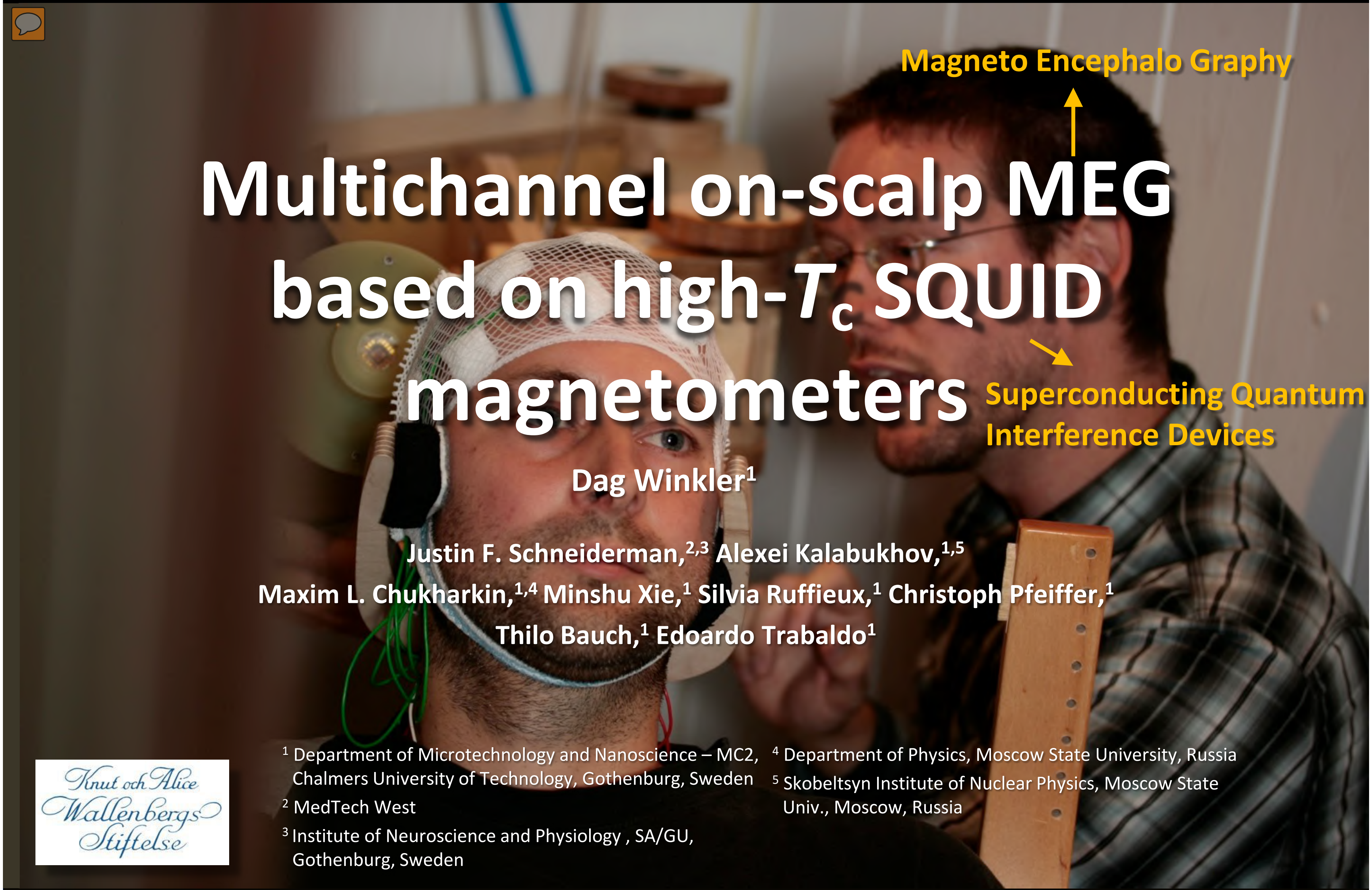
IEEE/CSC & ESAS SUPERCONDUCTIVITY NEWS FORUM (global edition), February 2018.
Invited presentation ED1-1-INV was given at ISS 2017, December 13-15, 2017, Tokyo, Japan.



Magneto Encephalo Graphy

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

Superconducting Quantum Interference Devices

Dag Winkler[1]

Justin F. Schneiderman,[2,3] Alexei Kalabukhov,[1,5]
Maxim L. Chukharkin,[1,4] Minshu Xie,[1] Silvia Ruffieux,[1] Christoph Pfeiffer,[1]
Thilo Bauch,[1] Edoardo Trabaldo[1]

[1] Department of Microtechnology and Nanoscience – MC2, Chalmers University of Technology, Gothenburg, Sweden
[2] MedTech West
[3] Institute of Neuroscience and Physiology , SA/GU, Gothenburg, Sweden
[4] Department of Physics, Moscow State University, Russia
[5] Skobeltsyn Institute of Nuclear Physics, Moscow State Univ., Moscow, Russia

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Göteborg at the West Coast of Sweden

The gateway to Scandinavia

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  - Magnetoencephalography (MEG) and focal MEG
  - High-T_c SQUIDs
  - Why high-T_c MEG
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  - 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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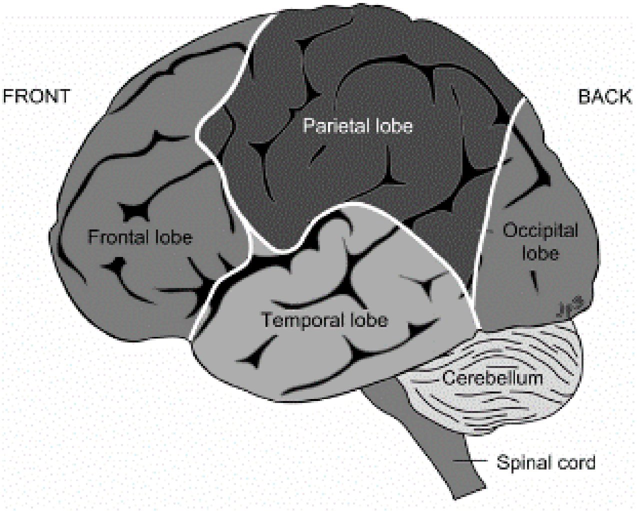
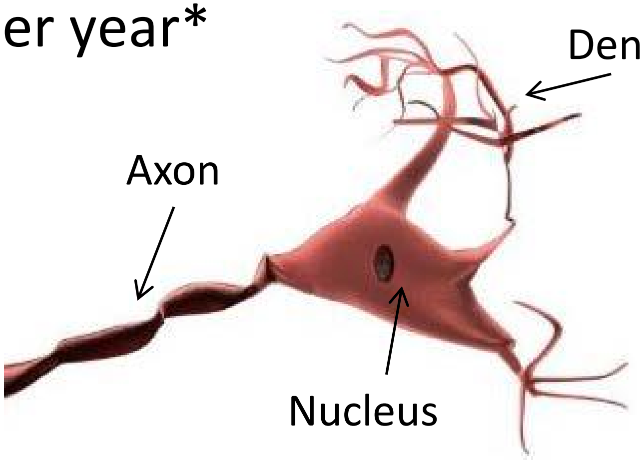
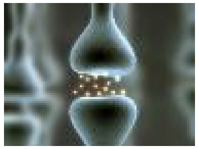
The human brain



- **Most complex organ known**
  - ~10^{11} neurons and ~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

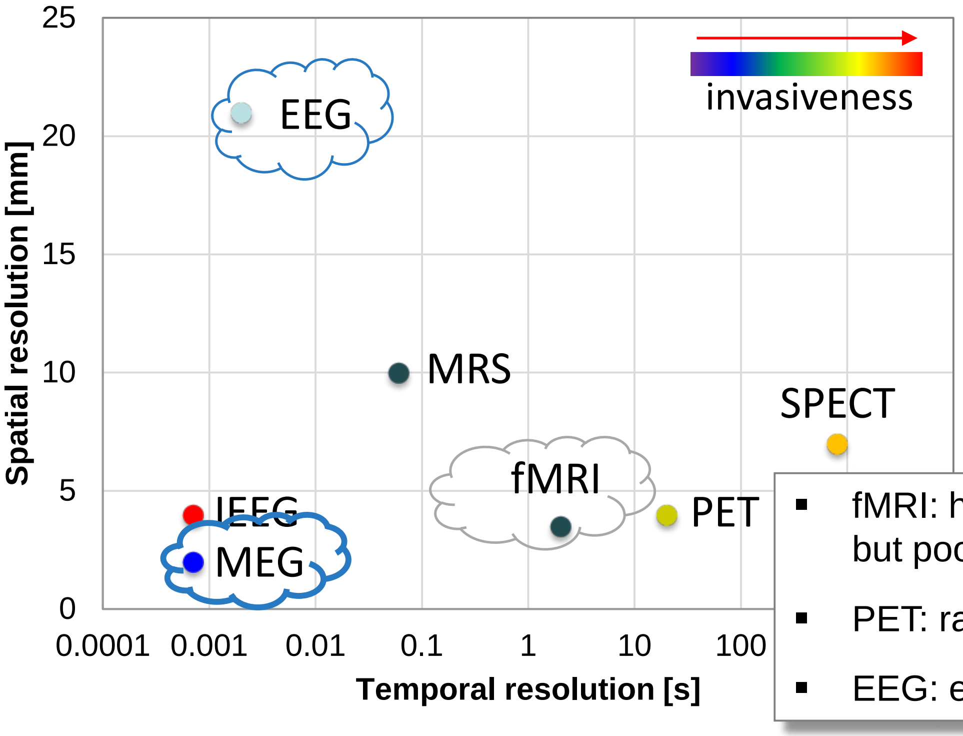




Synapse

*) Olesen et al., 2012

How to interrogate the brain



- fMRI: 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

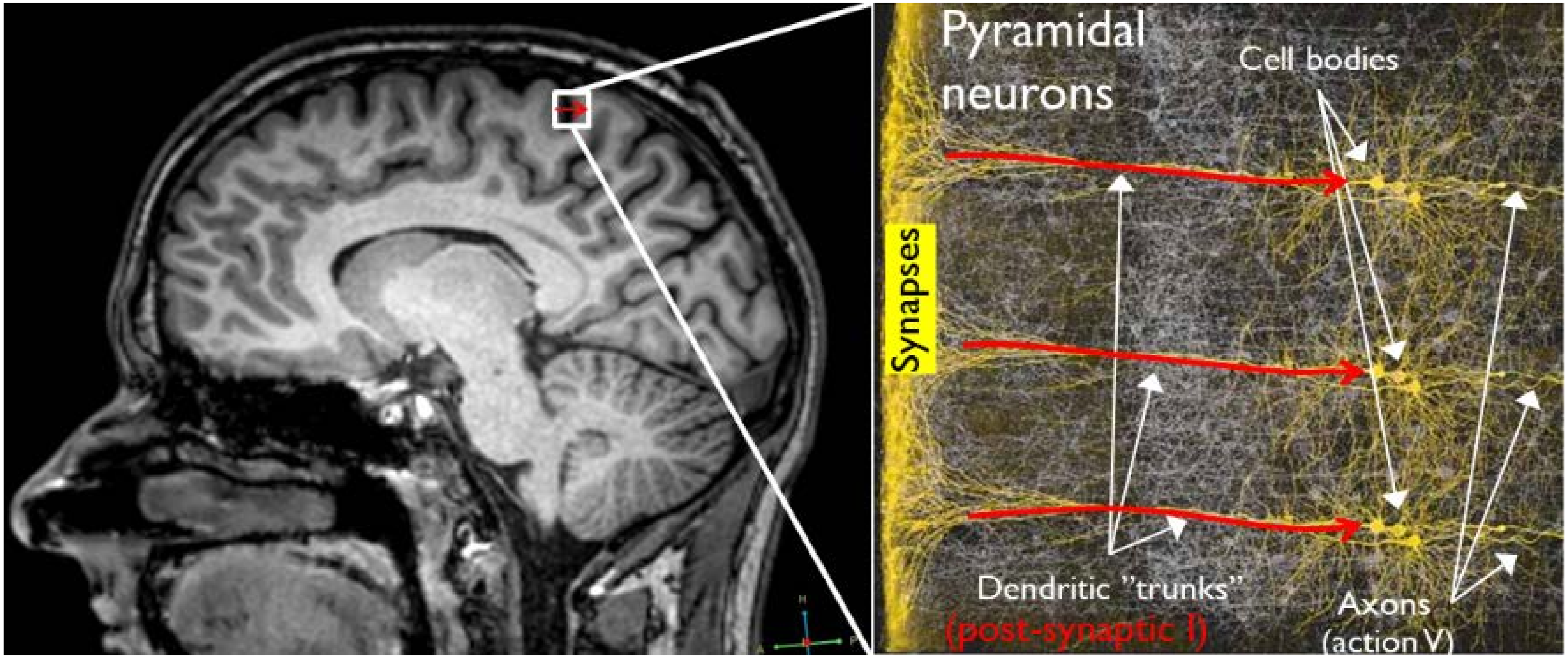
fMRI: functional MRI
SPECT: Single Photon Emission Cranial Tomography
PET: Positron Emission Tomography

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

SAGE-Hindawi Access to Research
International Journal of Alzheimer's Disease
Volume 2011, Article ID 280289, 10 pages
doi:10.4061/2011/280289

The Brain


Pyramidal neurons
Cell bodies
Synapses
Dendritic "trunks"
(post-synaptic I)
Axons
(action V)

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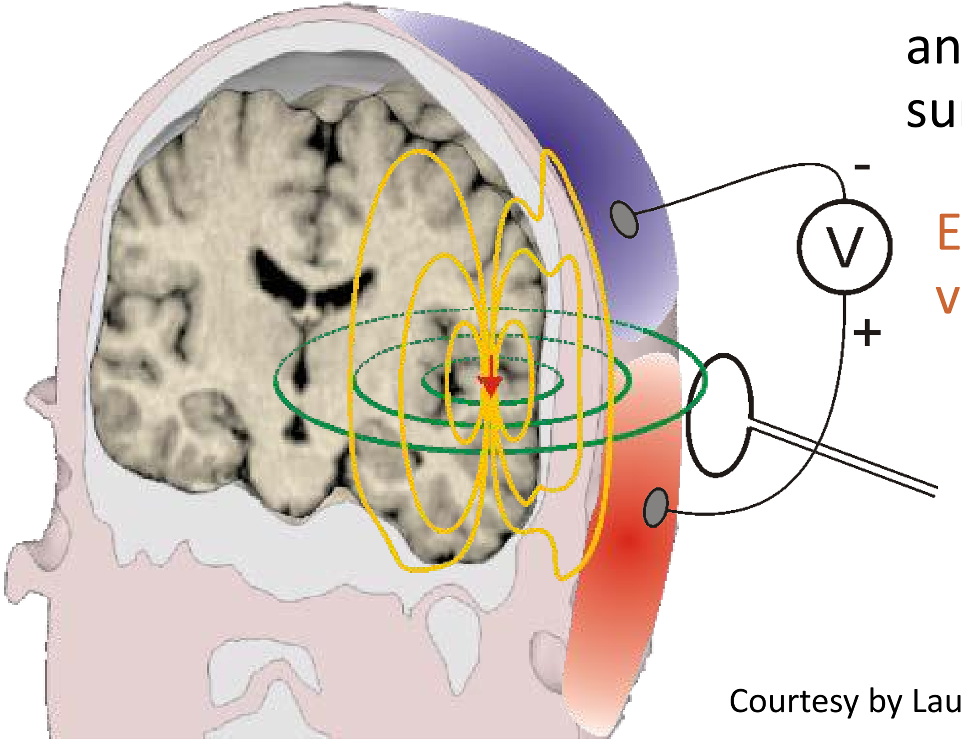
Magneto- and electroencephalography (MEG/EEG) – measuring electric brain activity

A single neuron: *B* ~ 0.01 fT

10 000 synchronous and parallel neurons: *B* ~100 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

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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

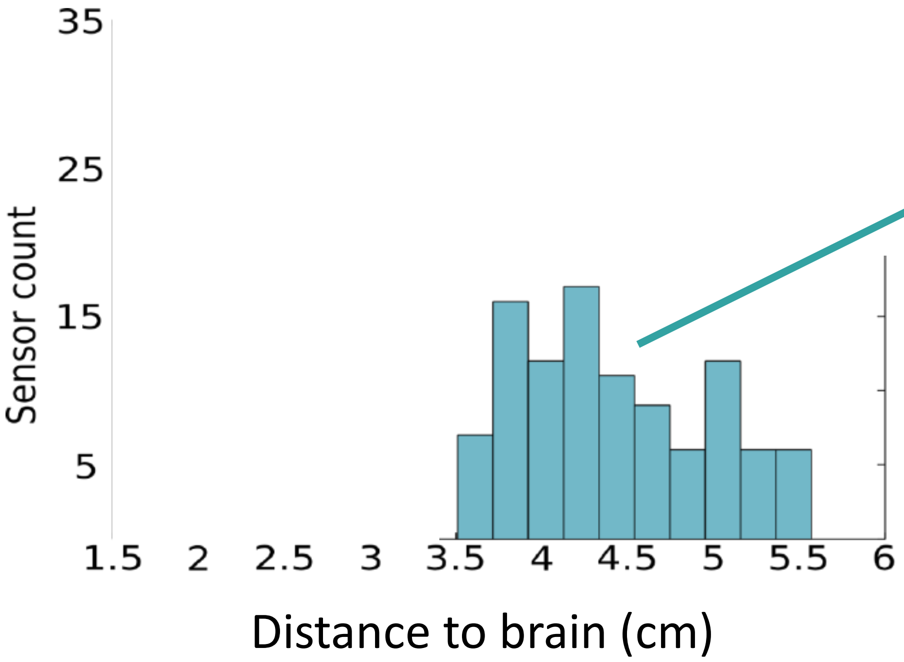
Mäkelä, Paetau & Parkkonen, SUST 2016

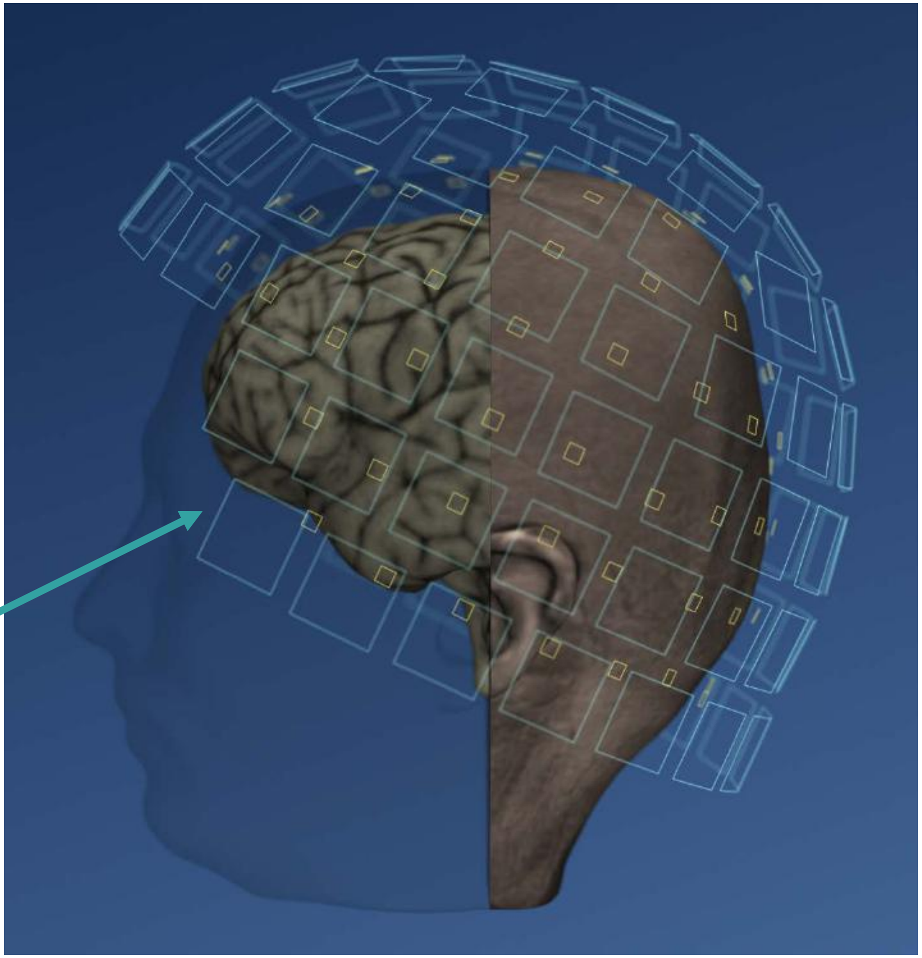
Courtesy by Lauri Parkkonen

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



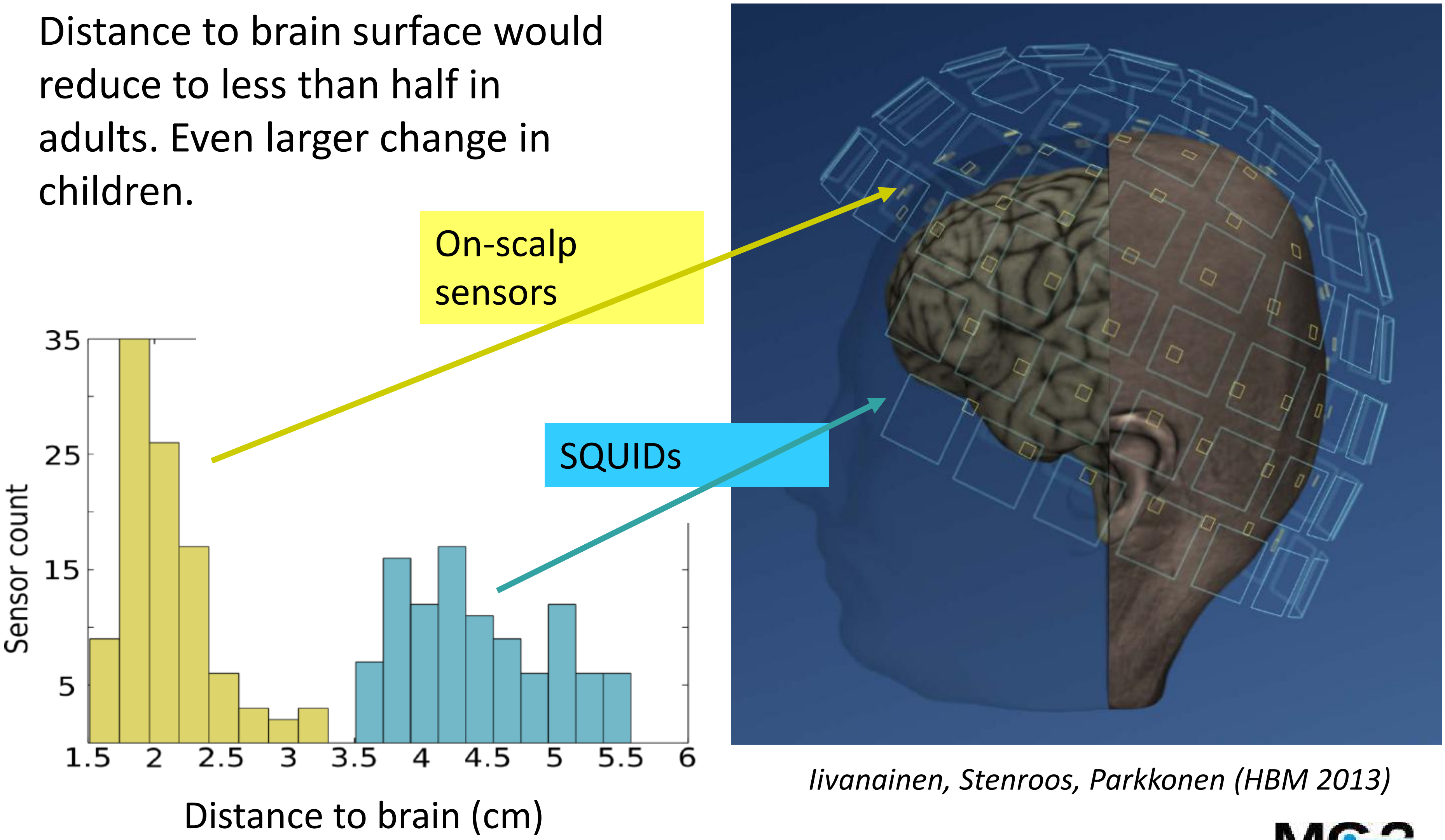


Iivanainen, Stenroos, Parkkonen (HBM 2013)

Courtesy by Lauri Parkkonen

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

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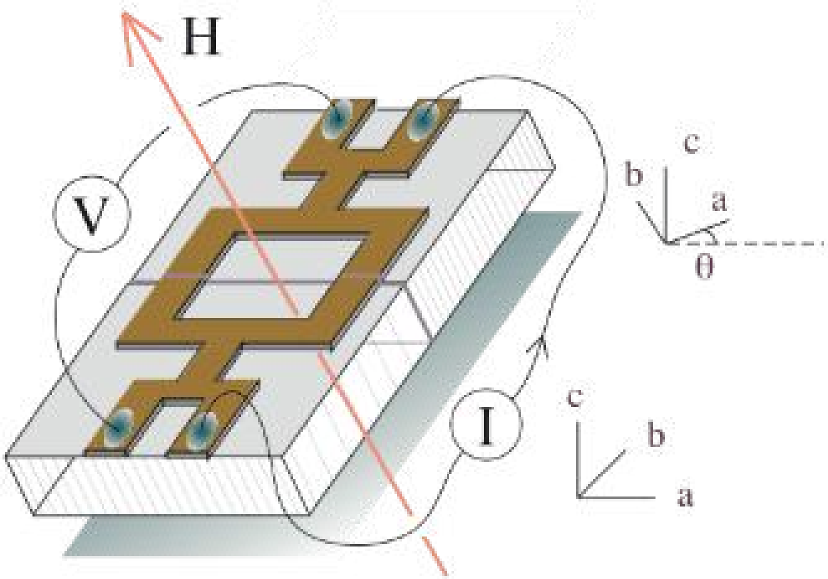
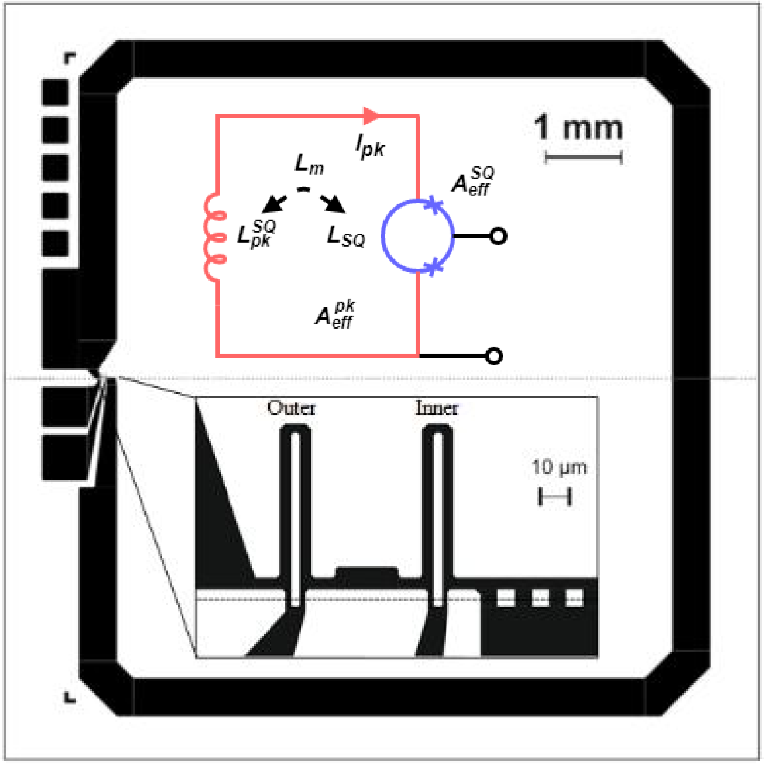
Why on-scalp MEG?

- 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



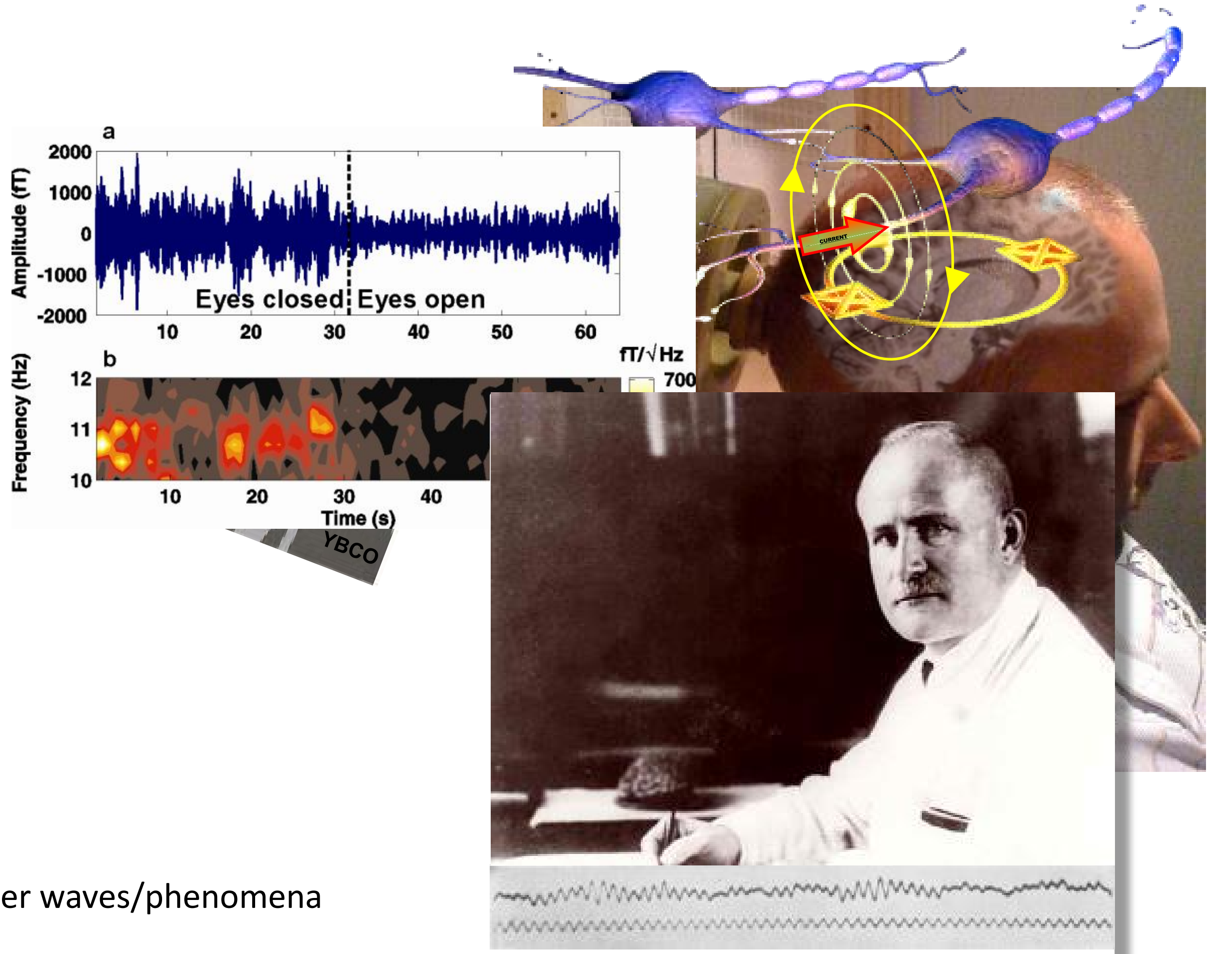


Weak links: bicrystal substrate → grain boundary → epitaxial YBCO film → microbridges crossing the grain boudary

D. Dimos, P. Chaudhari, and J. Mannhart, Phys. Rev. B 41, 4038 (1990)

High-T_c SQUID magnetometers for MEG in an ILK dewar

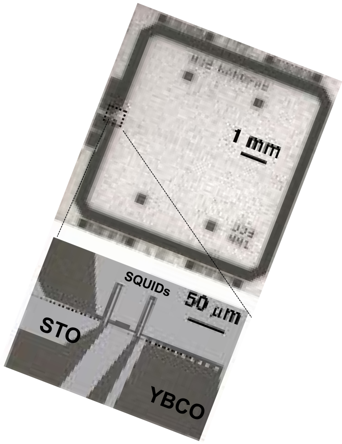
Graduate student & SQUID & FFT

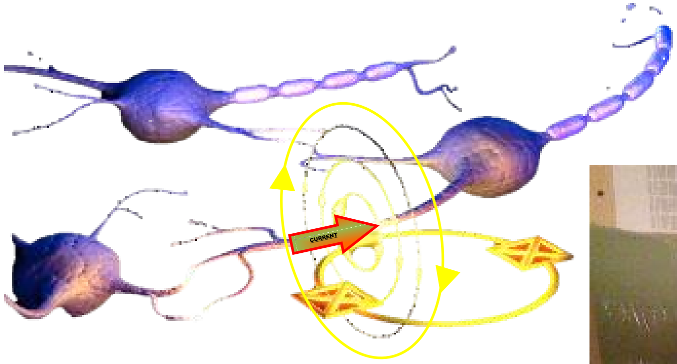


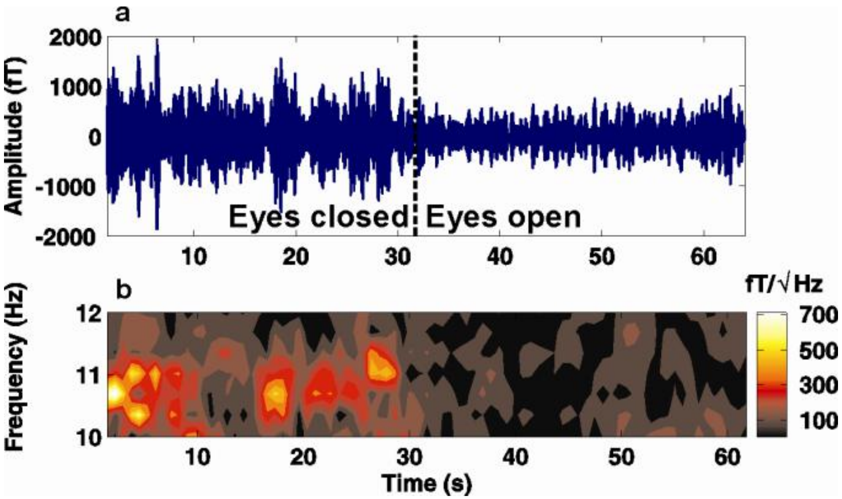
Berger waves/phenomena

Hans Berger and early EEG recordings from the 1930s

Graduate student & SQUID & FFT







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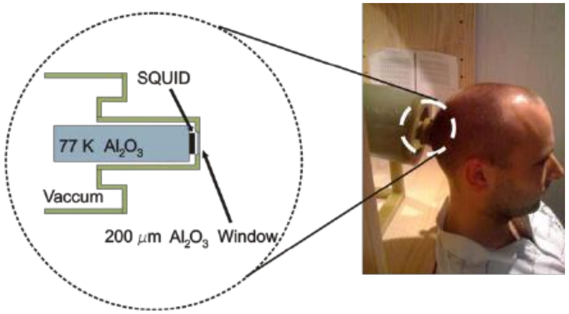
EEG recordings from 1930s

Hans Berger and early EEG recordings from the 1930s

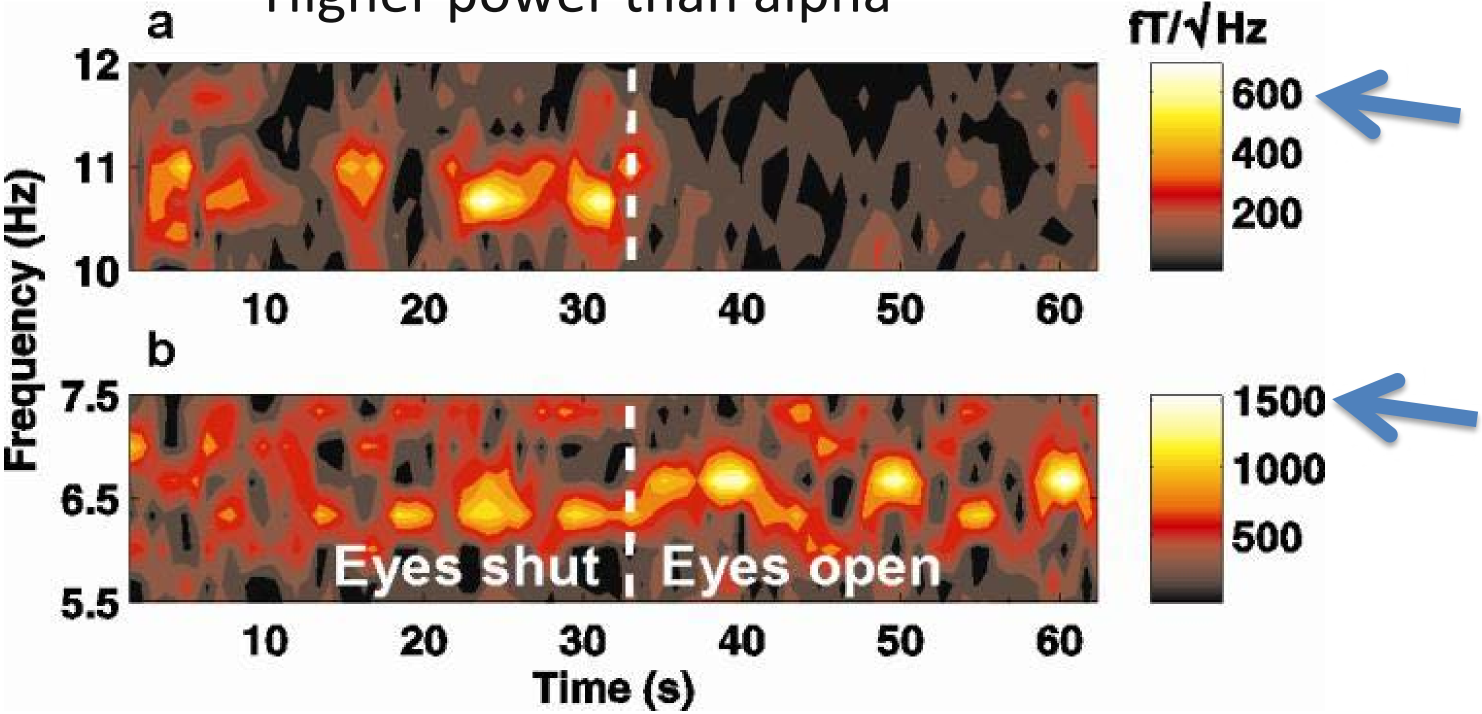
Berger waves/phenomena

Alpha and theta bands…



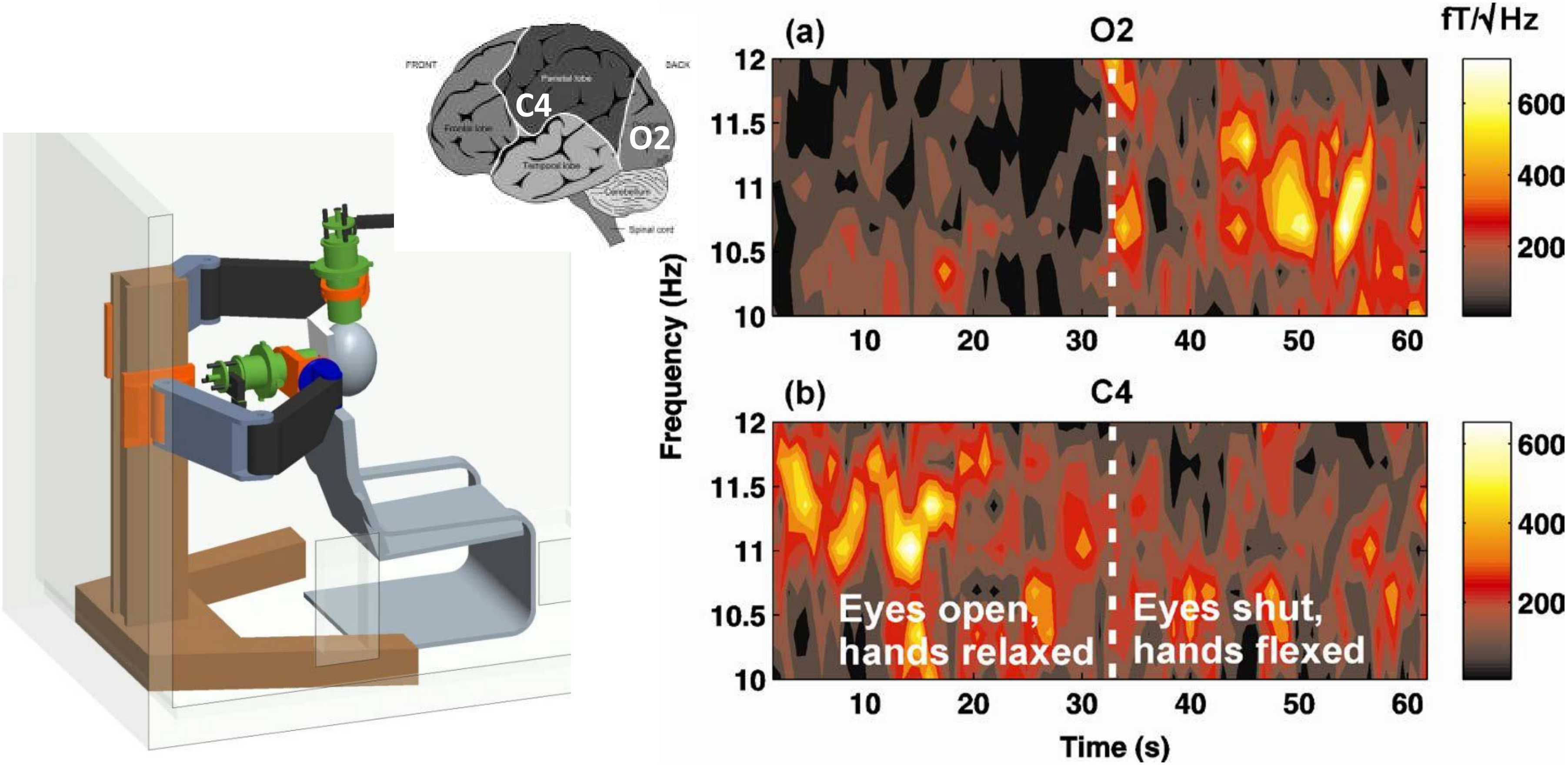
Our first high-T_c SQUID-based MEG recordings

- 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



Öisjöen et al, High-Tc superconducting quantum interference device..., *App. Phys. Lett.* 2012, DOI:10.1063/1.3698152

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1270 IEEE TRANSACTIONS ON BIOMEDICAL ENGINEERING, VOL. 64, NO. 6, JUNE 2017

EMB

Benchmarking for On-Scalp MEG Sensors

Minshu Xie, Justin F. Schneiderman*, Maxim L. Chukharkin, Alexei Kalabukhov, Bushra Riaz,
Daniel Lundqvist, Stephen Whitmarsh, Matti Hämäläinen, Veikko Jousmäki, Robert Oostenveld,
and Dag Winkler

    - Single-layer device
    - Flip-chip devices
- Conclusion

Work done in collaboration with NatMEG @ KI

Minshu Xie,[1] Justin F. Schneiderman,[2,3] Alexei Kalabukhov,[1,5] Maxim L. Chukharkin,[1,4] Silvia Ruffieux,[1] Christoph Pfeiffer,[1] Bushra Riaz, [2,3] Daniel Lundqvist,[6] Stephen Whitmarsh,[6] Matti Hämäläinen,[7] Veikko Jousmäki,[8] Robert Oostenveld[9], Dag Winkler[1]

1) Department of Microtechnology and Nanoscience – MC2, Chalmers University of Technology, Gothenburg, Sweden
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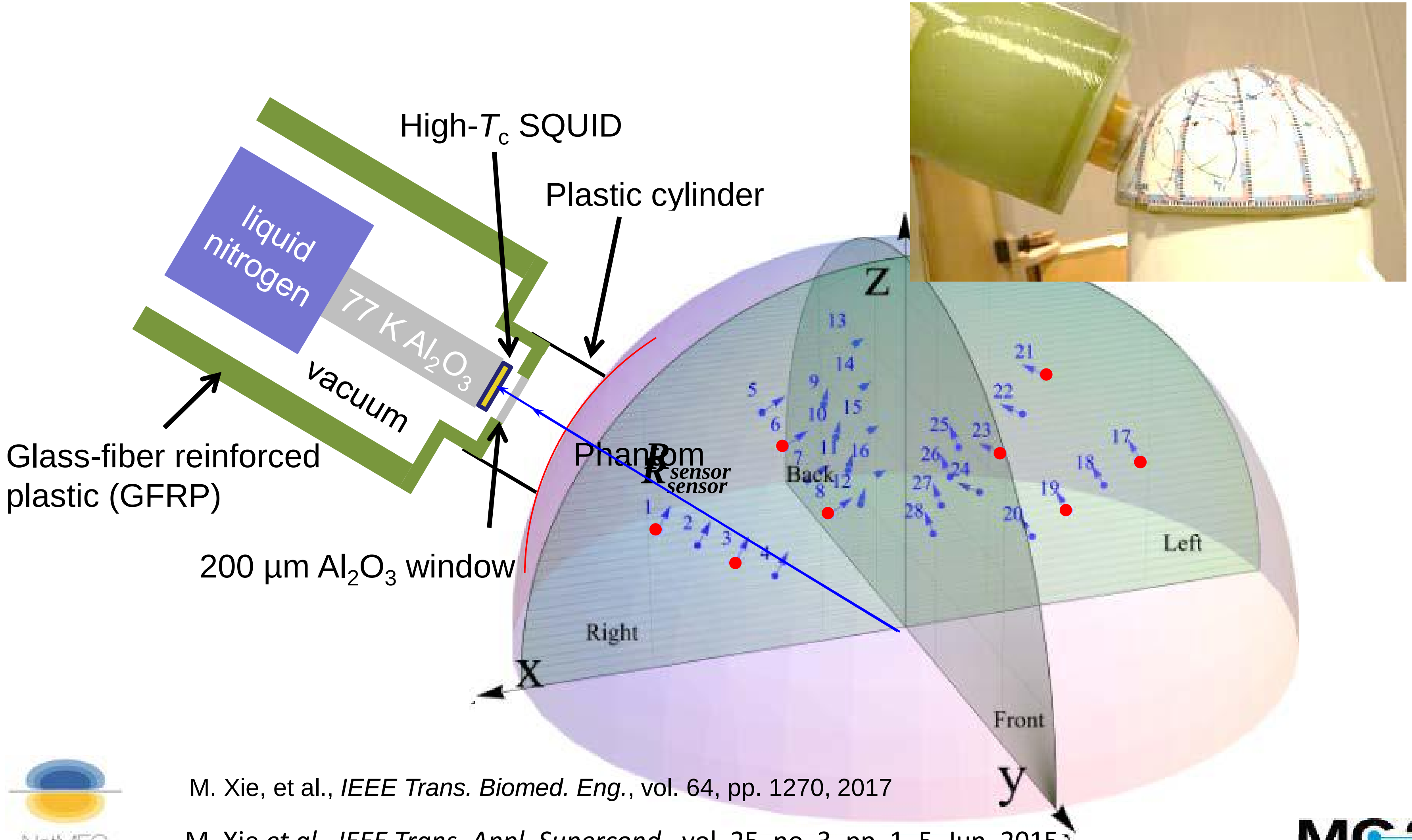
5) Skobeltsyn Institute of Nuclear Physics, Moscow State Univ., Moscow, Russia
6) Swedish National Facility for Magnetoencephalography (NatMEG), Karolinska Institutet (KI)
7) NatMEG, KI and A.A. Martinos Center for Biomedical Imaging, Mass. Gen. Hospital & Aalto Univ.
8) NatMEG, KI & Aalto University
9) NatMEG, KI & Radboud University

Benchmarking on phantoms (courtesy of Elekta)



High-T_c SQUID

Plastic cylinder

Glass-fiber reinforced plastic (GFRP)

200 µm Al_2O_3 window

M. Xie, et al., *IEEE Trans. Biomed. Eng.*, vol. 64, pp. 1270, 2017

M. Xie *et al.*, *IEEE Trans. Appl. Supercond.*, vol. 25, no. 3, pp. 1–5, Jun. 2015.

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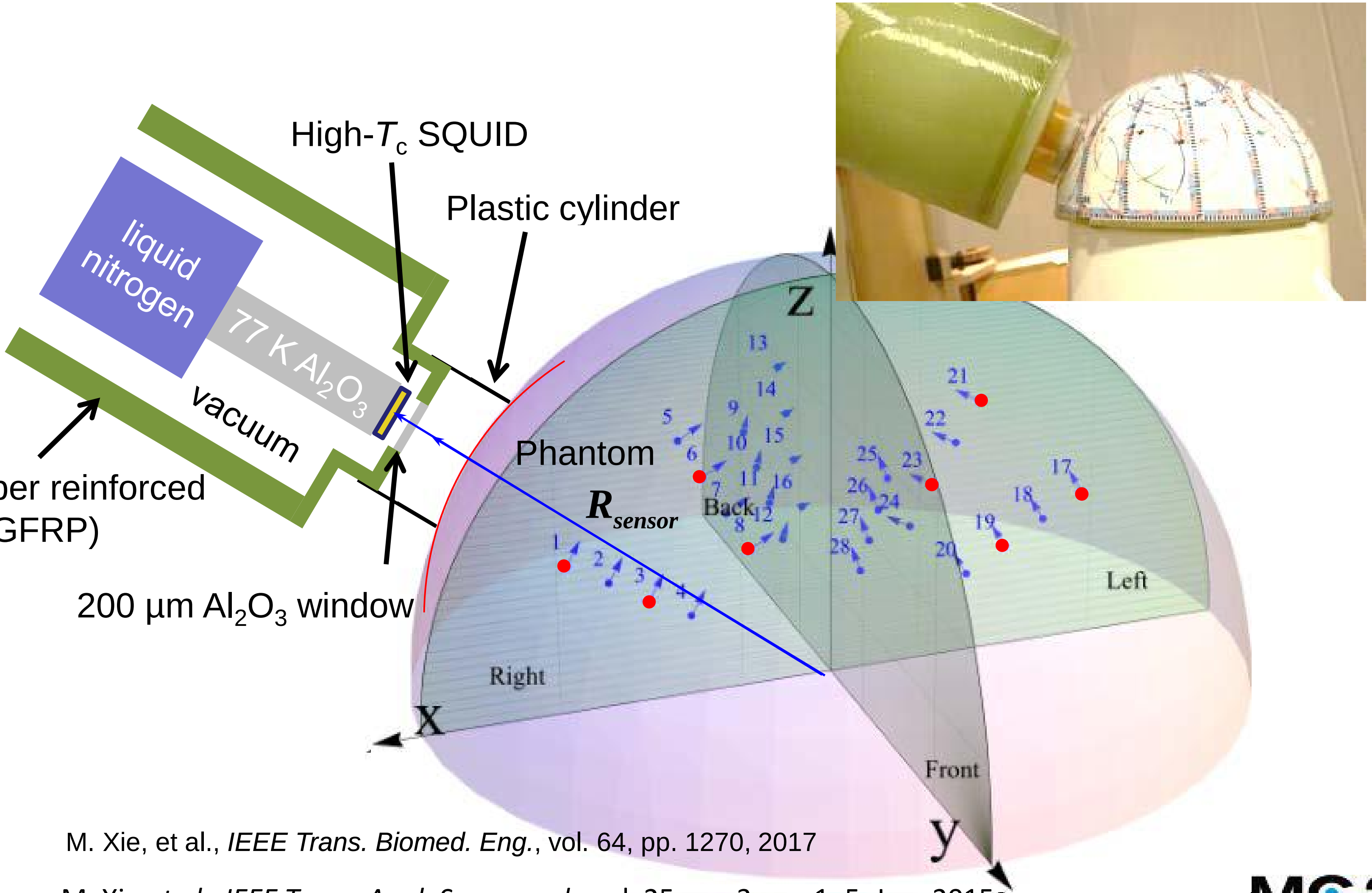

M. Xie, et al., *IEEE Trans. Biomed. Eng.*, vol. 64, pp. 1270, 2017

M. Xie *et al.*, *IEEE Trans. Appl. Supercond.*, vol. 25, no. 3, pp. 1–5, Jun. 2015.

NatMEG

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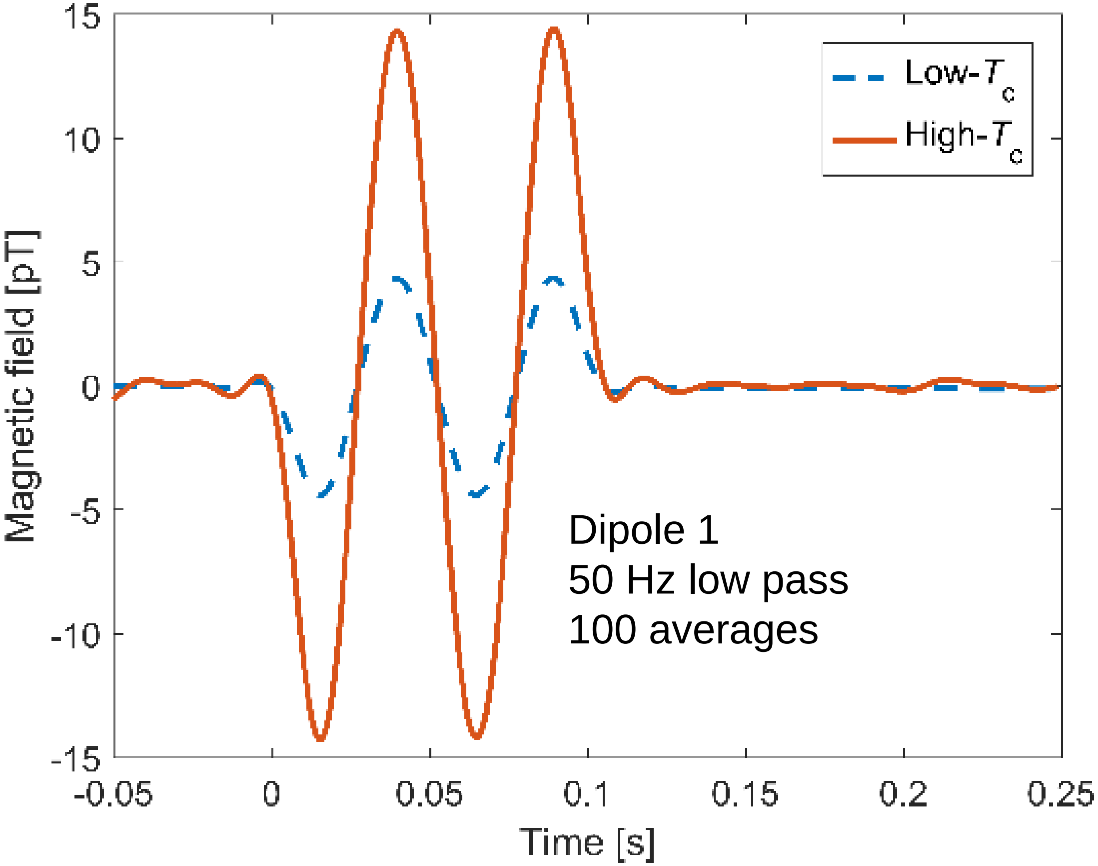
Results

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: ~3 times



M. Xie, et al., *IEEE Trans. Appl. Supercond.*, vol. 25, pp. 1601905, 2015

Benchmarking on human subjects

A new benchmarking protocol is needed!

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

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Benchmarking for On-Scalp MEG Sensors

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State-of-the-art vs. bicrystal grain boundary high-T_c MEG system

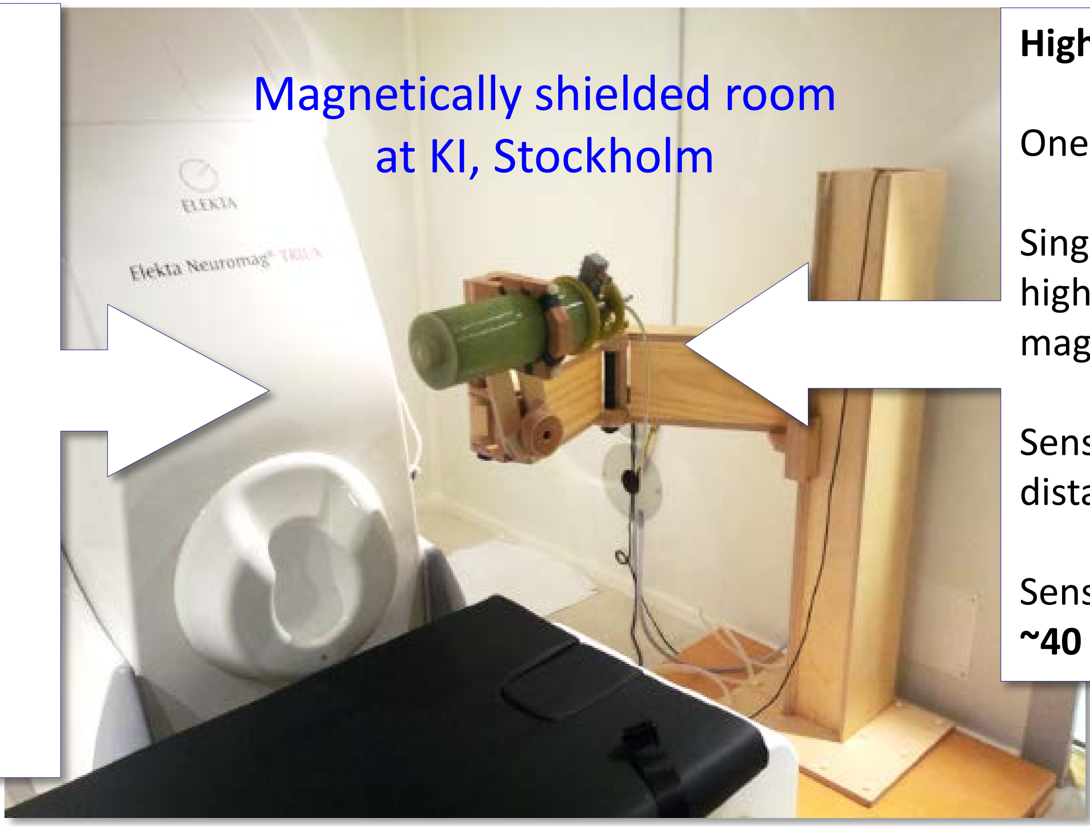
Elekta Neuromag® TRIUX

102 low-T_c SQUID magnetometers and 204 gradiometers

Capable of full head mapping

Sensor-to-subject distance ~**20 mm**

Sensitivity
1–5 fT/√Hz



Magnetically shielded room at KI, Stockholm

High-T_c MEG system

One or two channels

Single-layer bicrystal high-T_c SQUID magnetometer

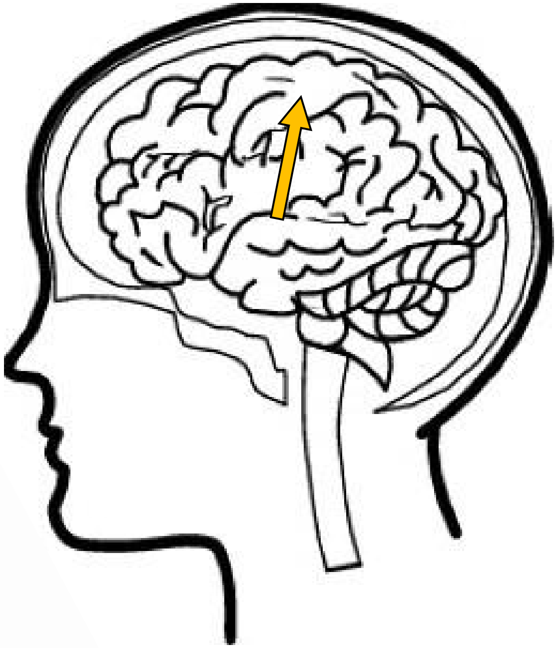
Sensor-to-subject distance ~**3 mm**

Sensitivity
~40 fT/√Hz

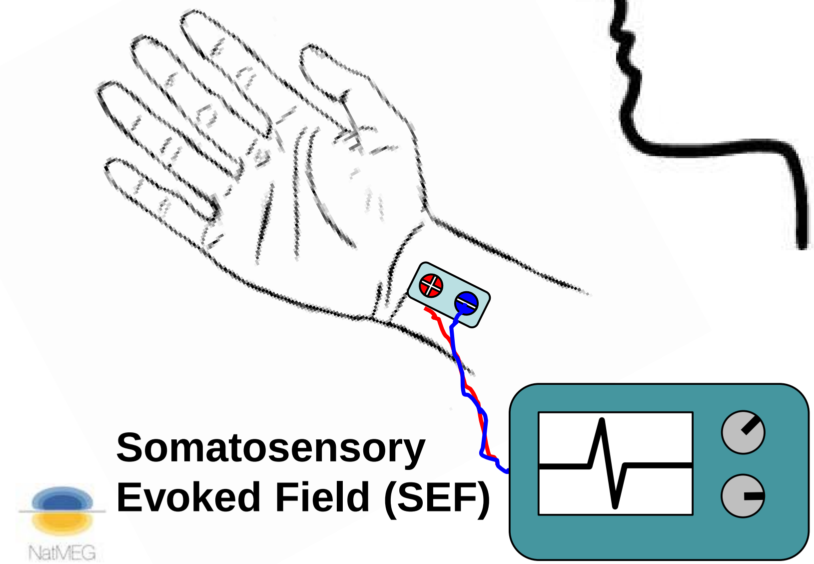
M. Xie, et al., *IEEE Trans. Appl. Supercond.*, vol. 25, pp. 1601905, 2015
M. Xie, et al., *IEEE Trans. Biomed. Eng.*, vol. 64, pp. 1270, 2017

Benchmarking protocol

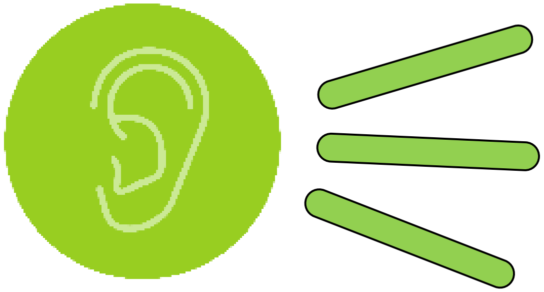
↑ Brain signal



Brain signal

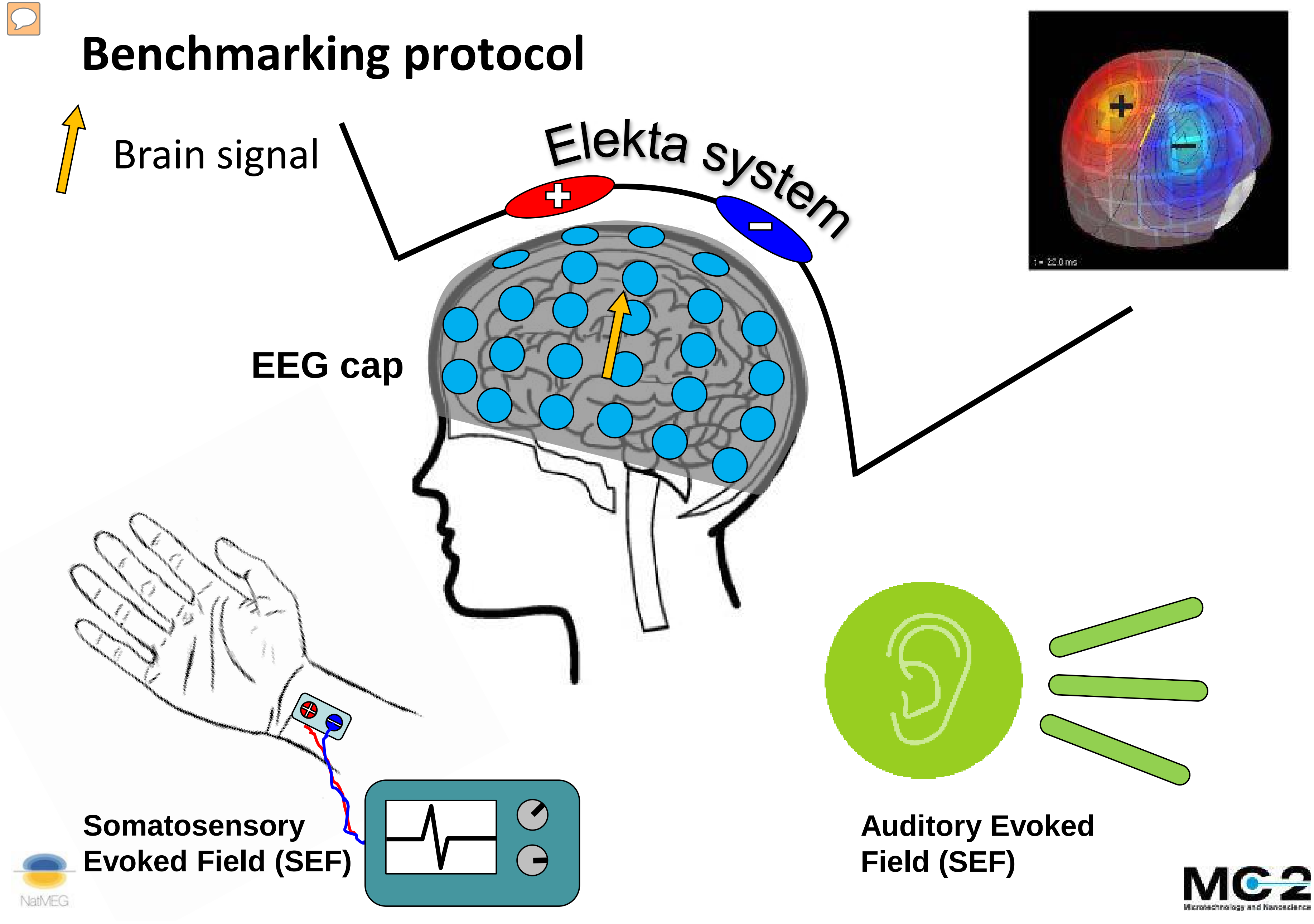


Somatosensory Evoked Field (SEF)



Auditory Evoked Field (SEF)

Benchmarking protocol



Brain signal

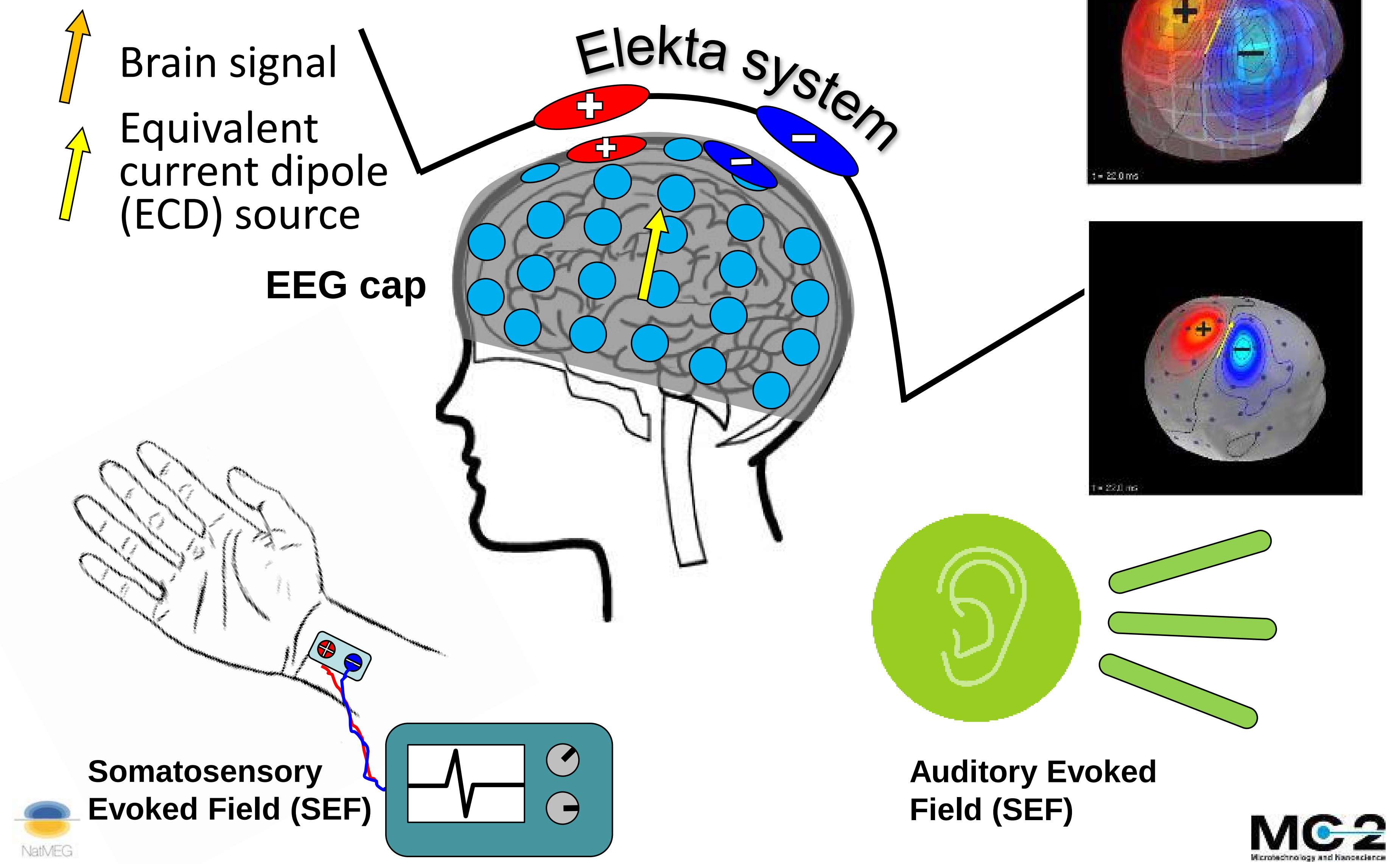
Elekta system

EEG cap

Somatosensory Evoked Field (SEF)

Auditory Evoked Field (SEF)

Benchmarking protocol



Brain signal

Equivalent current dipole (ECD) source

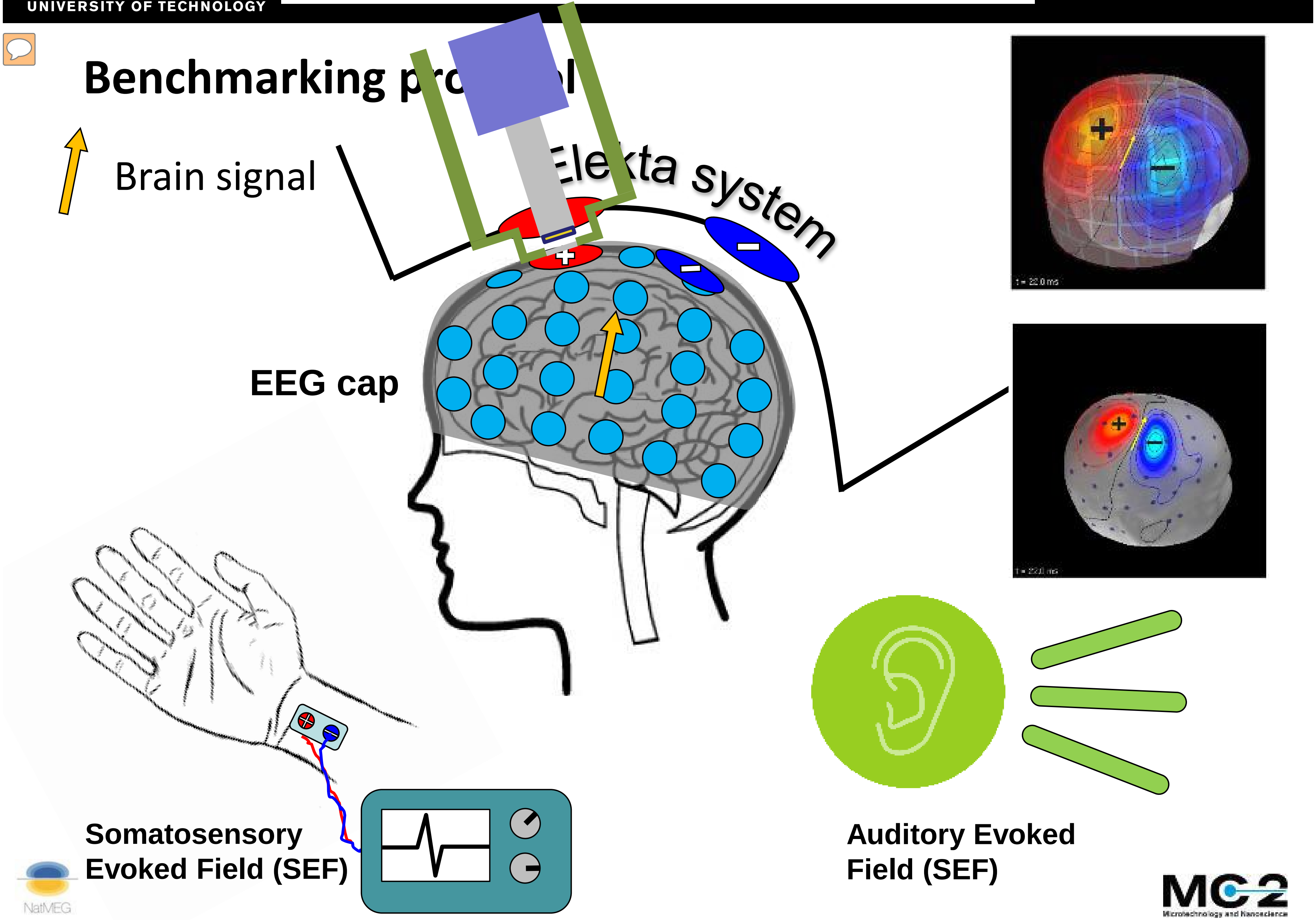
Elekta system

EEG cap

Somatosensory Evoked Field (SEF)

Auditory Evoked Field (SEF)

Benchmarking pr l



Brain signal

Elekta system

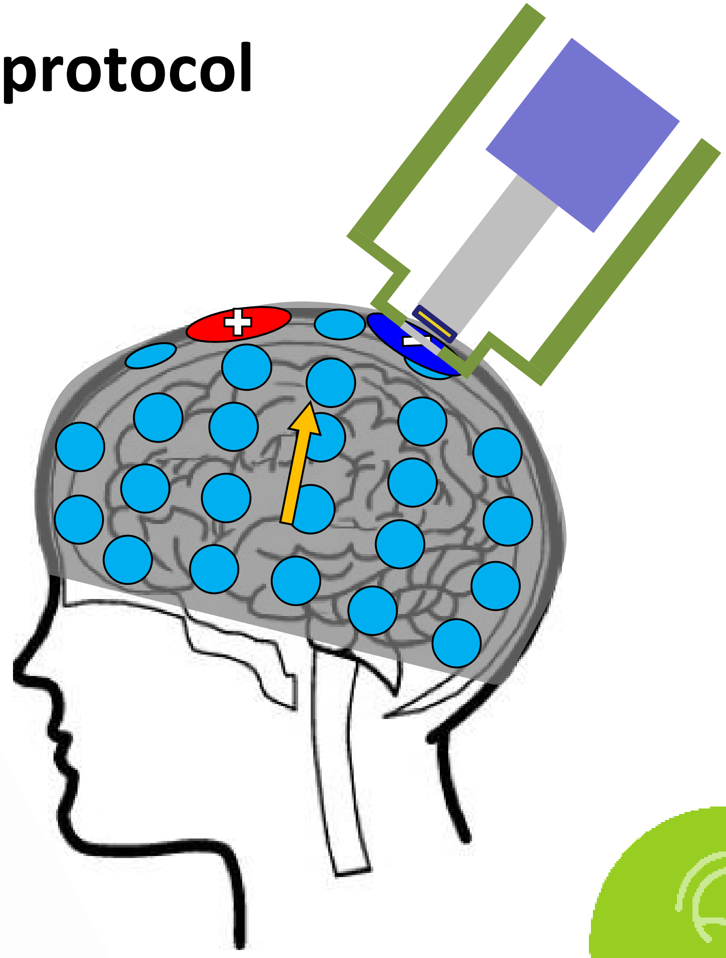
EEG cap

Somatosensory Evoked Field (SEF)

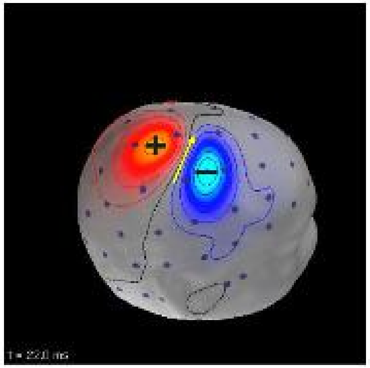
Auditory Evoked Field (SEF)

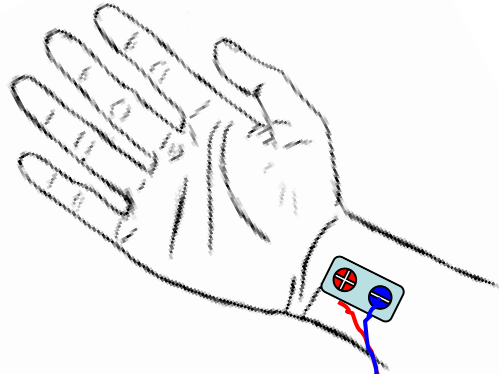
Benchmarking protocol

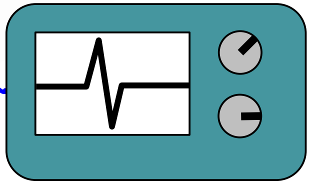
Brain signal



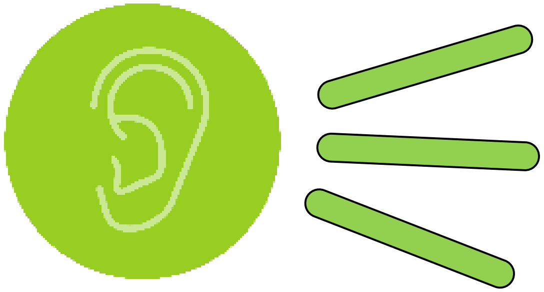
EEG cap







Somatosensory Evoked Field (SEF)

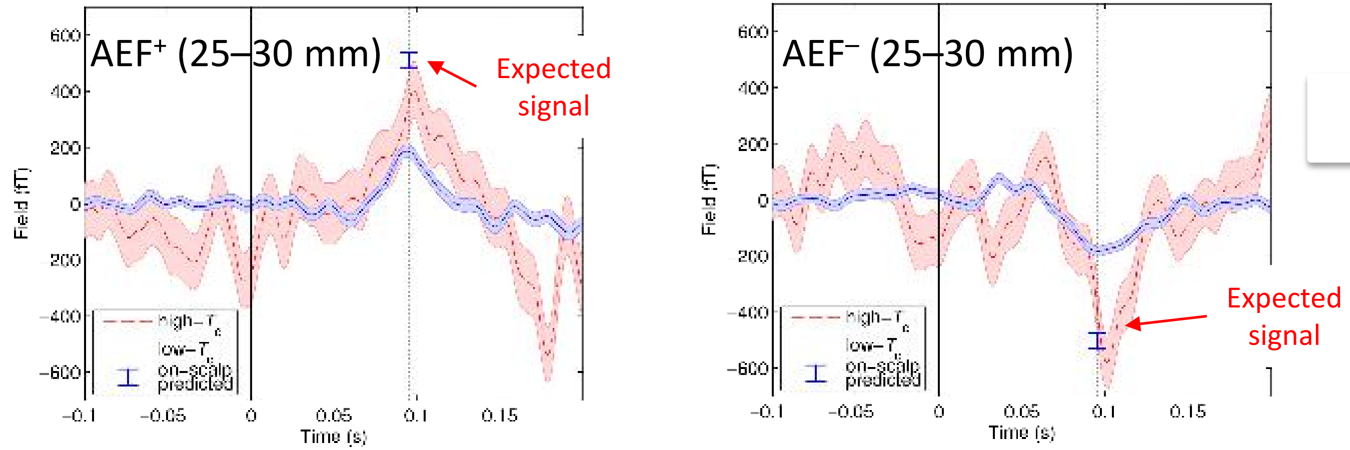


Auditory Evoked Field (SEF)

NatMEG

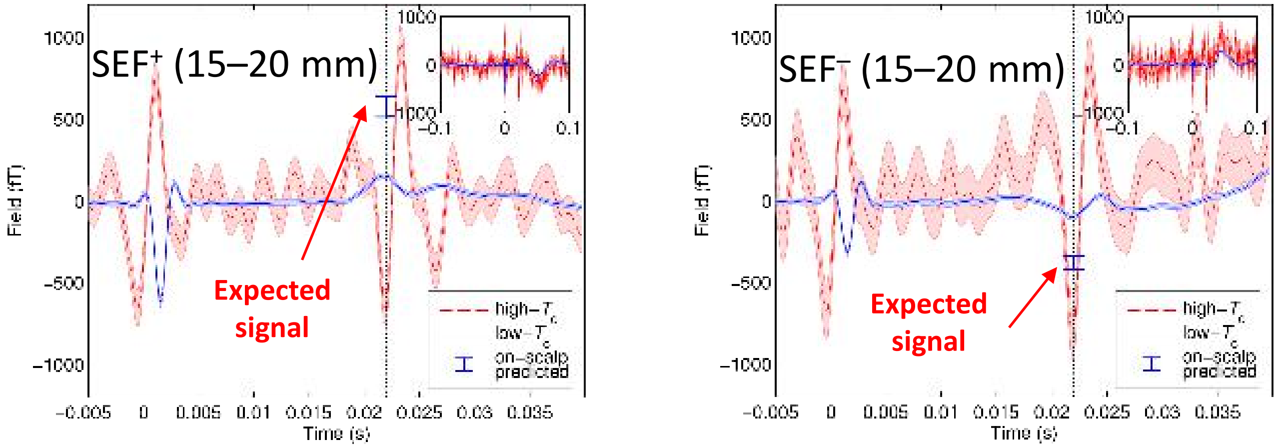
MC2 Microtechnology and Nanoscience

Results on AEF & SEF



Deep source

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



Shallow source

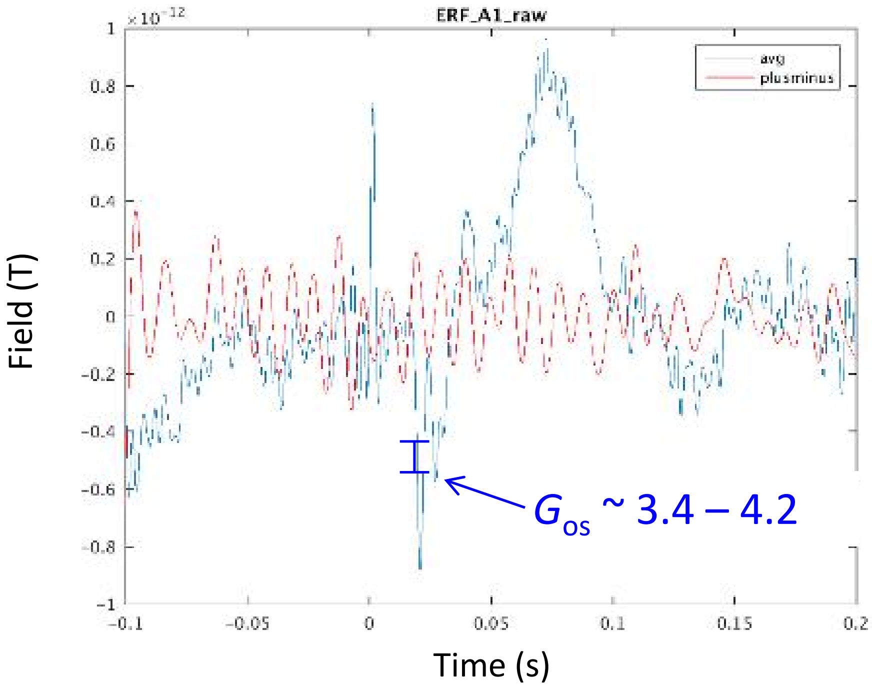
Somatosensory evoked field after ~616 averages and 1–500 Hz band pass filtering

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

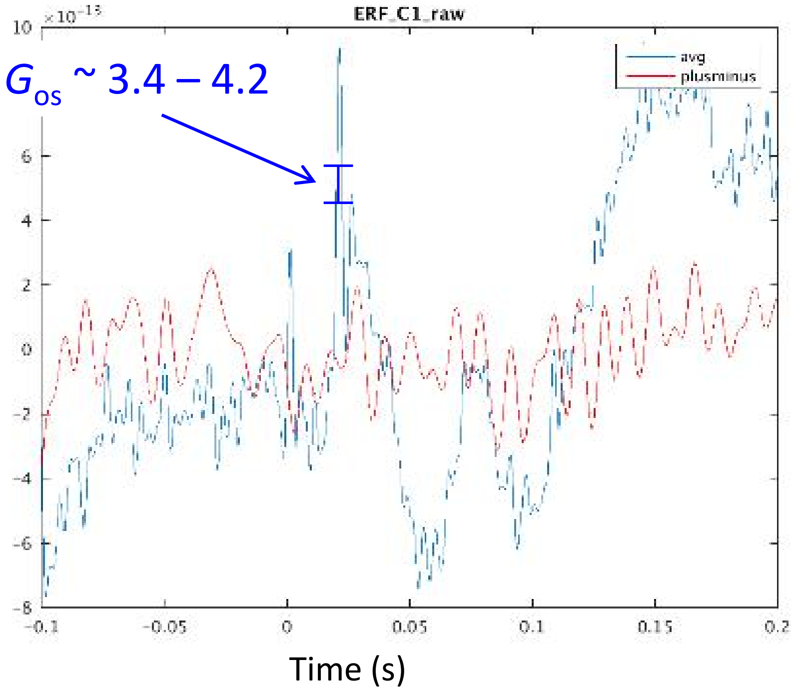
M. Xie, et al., *IEEE Trans. Biomed. Eng.*, vol. 64, pp. 1270, 2017

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



G_{os} ~ 3.4 – 4.2



G_{os} ~ 3.4 – 4.2

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  - 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

Knut och Alice Wallenbergs Stiftelse

Projekt: **"Nanoscale superconducting devices for a closer look at brain activity".**
Beviljat anslag: 34 397 000 kronor under fem år

NeuroSQUID
Nanoscale superconducting devices for a closer look at brain activity

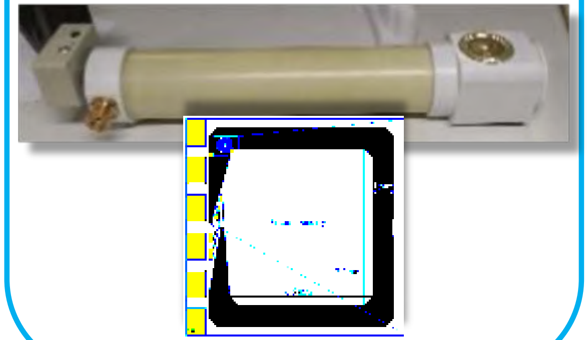
Vision: To make the most sensitive magnetometer capable of operation above 77 K by employing superconducting quantum effects at the nanoscale. Sensors based on this technology will lead to a paradigm shift in neuroimaging. World-leading competences and facilities will come together to explore the fundamental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

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

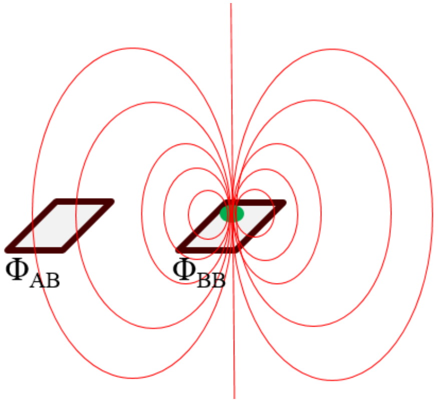
NatMEG
Karolinska Institutet
MedTech West
GÖTEBORGS UNIVERSITET
CHALMERS
MC2 Microtechnology and Nanoscience

NeuroSQUID

Cryostat and sensors

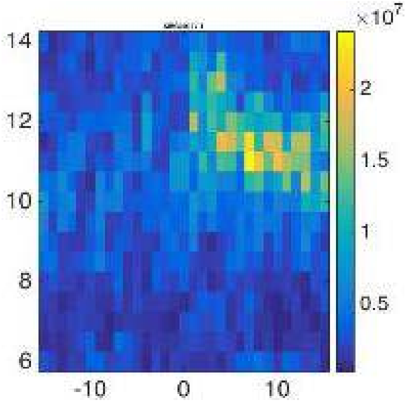


Crosstalk



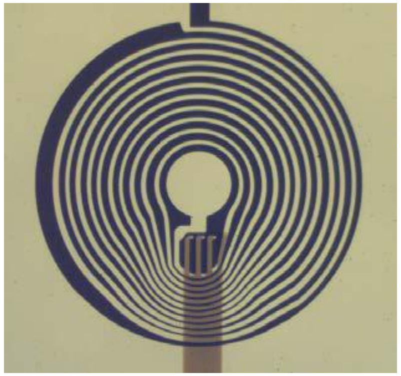
Head phantom measurements

Preliminary alpha



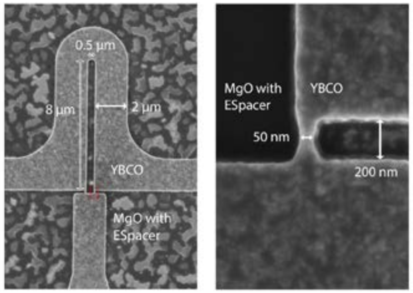
Next step:

Flux transformers



Next step:

Nanowire-based SQUIDs



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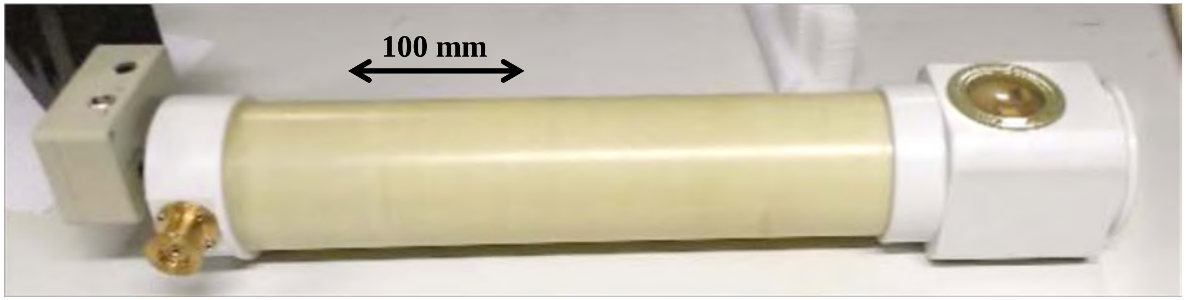
NeuroSQUID

Cryostat

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

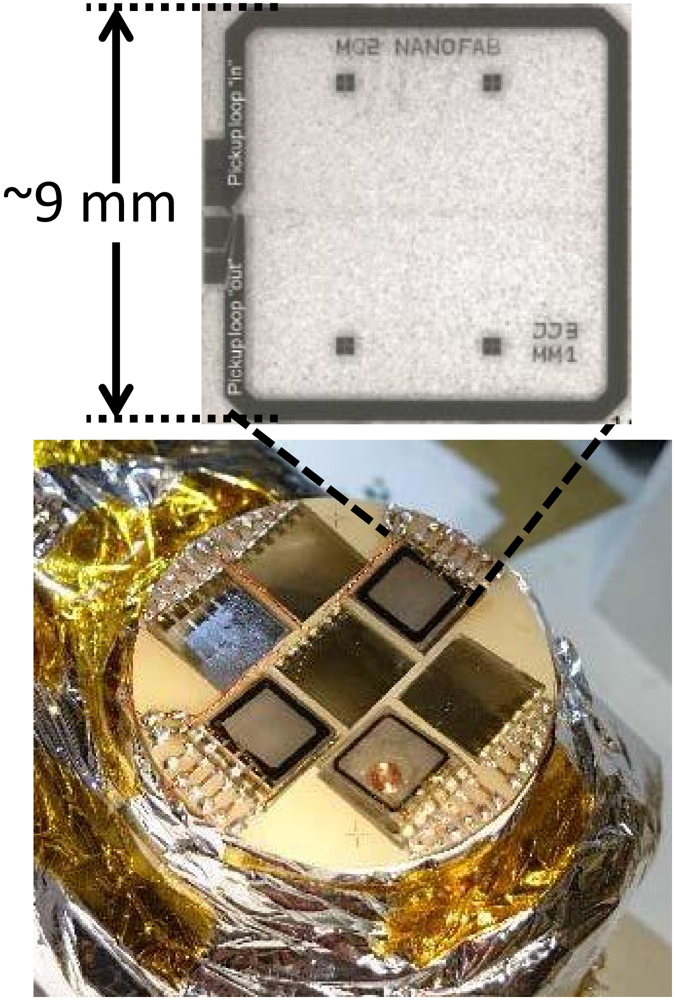
Cryostat – outer part and inner guts

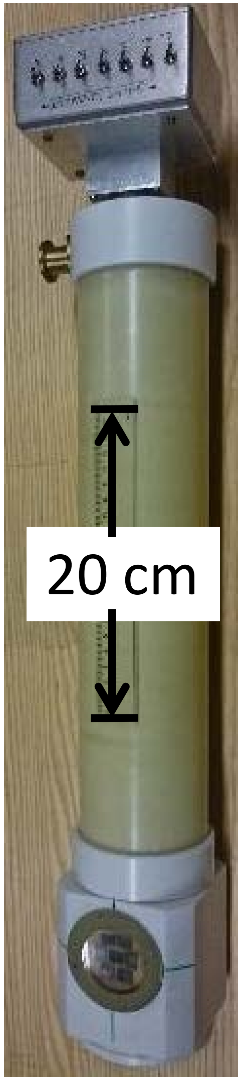
- Sapphire window on inner LN2 container
- 7 sapphire wedges on d.o. holding SQUIDs
  - Dense, hexagonal pattern (2 mm edge-to-edge)
  - Tilted towards center
- 3 x 3-channel electronics from Magnicon



NeuroSQUID

Parts and pieces

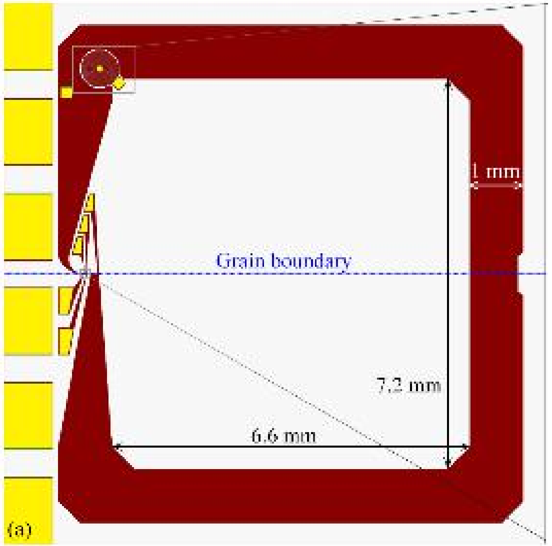


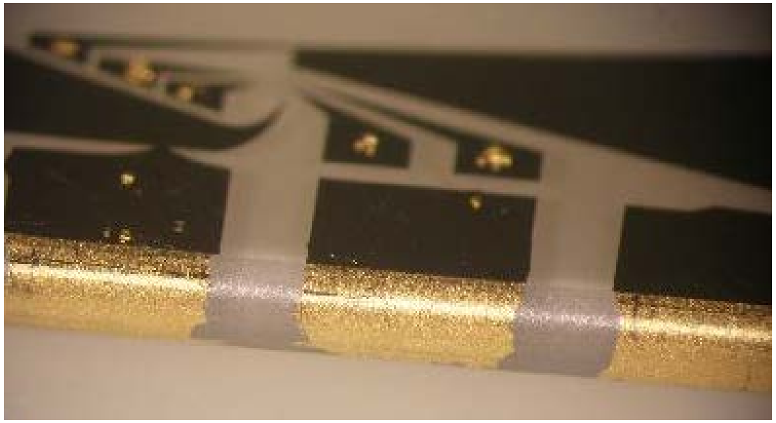


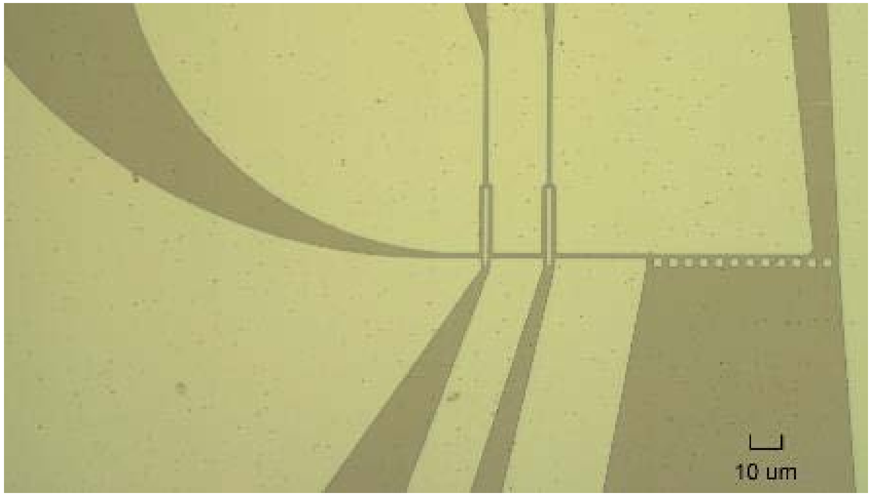
NeuroSQUID

High-T_c SQUID magnetometer

- Single layer $YBa_2Cu_3O_{7-x}$ (YBCO) thin film magnetometer with directly coupled pickup loop
- 10×10 mm^2 STO bicrystal substrate
- 2 grain boundary Josephson junction dc SQUIDs per chip
- High I_CR_n product: 120 – 250 µV at 77 K
- Rounded gold edges to contact from the side

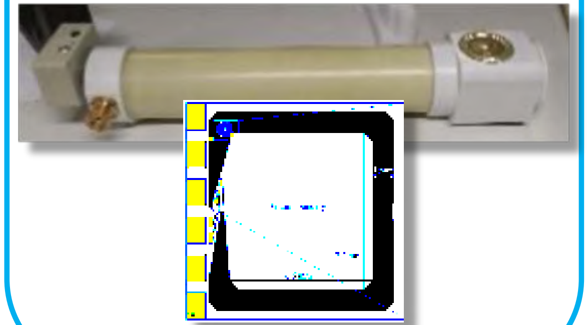




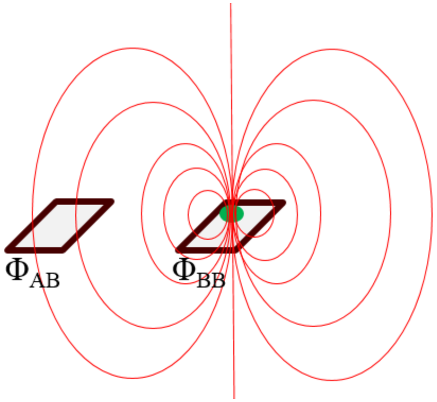


NeuroSQUID

Cryostat and sensors

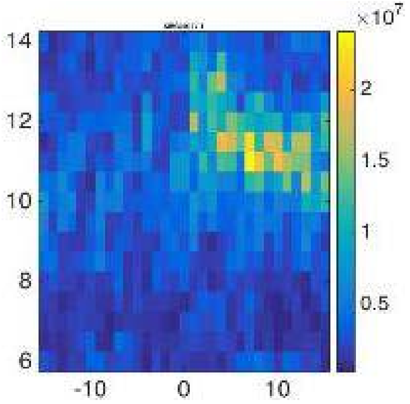


Crosstalk



Head phantom measurements

Preliminary alpha



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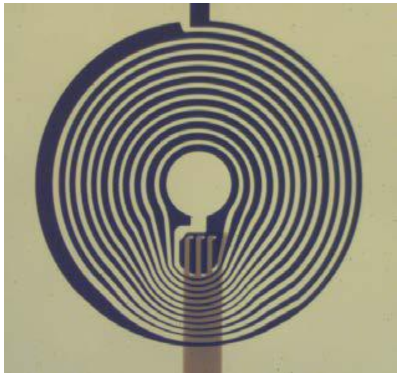

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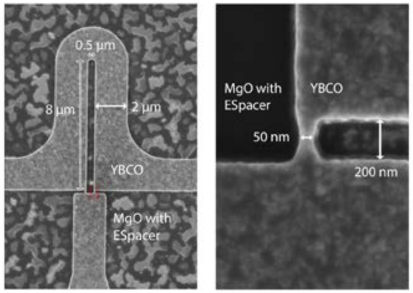
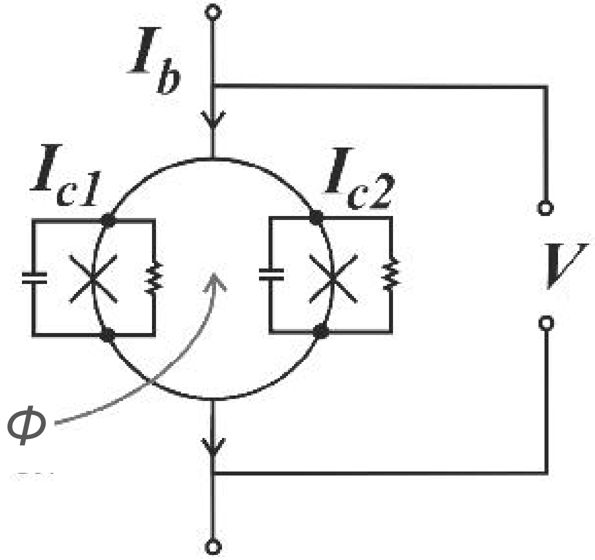
Nanowire-based SQUIDs



NeuroSQUID



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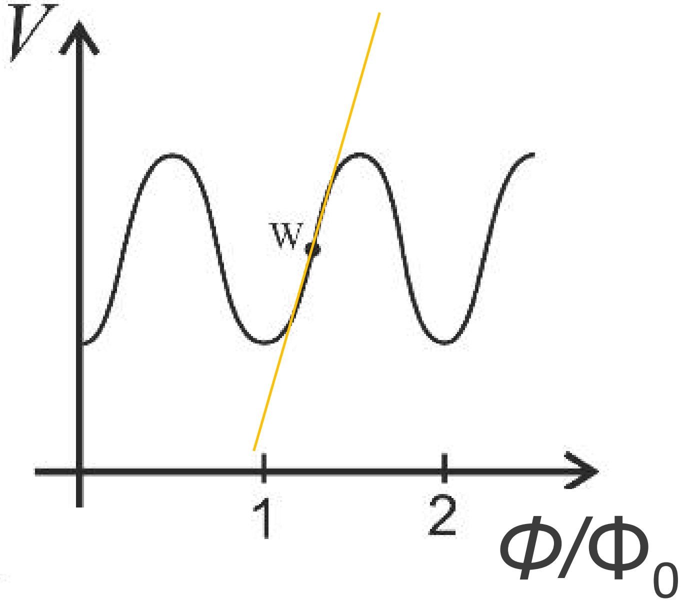
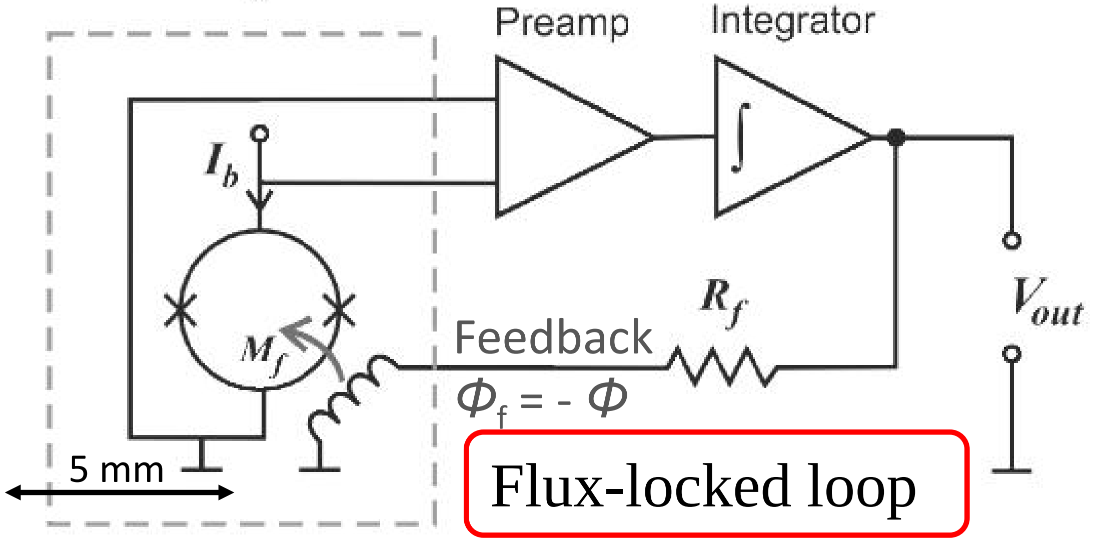
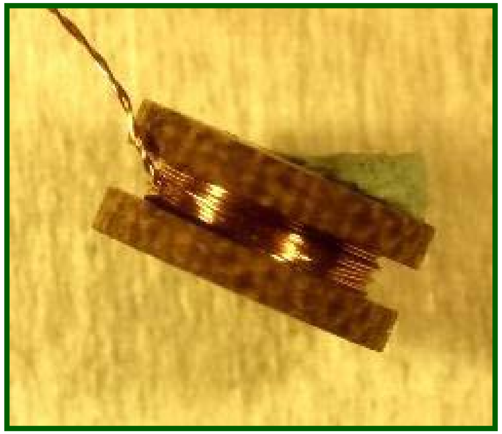




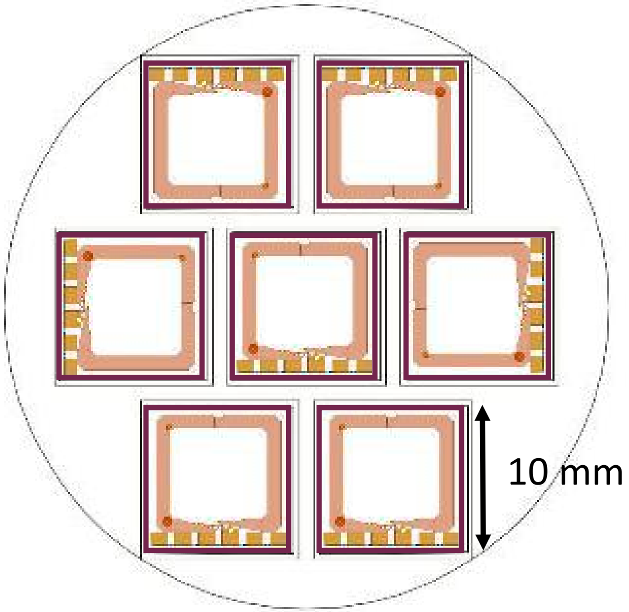
Flux-locked loop

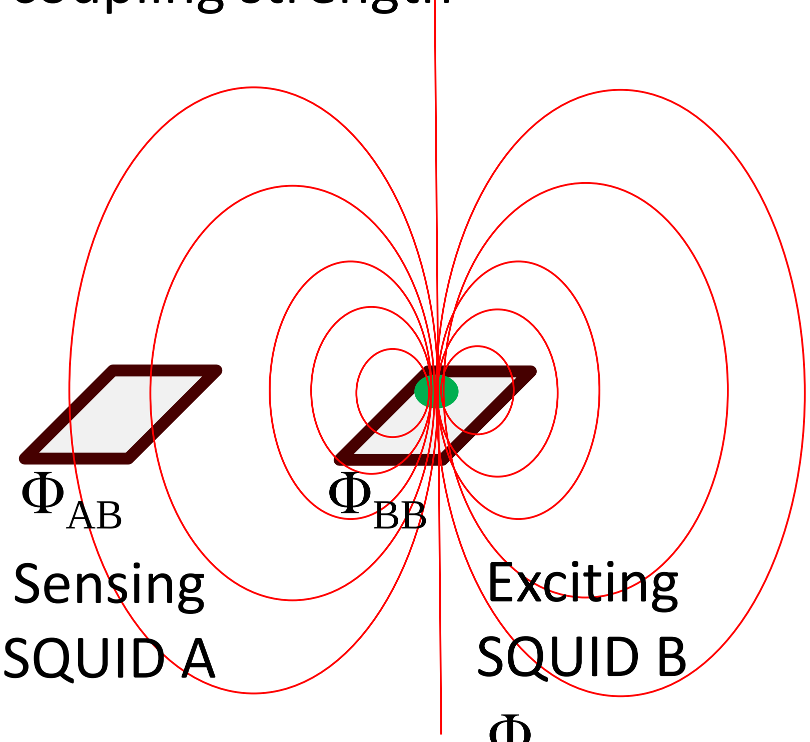


NeuroSQUID

Criteria for feedback

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





$$\text{Crosstalk } C_{AB} = \frac{\Phi_{AB}}{\Phi_{BB}}$$

Paper: S. Ruffieux et al., Supercond. Sci. Technol. **30** (2017) 054006

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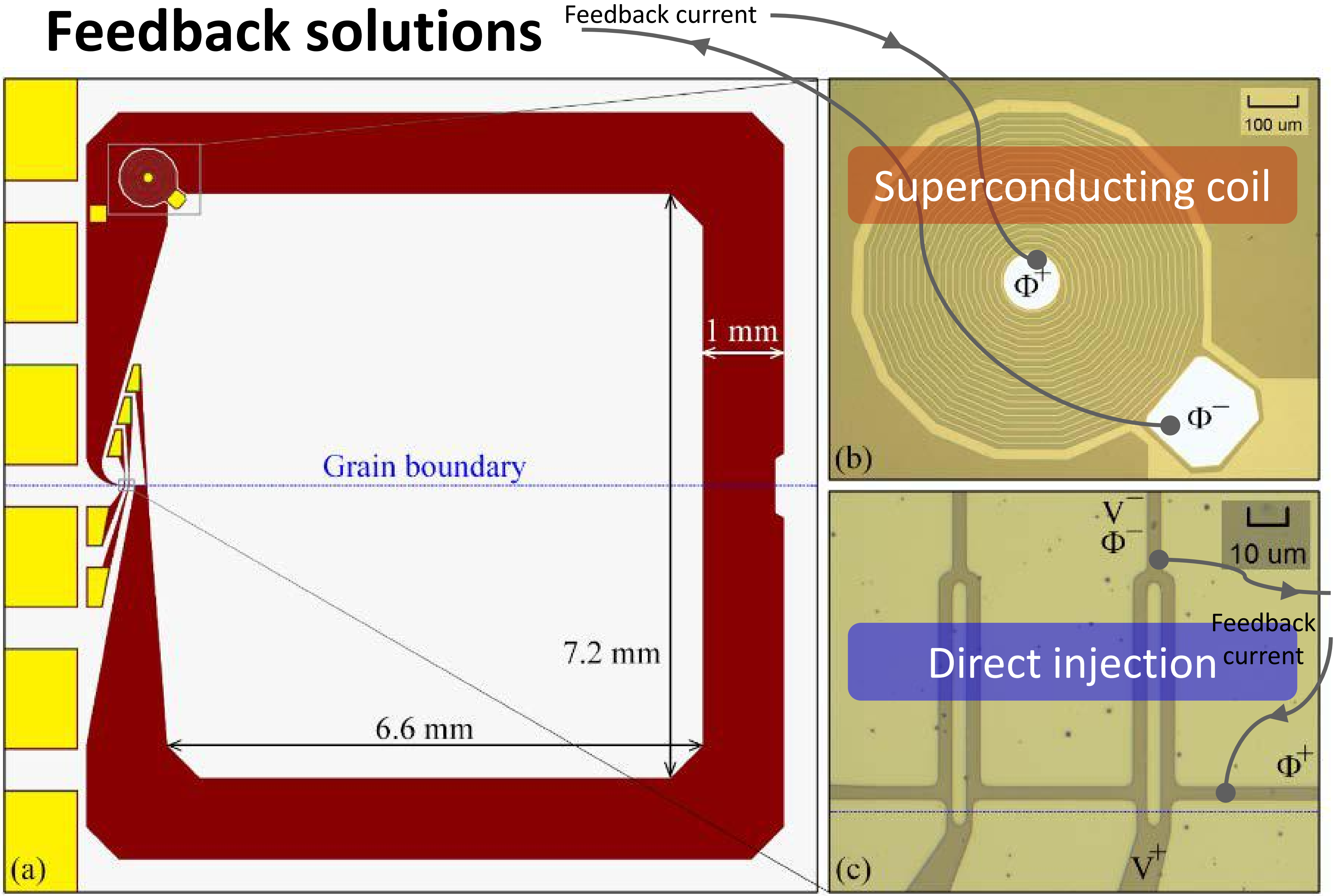
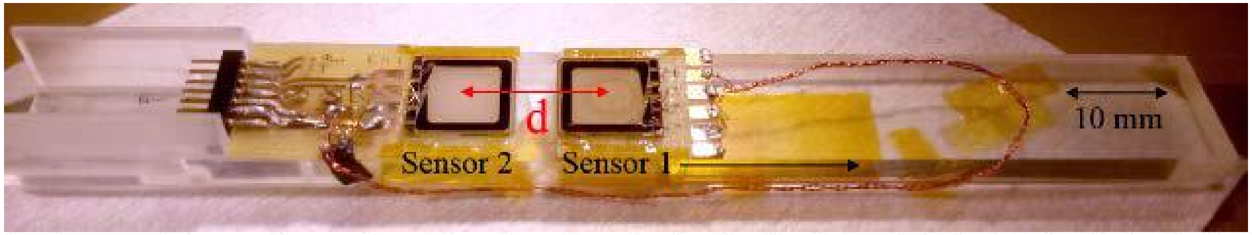
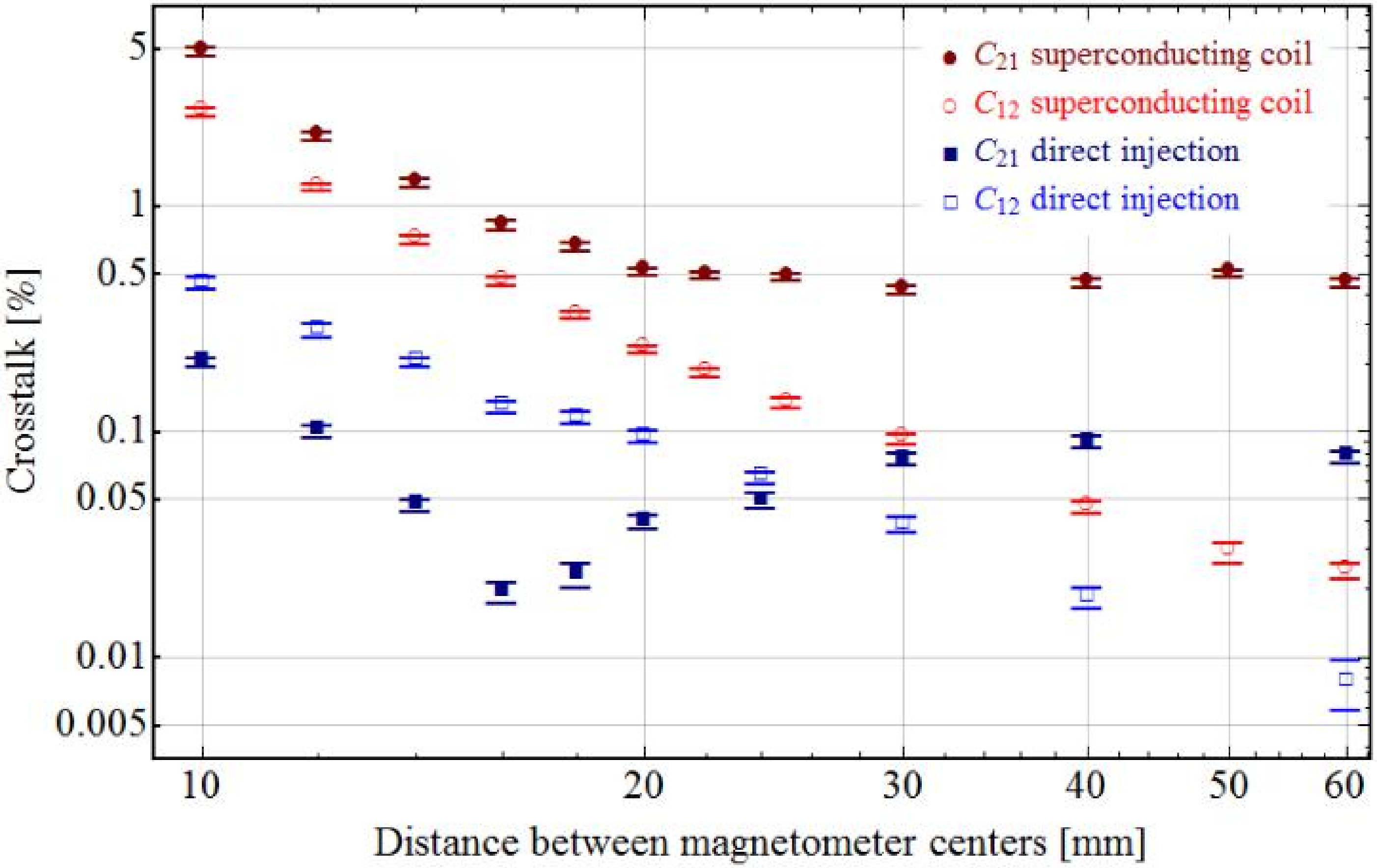
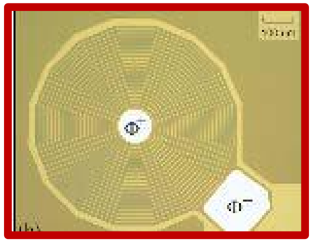
Feedback solutions

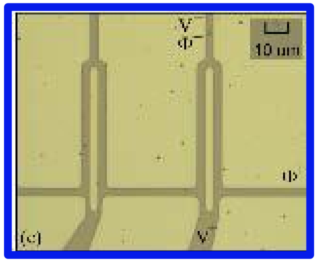


Crosstalk NeuroSQUID









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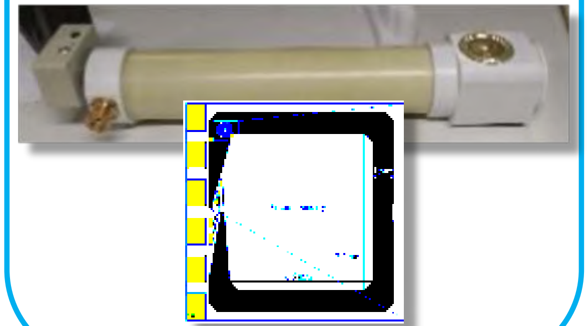
NeuroSQUID

Cryostat and sensors



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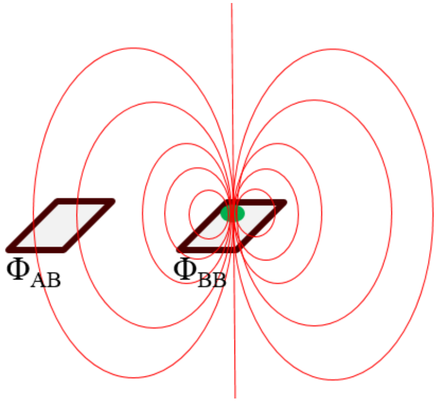
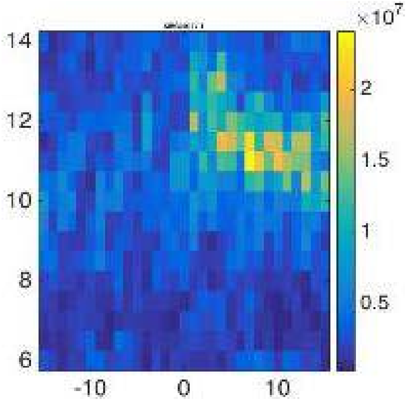


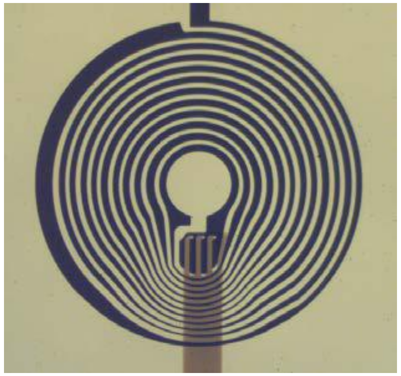
Head phantom measurements

Preliminary alpha



Next step:

Flux transformers



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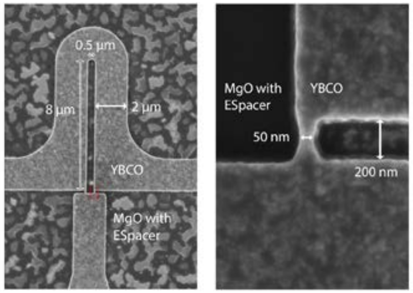
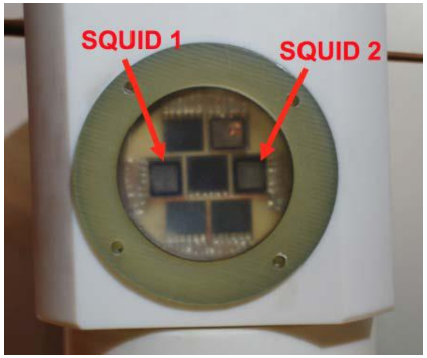
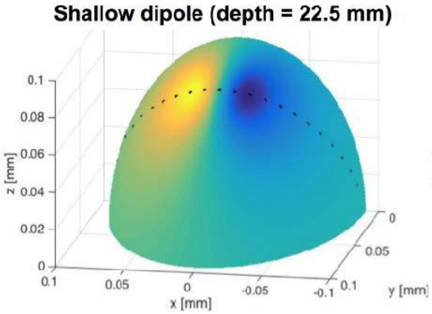
Nanowire-based SQUIDs

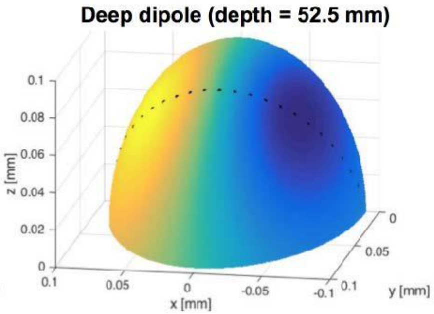


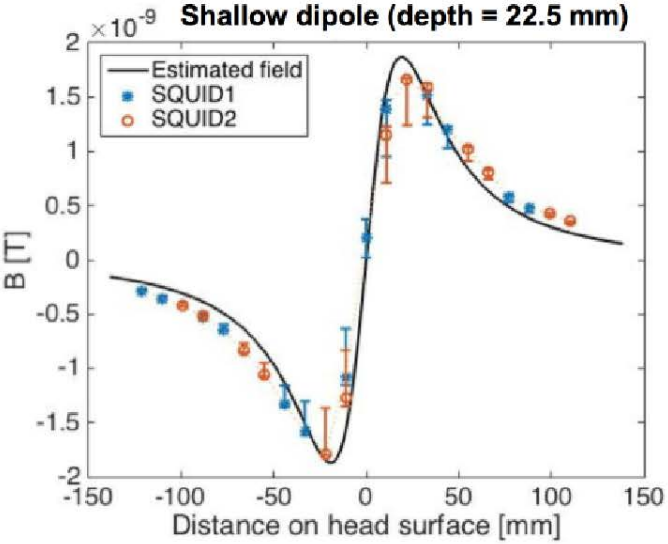
NeuroSQUID

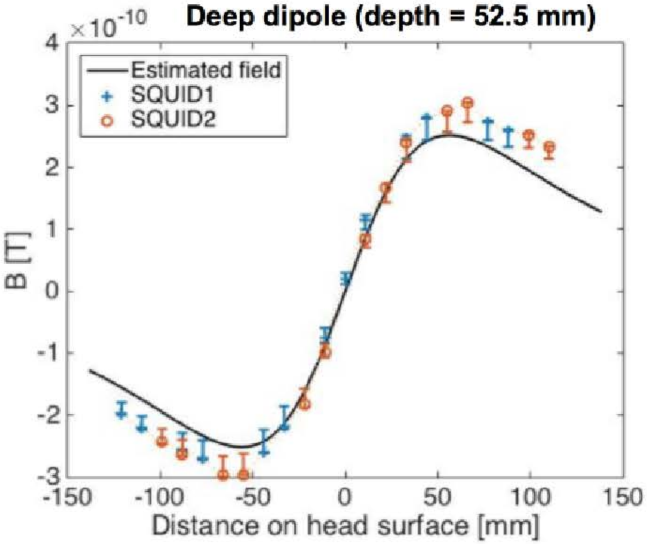
2 Channel phantom measurements











NeuroSQUID

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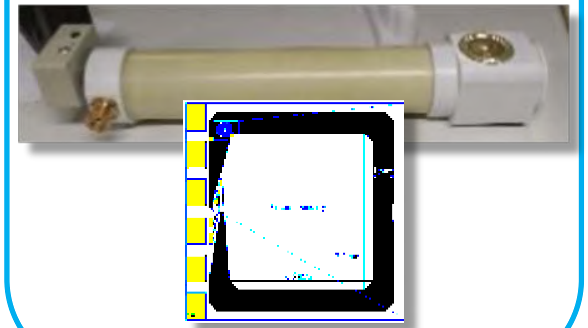

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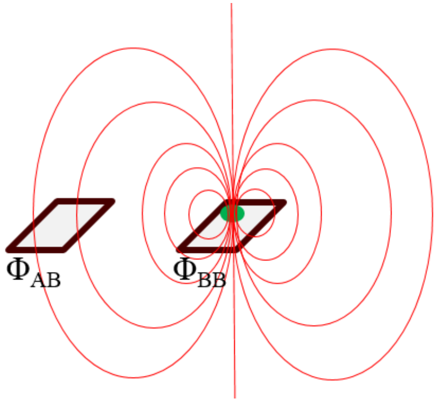

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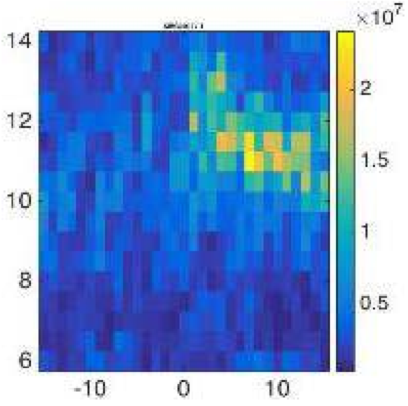

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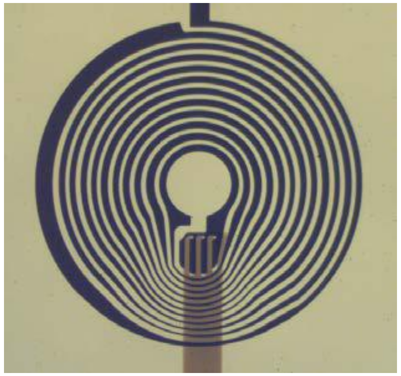
Flux transformers



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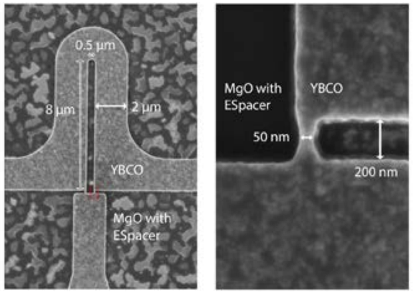

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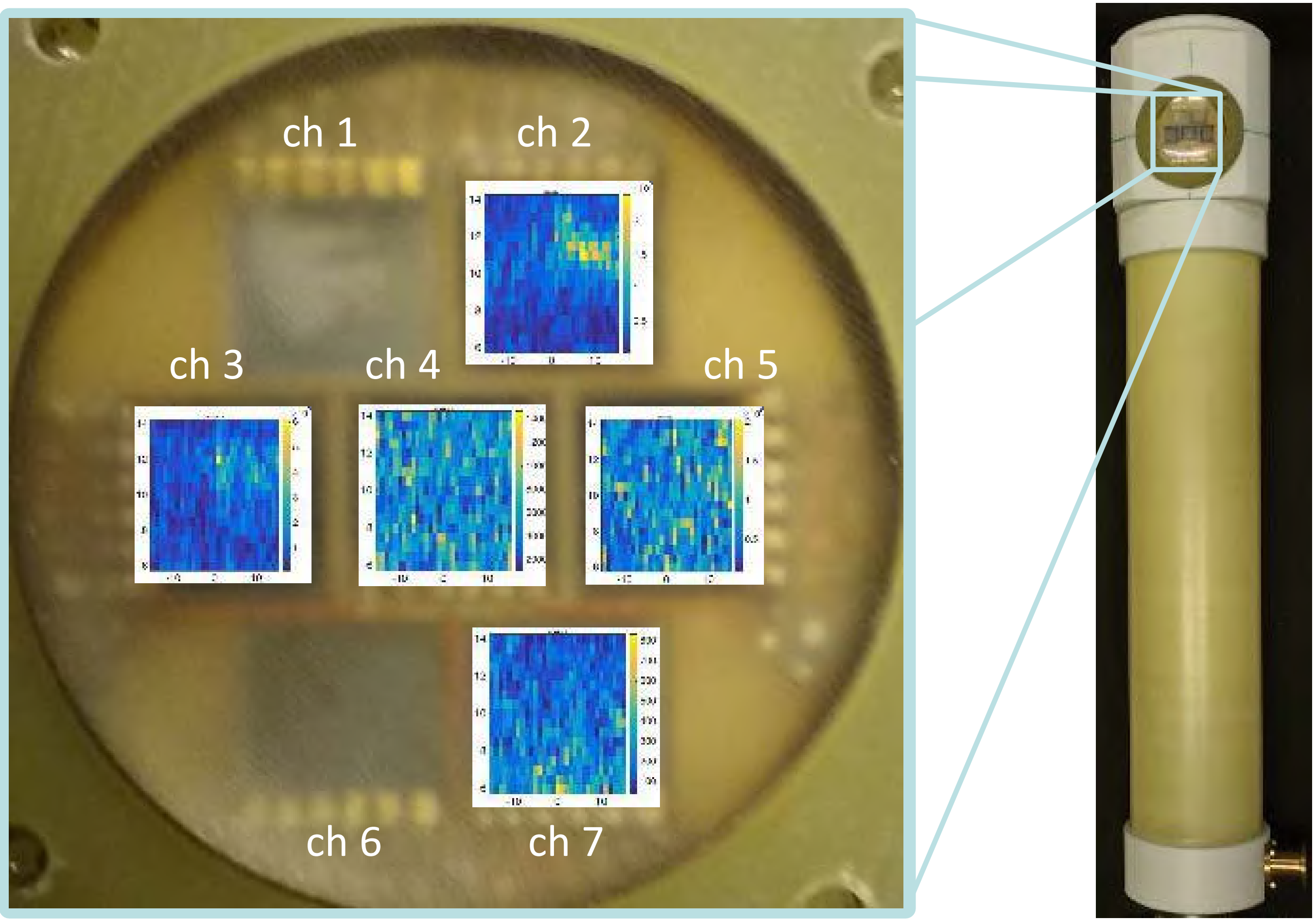
NeuroSQUID

Preliminary measurements on alpha

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

NeuroSQUID

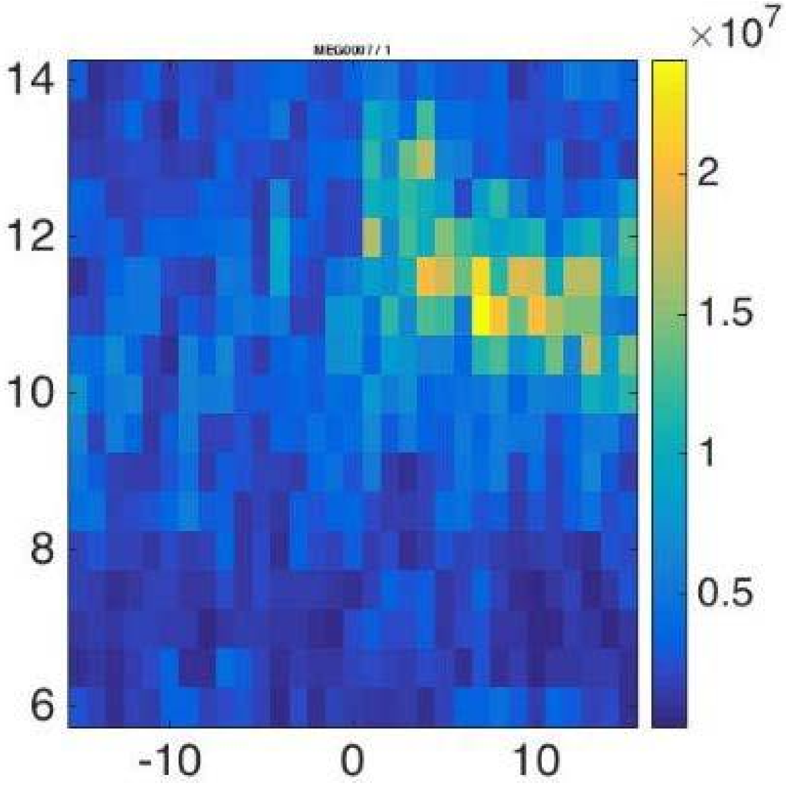
Preliminary measurements on alpha



NeuroSQUID

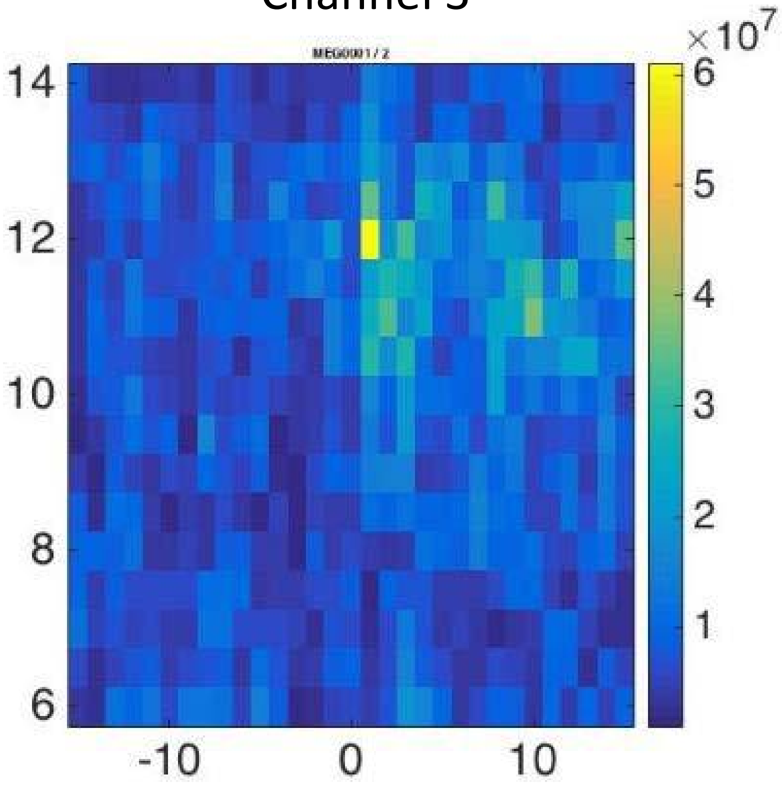
Preliminary measurements – increase in alpha seen in channel 2 & 3

Channel 2



eyes open | eyes closed
30 seconds 30 seconds

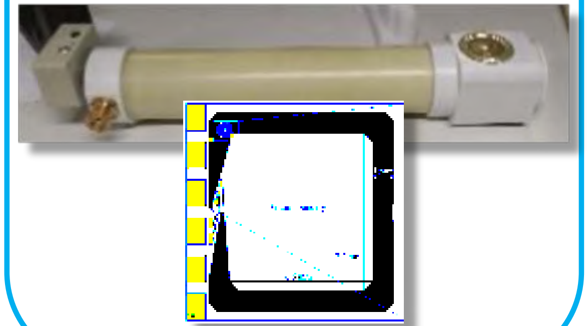
Channel 3



eyes open | eyes closed
30 seconds 30 seconds

NeuroSQUID

Cryostat and sensors



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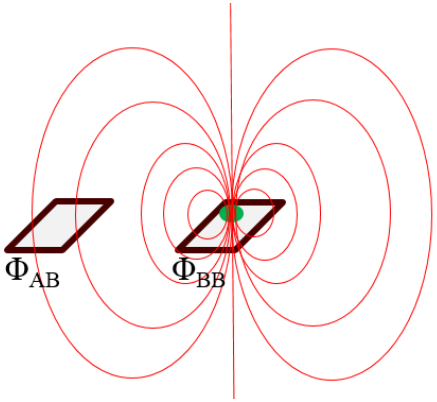

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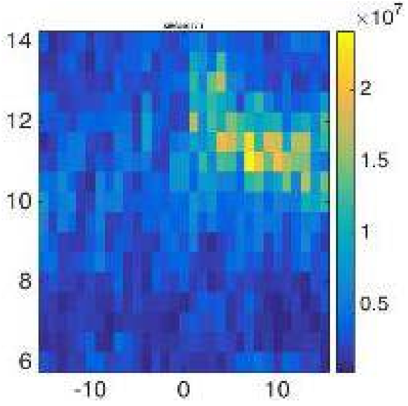

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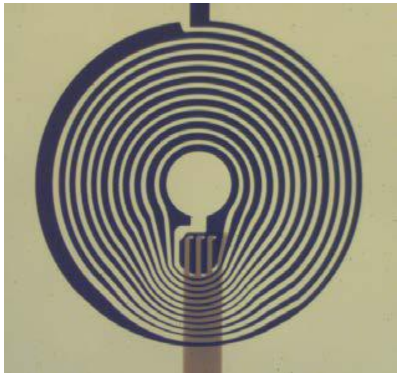
Flux transformers



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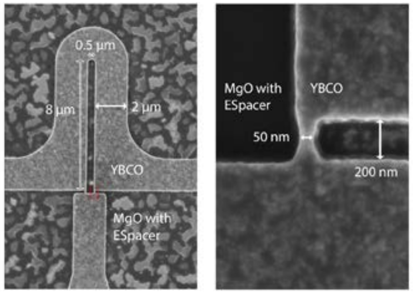
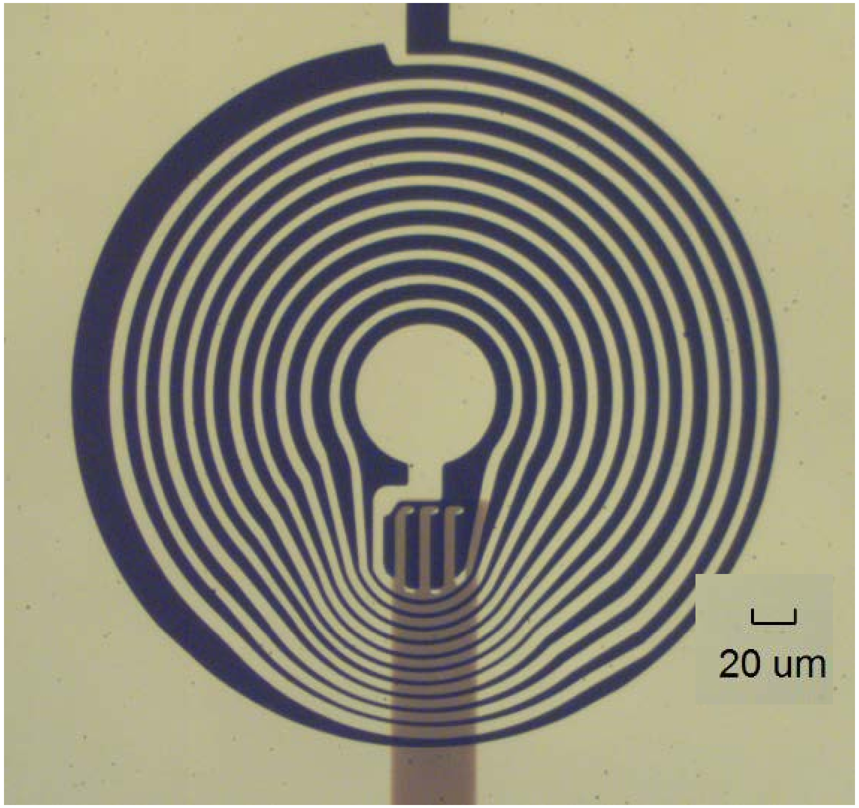
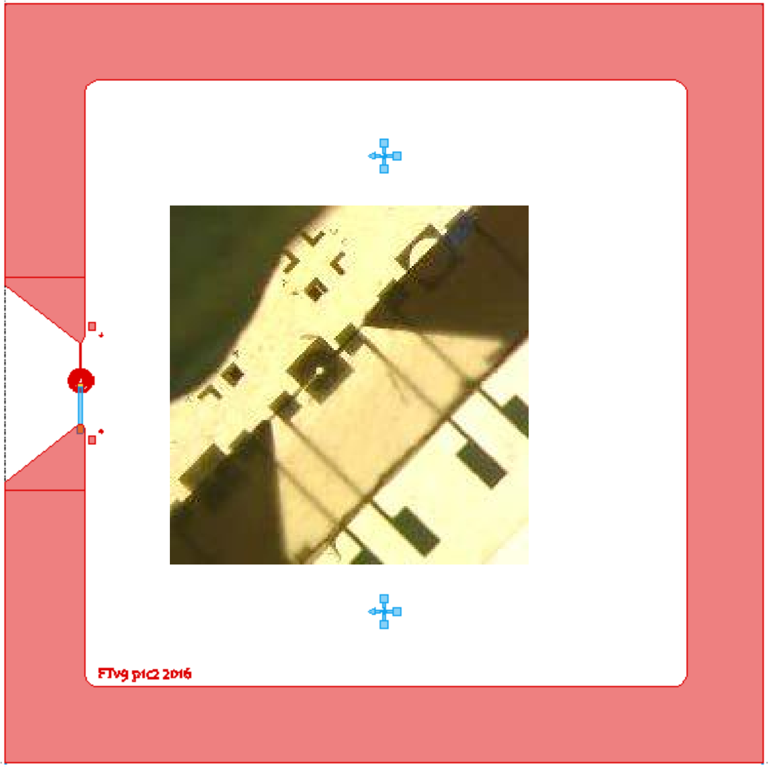


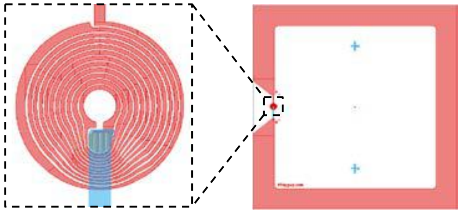
NeuroSQUID

Flux transformers

- Increase effective area A_{eff}
- Multi-layer device

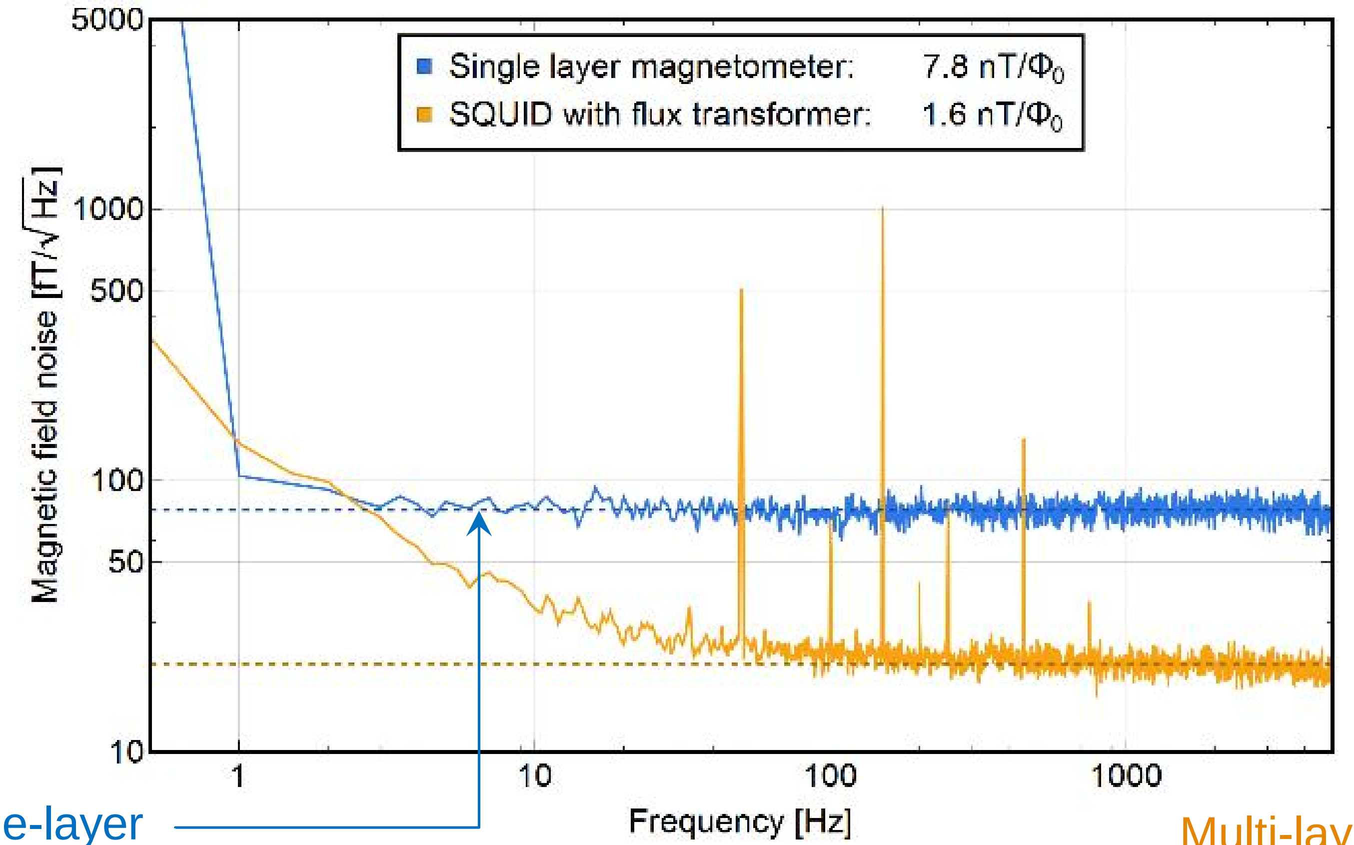






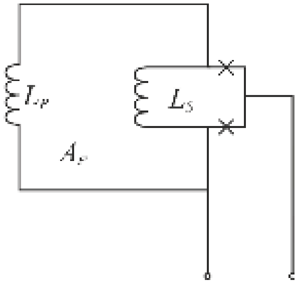
Flip-chip device

Flux transformers (for flip-chip) NeuroSQUID



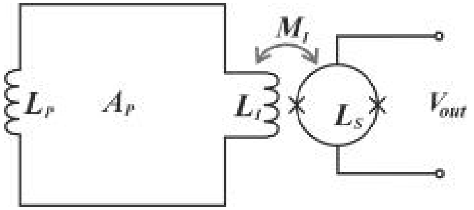
Single-layer

Multi-layer FT flip-chip



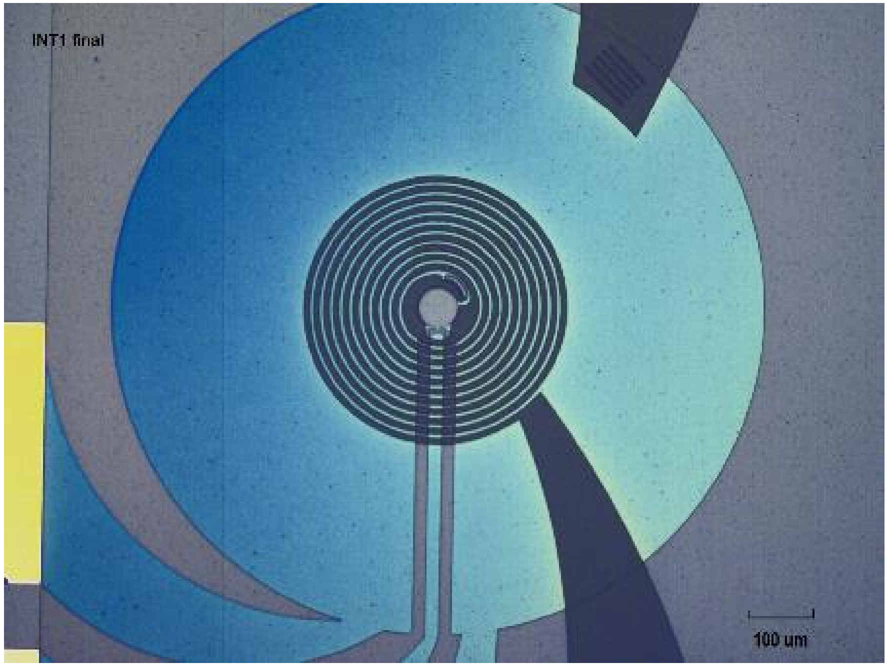
- Easy to fabricate
- Limited effective area / sensitivity

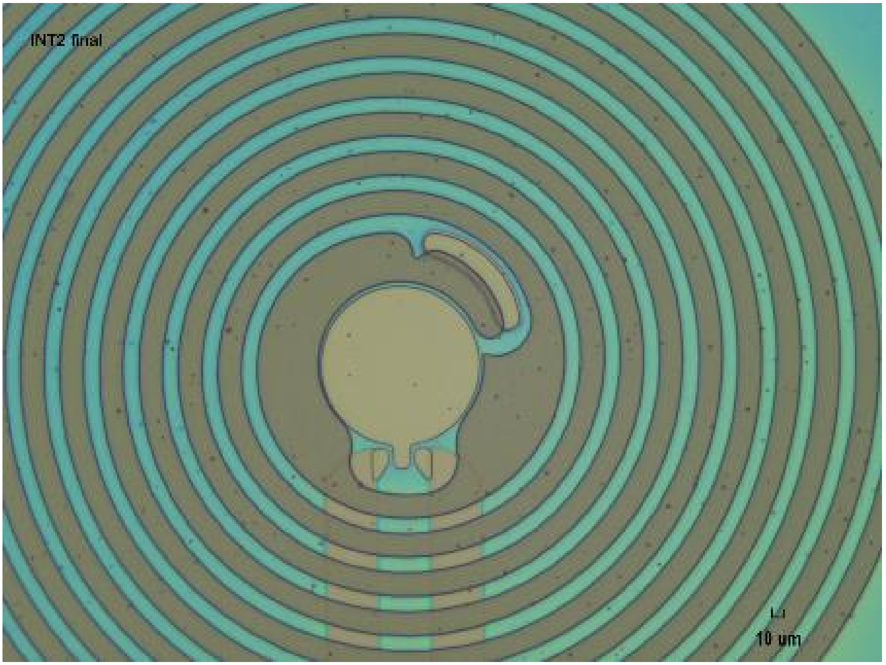
- Better effective area / sensitivity
- Challenging fabrication



Integrated flux transformer

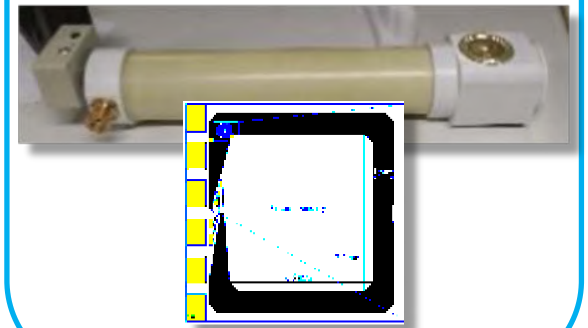
- Single chip
- Increased coupling





NeuroSQUID

Cryostat and sensors



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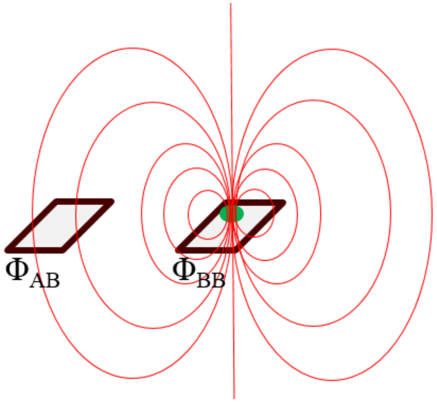

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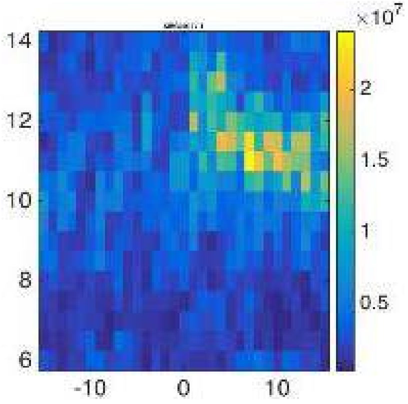
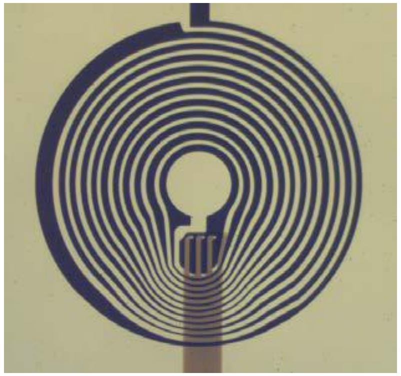


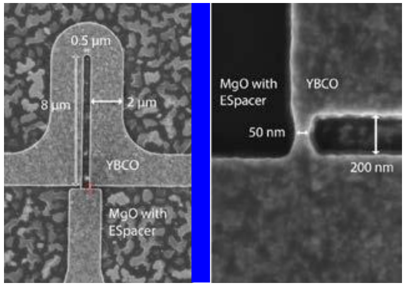
Next step:

Flux transformers



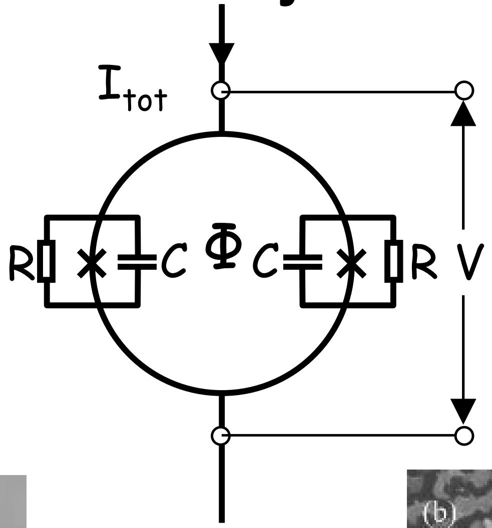
Next step:

Nanowire-based SQUIDs

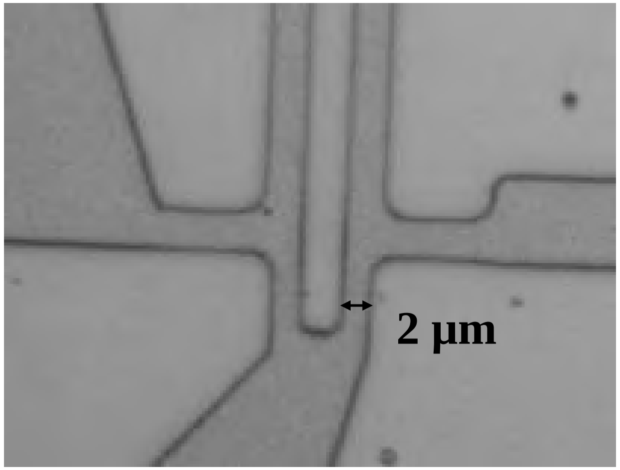


NeuroSQUID

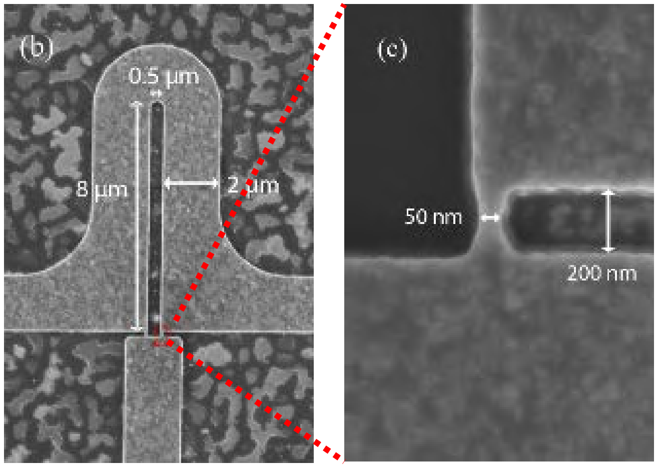
Moving from bicrystal grain boundary to nanowire junctions



Bicrystal grain boundary junctions



Nanowire junctions



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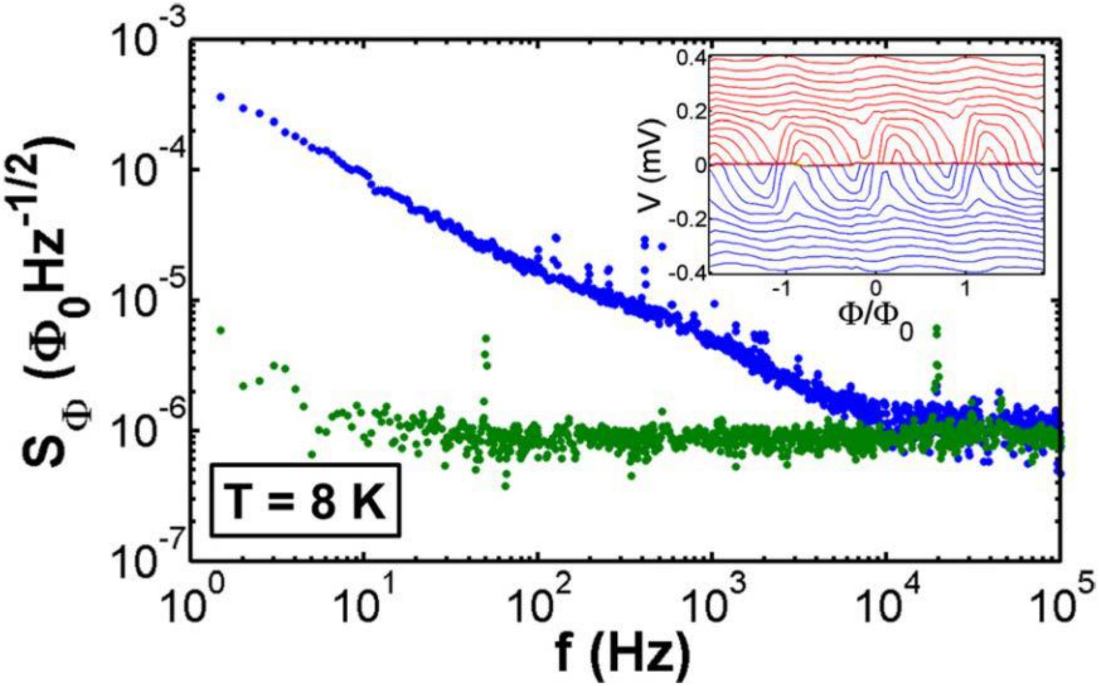
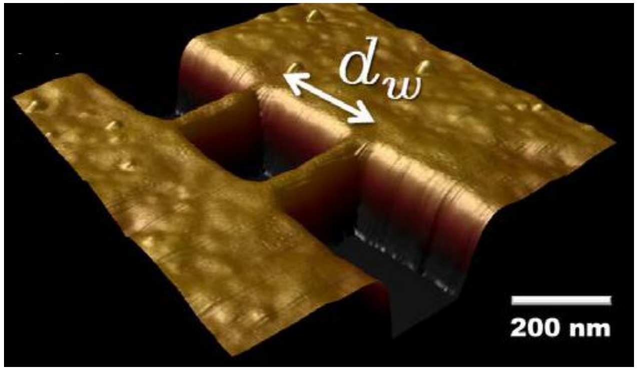
Motivation: Previous work* on high-T_c nano-SQUIDs





- 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?

*) R. Arpaia, et al., *Appl. Phys. Lett.*, vol.104, 2014

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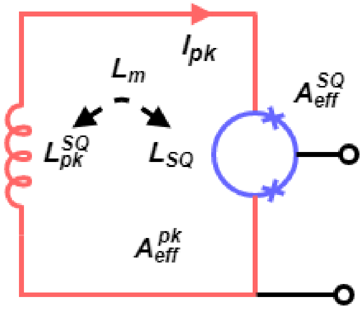
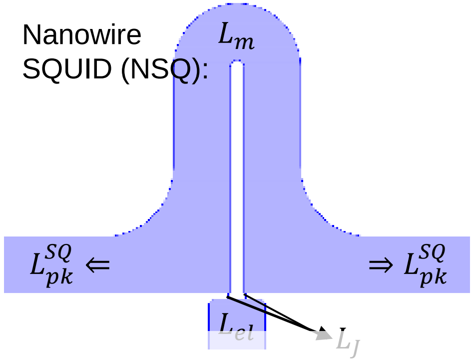
NeuroSQUID

Three approaches for coupling

Approach I

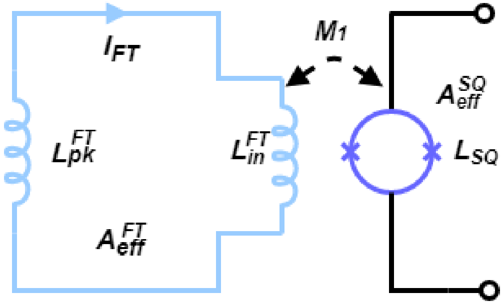


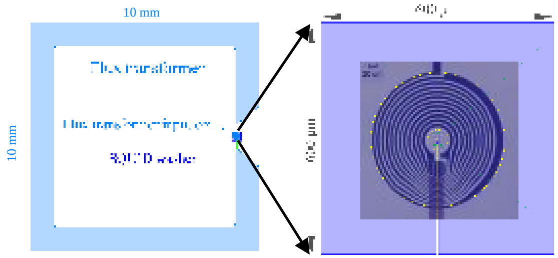
Nanowire SQUID (NSQ):



A_{eff} = 0.09 mm²
$S_\Phi^{1/2}$ = 55 μΦ$_0$/√Hz
$S_B^{1/2}$ = **1200 fT/√Hz**

Approach II: with a flux transformer

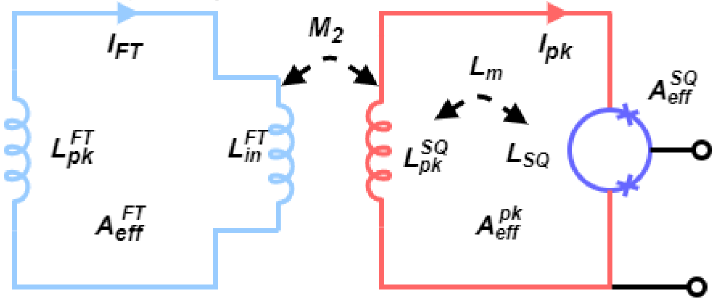




M. Chukharkin, et al., *IEEE Trans. Appl. Supercond.*, vol. 23, pp. 1602704, 2013

A_{eff} = 0.16 mm²
$S_\Phi^{1/2}$ = 35 μΦ$_0$/√Hz
$S_B^{1/2}$ = **480 fT/√Hz**

Approach III: A two-level coupling method

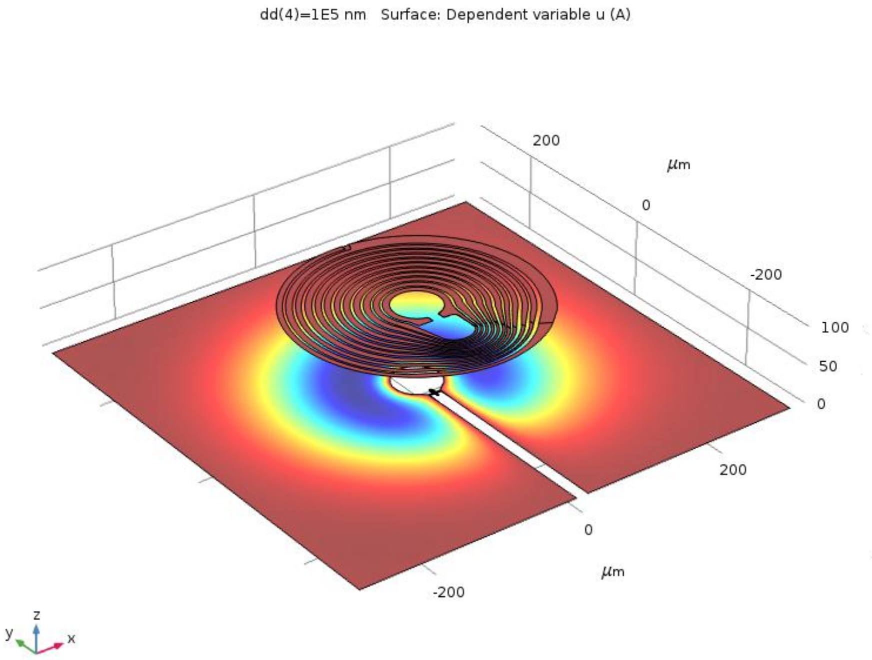


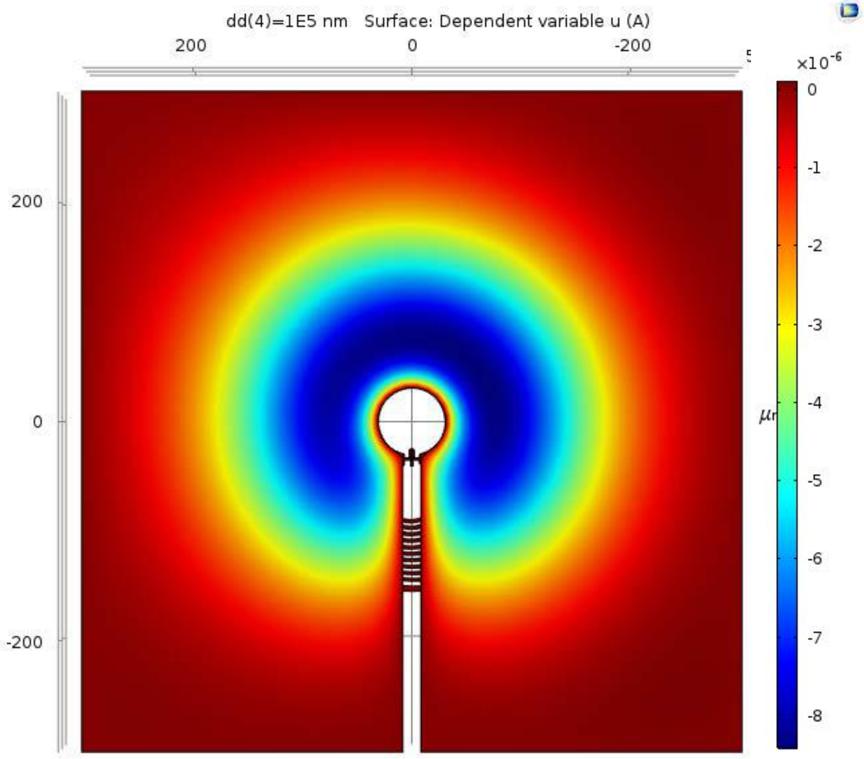
A_{eff} = 0.46 mm²
$S_\Phi^{1/2}$ = 55 μΦ$_0$/√Hz
$S_B^{1/2}$ = **240 fT/√Hz**

M. Xie, et al., *Supercond. Sci. Technol.*, vol. 30, pp. 115014, 2017

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

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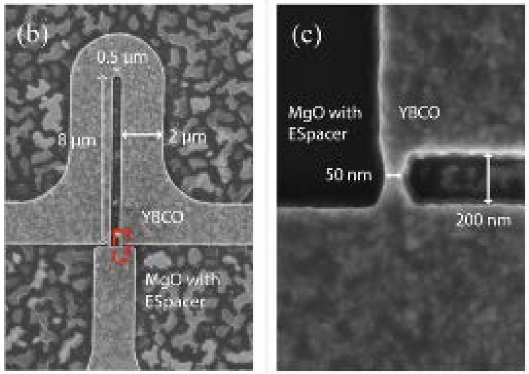
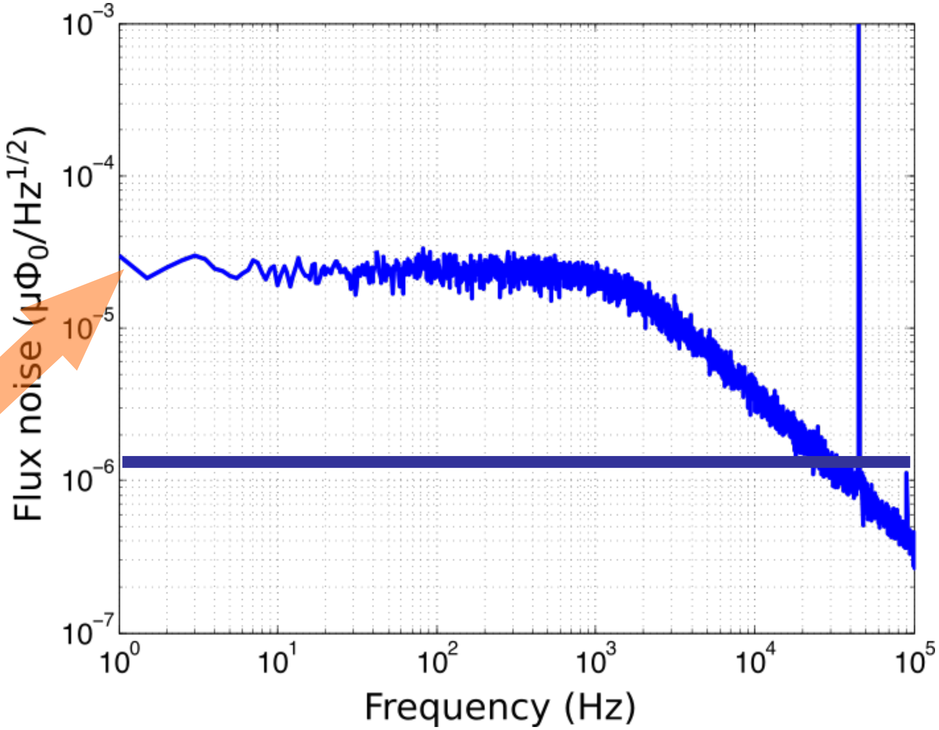
NeuroSQUID

Noise at 77 K without Au top layer



50 nm YBCO:

- no Au capping
- no pick up loop
- $V_\phi \sim 15\ \mu V/\phi_0$
- Amp: $S_V^{1/2} \sim 0.4\ nV/Hz^{1/2}$



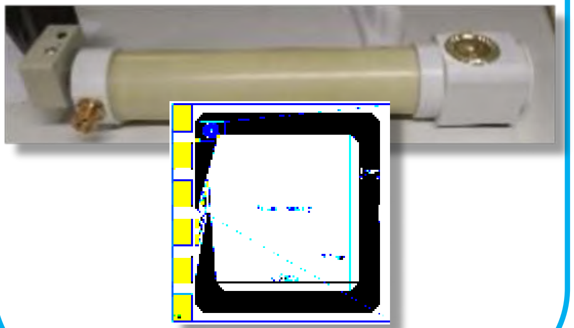
Expected field noise taking achieved effective area $A_{eff} \sim 0.1\ mm^2$: $S_\phi^{1/2} \sim 500\ fT/Hz^{1/2}$

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

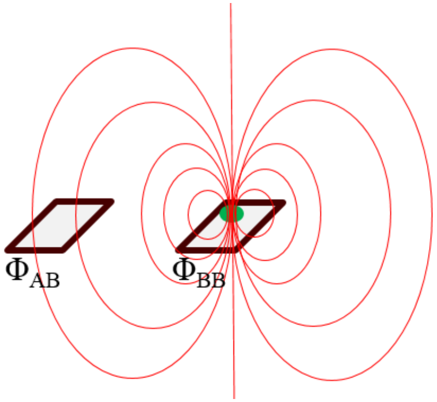
➔SQUID electronics with lower input noise (Cryoton)

NeuroSQUID

Cryostat and sensors

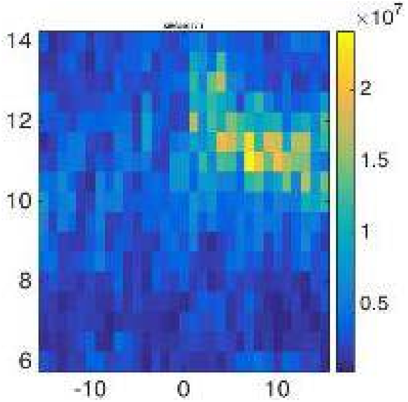


Crosstalk



Head phantom measurements

Preliminary alpha



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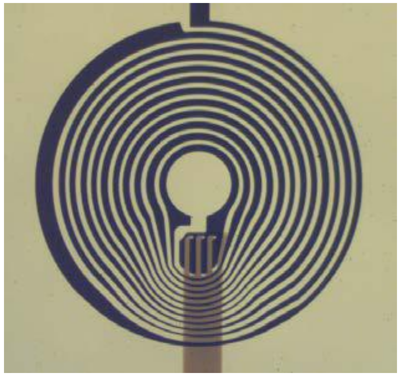
Flux transformers



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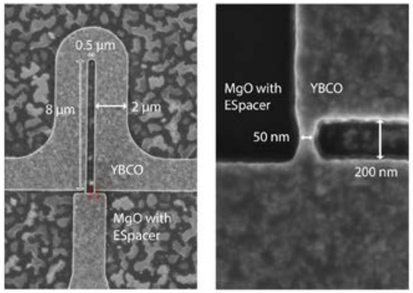

CONCLUSIONS

- We still have to struggle a bit to get further down the road…

- 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 $10\ \mathrm{fT}/\sqrt{\mathrm{Hz}}$ for Ketchen-type coupling

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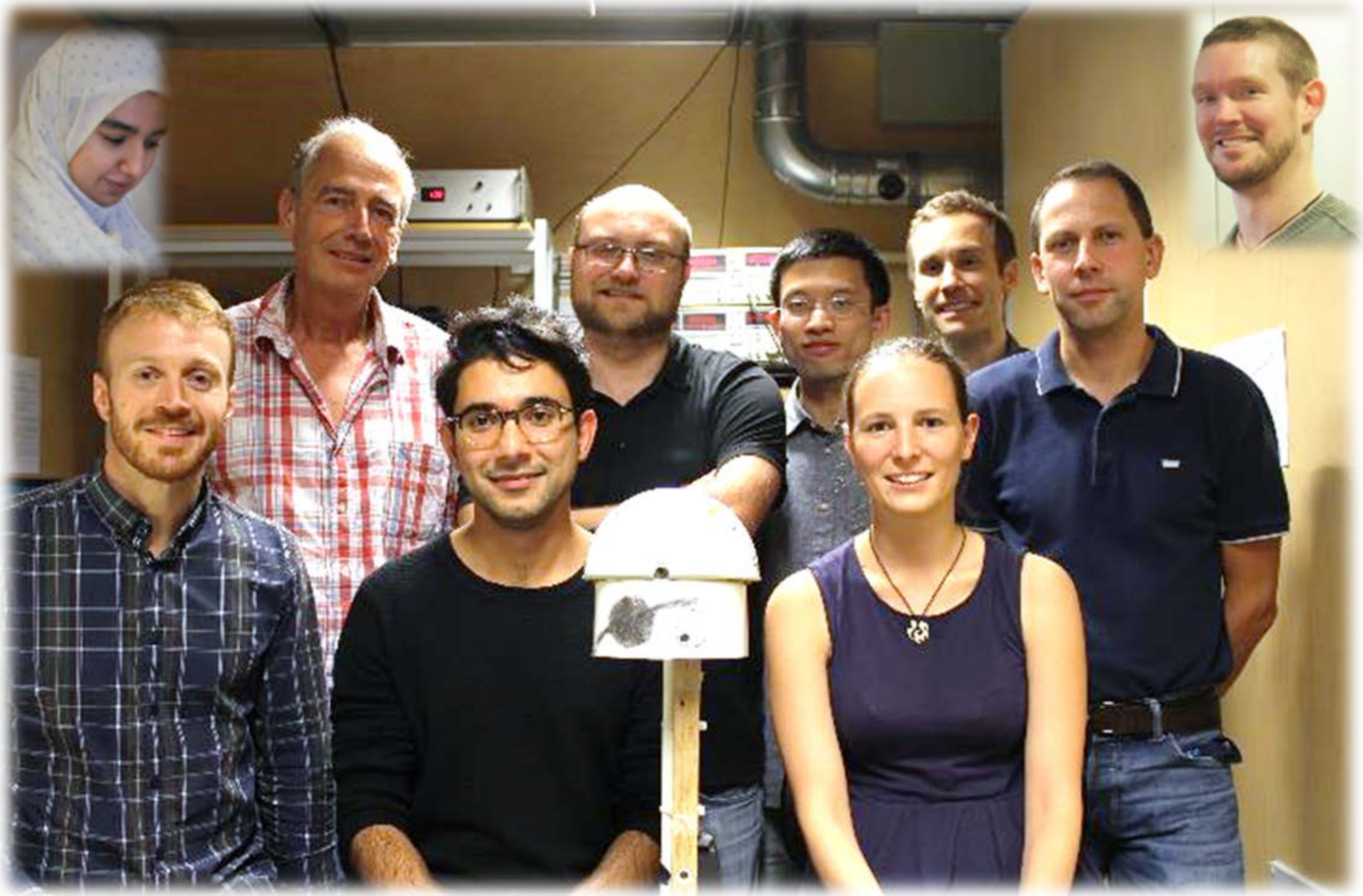
The Chalmers SQUID group



Knut och Alice Wallenbergs Stiftelse

MedTech West

GÖTEBORGS UNIVERSITET

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MC2 Microtechnology and Nanoscience

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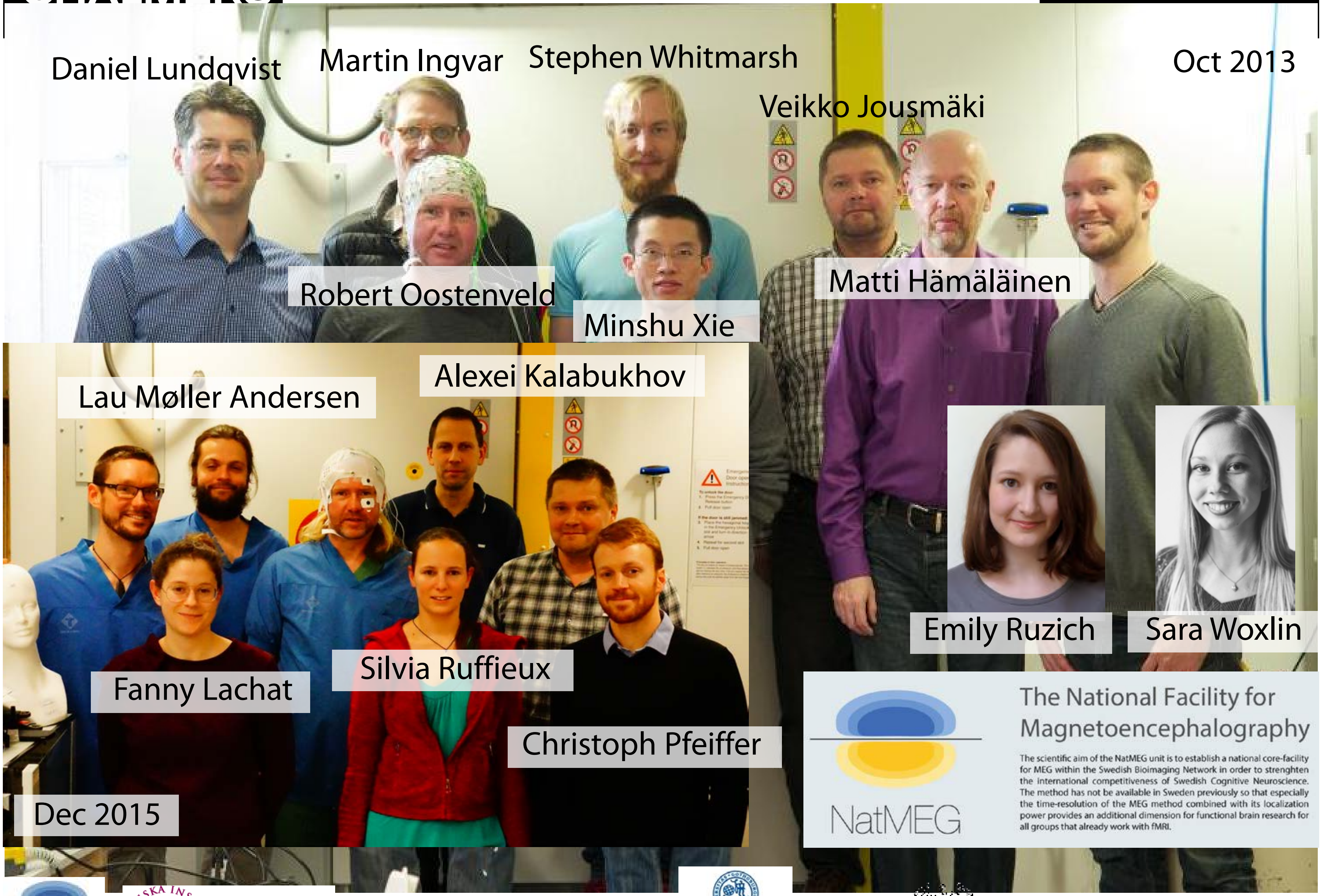

The National Facility for Magnetoencephalography

NatMEG

The scientific aim of the NatMEG unit is to establish a national core-facility for MEG within the Swedish Bioimaging Network in order to strenghten the international competitiveness of Swedish Cognitive Neuroscience. The method has not be 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.

NatMEG Karolinska Institutet MedTech West GÖTEBORGS UNIVERSITET CHALMERS MC2 Microtechnology and Nanoscience

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Thanks!

¿QUESTIONS?