN2 container
- 7 sapphire wedges on d.o. holding SQUIDs
  - Dense, hexagonal pattern (2 mm edge-to-edge)
  - Tilted towards center
- 3 x 3-channel electronics from Magnicon
Parts and pieces

NeuroSQUID

~9 mm

20 cm
NeuroSQUID

High-\(T_c\) SQUID magnetometer

- Single layer \(\text{YBa}_2\text{Cu}_3\text{O}_{7-x}\) (YBCO) thin film magnetometer with directly coupled pickup loop
- \(10 \times 10\) mm\(^2\) STO bicrystal substrate
- 2 grain boundary Josephson junction dc SQUIDs per chip
- High \(I_CR_n\) product: 120 – 250 \(\mu\)V at 77 K
- Rounded gold edges to contact from the side
NeuroSQUID

Cryostat and sensors

Crosstalk

Head phantom measurements

Preliminary alpha

Next step: Flux transformers

Next step: Nanowire-based SQUIDs
NeuroSQUID

Flux-locked loop

$I_b$

$V$

$\Phi$

$I_{c1}$

$I_{c2}$

$\Phi / \Phi_0$

$V_{out}$

$R_f$

Feedback

$\Phi_f = - \Phi$

Preamp

Integrator
Criteria for feedback

- On-scalp MEG → minimize standoff distance
- Flux-locked loop → high enough coupling strength
- Low noise
- Low crosstalk → densely packed

\[ \text{Crosstalk } C_{AB} = \frac{\Phi_{AB}}{\Phi_{BB}} \]

Feedback solutions

- Feedback current
- Superconducting coil
- Direct injection

(a) Grain boundary
(b) Superconducting coil
(c) Direct injection

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Crosstalk

NeuroSQUID

![Graph showing crosstalk percentage versus distance between magnetometer centers.]

- **C21** superconducting coil
- **C12** superconducting coil
- **C21** direct injection
- **C12** direct injection

Parameters:
- **d** (distance between sensors)
- **10 mm**

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2 Channel phantom measurements
Preliminary measurements on alpha

- 5 (7) SQUIDs
- Alpha (8-12 Hz)
- Eyes open – eyes closed
- Time-frequency spectra (using multitapers)
- Average over 5 trials
Preliminary measurements on alpha
NeuroSQUID

Preliminary measurements – increase in alpha seen in channel 2 & 3

Channel 2

eyes open     |     eyes closed
30 seconds   |     30 seconds

Channel 3

eyes open     |     eyes closed
30 seconds   |     30 seconds
NeuroSQUID

Cryostat and sensors

Crosstalk

Head phantom measurements

Preliminary alpha

Next step: Flux transformers

Next step: Nanowire-based SQUIDs
Flux transformers
- Increase effective area $A_{\text{eff}}$
- Multi-layer device
Flux transformers (for flip-chip)

- Easy to fabricate
- Limited effective area / sensitivity
- Better effective area / sensitivity
- Challenging fabrication

NeuroSQUID

- Single-layer magnetometer: 7.8 nT/Φ₀
- SQUID with flux transformer: 1.6 nT/Φ₀

Graph showing magnetic field noise [T/√Hz] vs. frequency [Hz] for single-layer and SQUID with flux transformer.
NeuroSQUID

Integrated flux transformer

- Single chip
- Increased coupling
NeuroSQUID

Cryostat and sensors

Head phantom measurements

Preliminary alpha

Next step: Flux transformers

Next step: Nanowire-based SQUIDs

Crosstalk

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Moving from bicrystal grain boundary to nanowire junctions

Bicrystal grain boundary junctions

Nanowire junctions

2 µm

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NeuroSQUID

Motivation: Previous work* on high-$T_c$ nano-SQUIDs

- Low flux noise at 8 K → what about at 77 K?
- Large 1/f noise → what about under bias-reversal condition?
- Small SQUID loop size → can it be used as a magnetometer?
- Scalable junction technology → potential for multi-channel MEG?

**NeuroSQUID**

Three approaches for coupling

**Approach I**

**Approach II: with a flux transformer**

**Approach III: A two-level coupling method**

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Nanowire SQUID (NSQ):

- \( A_{eff} = 0.09 \text{ mm}^2 \)
- \( S_{\phi}^{1/2} = 55 \, \mu\Phi_0/\sqrt{\text{Hz}} \)
- \( S_{B}^{1/2} = 1200 \, \text{fT}/\sqrt{\text{Hz}} \)

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Flip-chip separation ~3 µm

- \( A_{eff} = 0.16 \text{ mm}^2 \)
- \( S_{\phi}^{1/2} = 35 \, \mu\Phi_0/\sqrt{\text{Hz}} \)
- \( S_{B}^{1/2} = 480 \, \text{fT}/\sqrt{\text{Hz}} \)

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- \( A_{eff} = 0.46 \text{ mm}^2 \)
- \( S_{\phi}^{1/2} = 55 \, \mu\Phi_0/\sqrt{\text{Hz}} \)
- \( S_{B}^{1/2} = 240 \, \text{fT}/\sqrt{\text{Hz}} \)

NeuroSQUID

Simulation toolbox for numerically calculating the inductances and coupling

- Software: AutoCAD and COMSOL Multiphysics
- Principle: Solving London and Maxwell Eqs with the concept of stream function

Minshu Xie: PhD thesis 2017
50 nm YBCO:
- no Au capping
- no pick up loop
- $V_\phi \sim 15 \mu V/\phi_0$
- Amp: $S_\nu^{1/2} \sim 0.4 \text{nV/Hz}^{1/2}$

Expected field noise taking achieved effective area $A_{\text{eff}} \sim 0.1 \text{mm}^2$: $S_\phi^{1/2} \sim 500 \text{fT/Hz}^{1/2}$

For HTS MEG applications: $S_\phi^{1/2} < 50 \text{fT/Hz}^{1/2}$ needed

➔ SQUID electronics with lower input noise (Cryoton)
NeuroSQUID

Cryostat and sensors

Head phantom measurements

Crosstalk

Preliminary alpha

Next step: Flux transformers

Next step: Nanowire-based SQUIDs
We still have to struggle a bit to get further down the road...

**CONCLUSIONS**

- **HTS vs. LTS MEG**
  - Benchmarking has been made with phantoms and humans
  - HTS MEG reveals strange theta at occipital region
  - HTS MEG shows larger than expected signals for shallow sources
  - HTS MEG shows more complex signals

- **A 7-channel high-Tc SQUID-based MEG system is being built:**
  - Crosstalk between two channels caused by feedback has been studied
  - Phantom and human subjects measured
  - System level benchmarking (source localization) to be carried out

- **Low-noise flux-transformers for**
  - Flip-chip and possibly integrated devices

- **To improve the sensitivity of nanowire-based high-Tc SQUID:**
  - Thicker washer in Ketchen-type coupling (coupling coeff. $k$: 0.05 → 0.7)
  - Integrated devices (smaller separation)
  - Projected sensitivity 10 fT/√Hz for Ketchen-type coupling
The Chalmers SQUID group
The National Facility for Magnetoencephalography

The scientific aim of the NatMEG unit is to establish a national core facility for MEG within the Swedish Biomaging Network in order to strengthen the international competitiveness of Swedish Cognitive Neuroscience. The method has not been available in Sweden previously so that especially the time-resolution of the MEG method combined with its localization power provides an additional dimension for functional brain research for all groups that already work with fMRI.

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Thanks!

¿QUESTIONS?

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