From ECoG to Magnetocorticography:

Optically Pumped Magnetometers for non-invasive, high-resolution imaging

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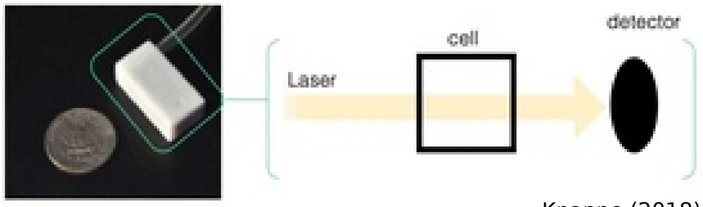
Optically Pumped Magnetometers

1. What are optically pumped magnetometers and what do they measure?
2. Neuroscientific applications around the world
3. Our project at NIH for high spatial and temporal resolution measurements/imaging

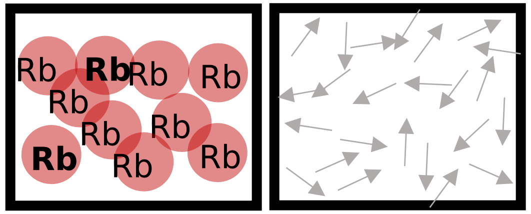
Principle of operation



FieldLine Inc.

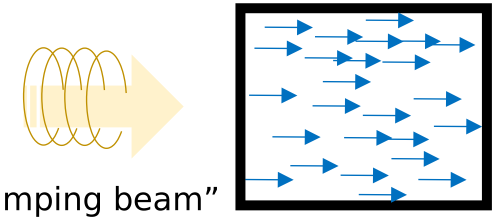
Knappe (2018)

Rubidium (^{87}Rb) vapor cell



^{87}Rb spins oriented randomly

Apply circularly polarized light

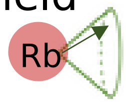


"Pumping beam"

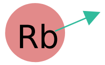
^{87}Rb spins aligned to laser

When aligned, light no longer transfers energy to atoms

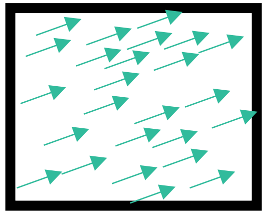
In the presence of a magnetic field

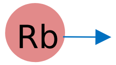


Spins will precess at a known frequency



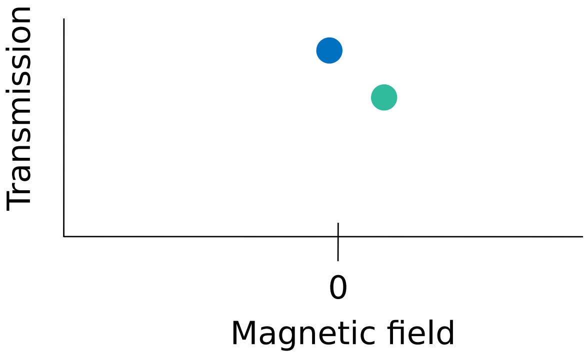
On average…



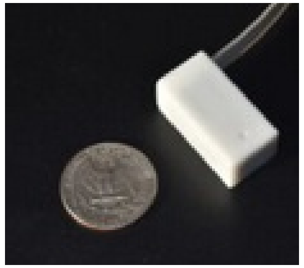


But pumping still occurring!

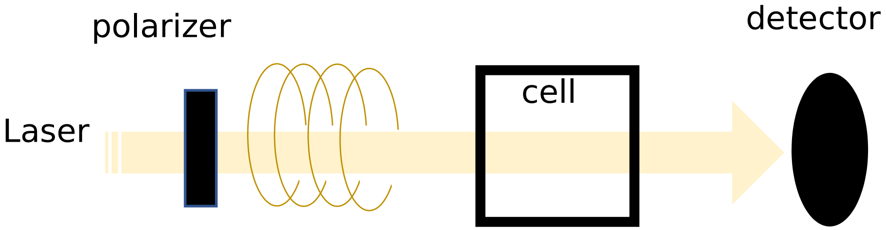
Optical detection through amount of transmitted light

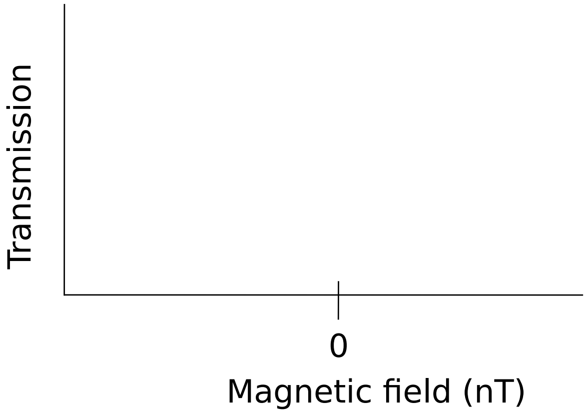


Principle of operation II

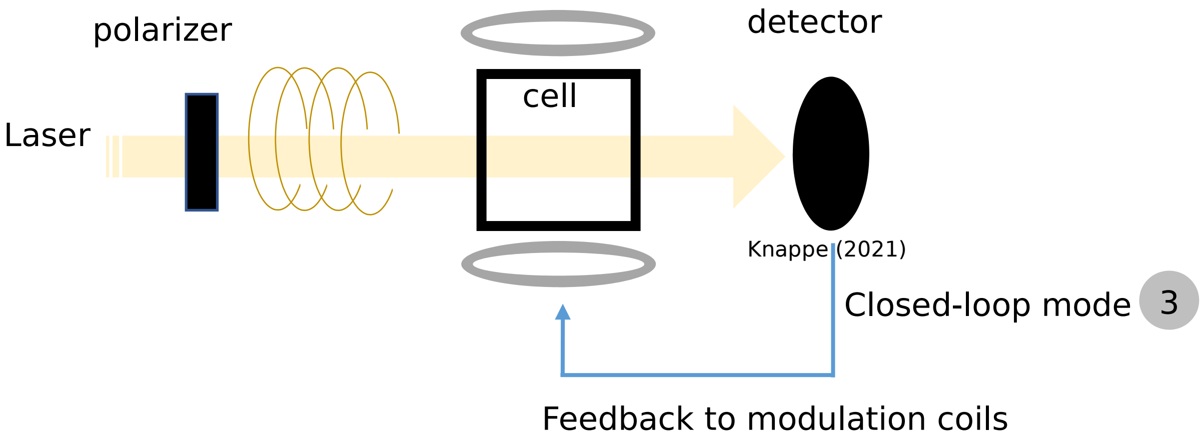


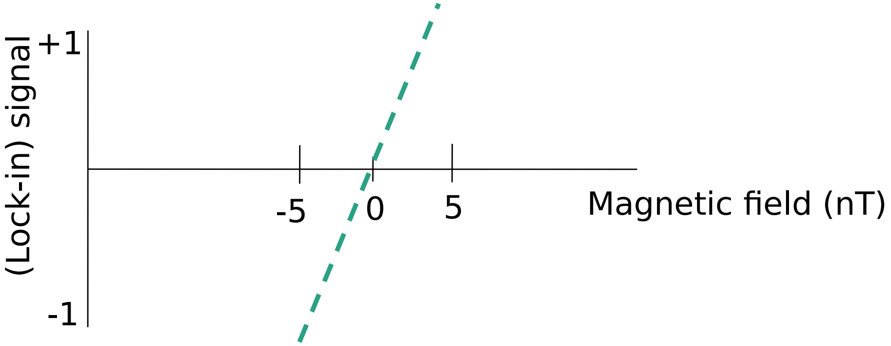
FieldLine Inc.





Magnetometer sensitive to the magnetic field in a specific direction

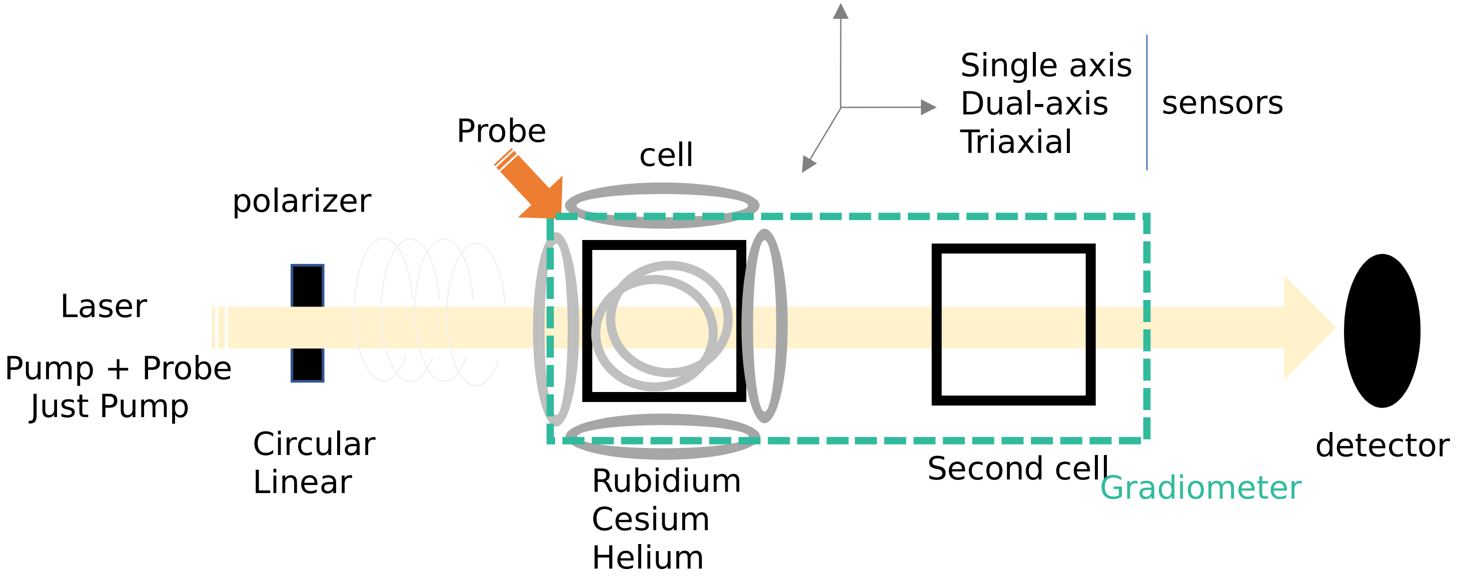


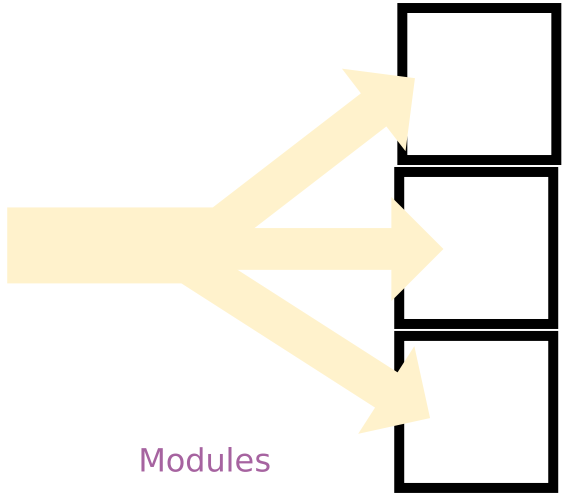


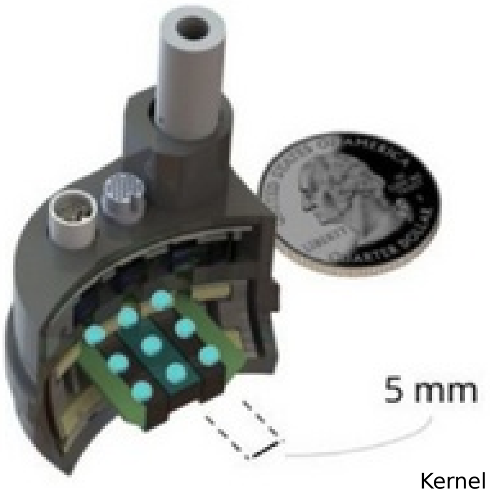
"Steep zero-crossing behavior" requires:

- 1 Warming up the cell to ~150ºC
- 2 Staying at very low magnetic fields
  Magnetically shielded room + Mu-coils

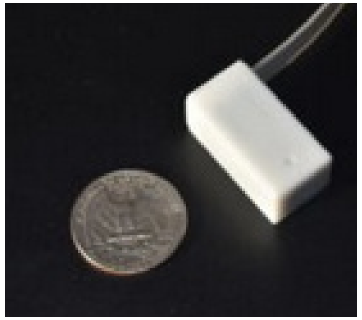
Variations of commercial OPMs and OPMs under development



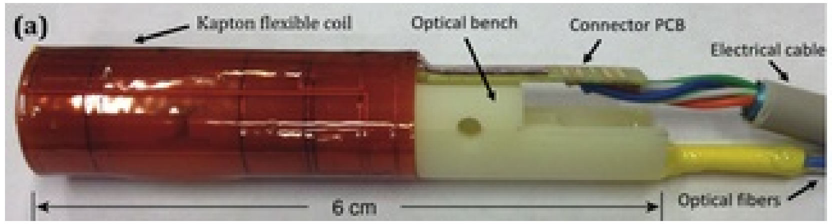




Kernel Flux



FieldLine Inc.

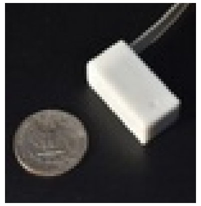


Nardelli et al, 2019

QuSpin Inc.

SQUID-based and OPM-based systems

MEG Core



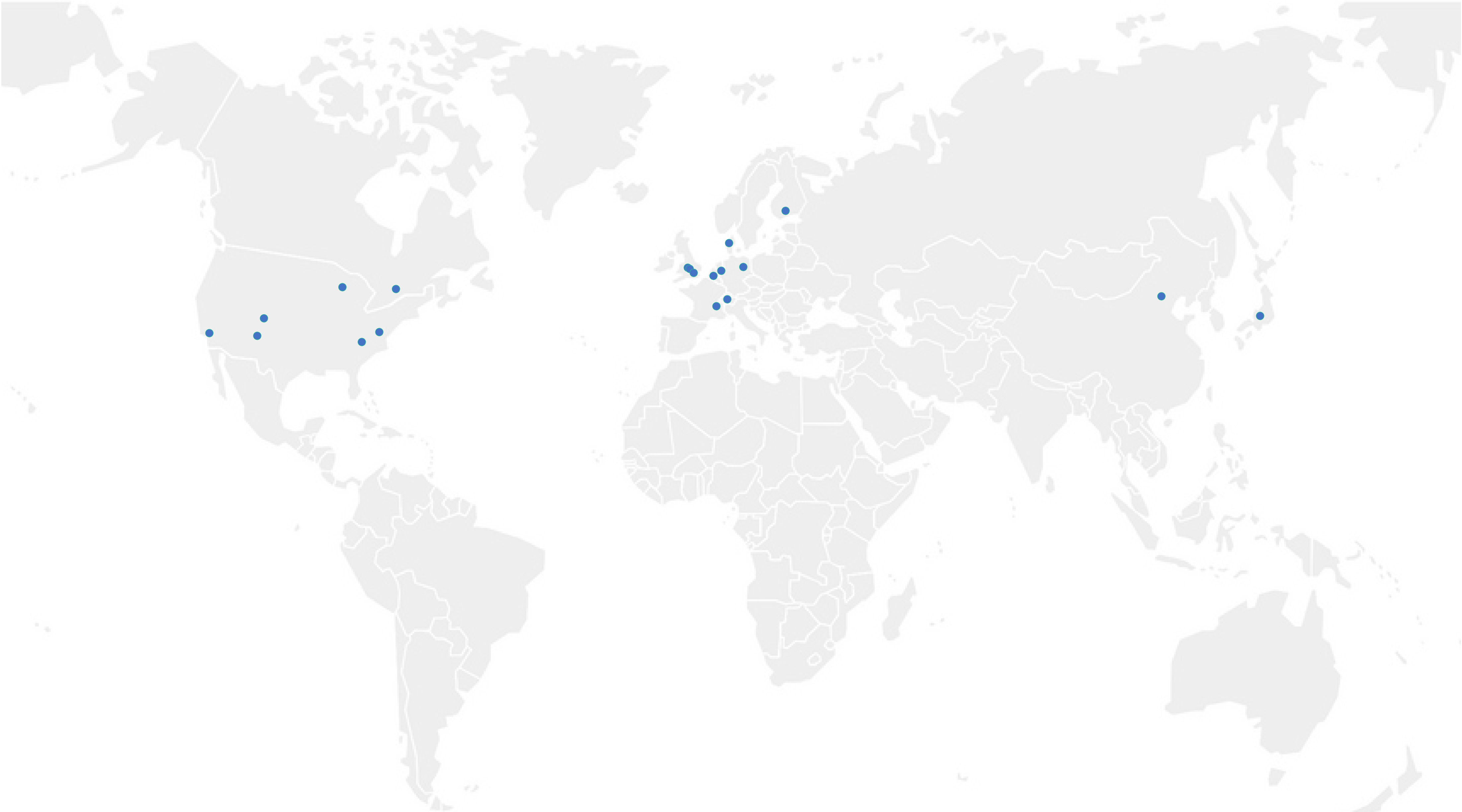
FieldLine Inc.

	SQUID based MEG	OPM based MEG
Operating temperature	5K, vacuum between head and coils needed	Room temperature
Sensitivity	5-10fT/√Hz	~10fT/√Hz**
Bandwidth	~600Hz*	~200Hz
Sensor array	Fixed, gap between scalp and sensor (~2cm)	Fixed or flexible, placed on subject’s scalp
Number of sensors	>100	10-60

* For a sampling rate of 2400 Hz

**Trade-off between sensor size and sensitivity

OPMs around the world

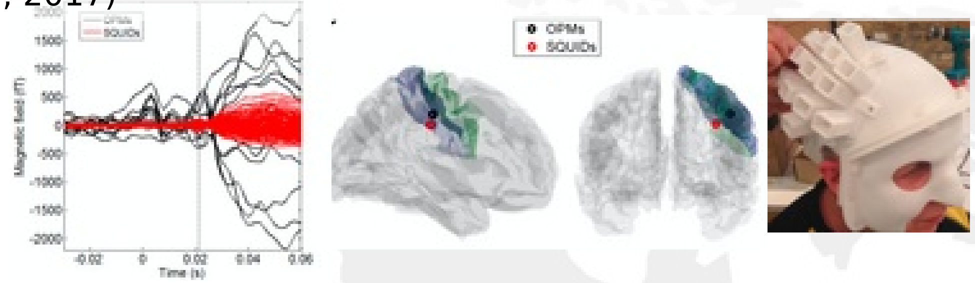


source

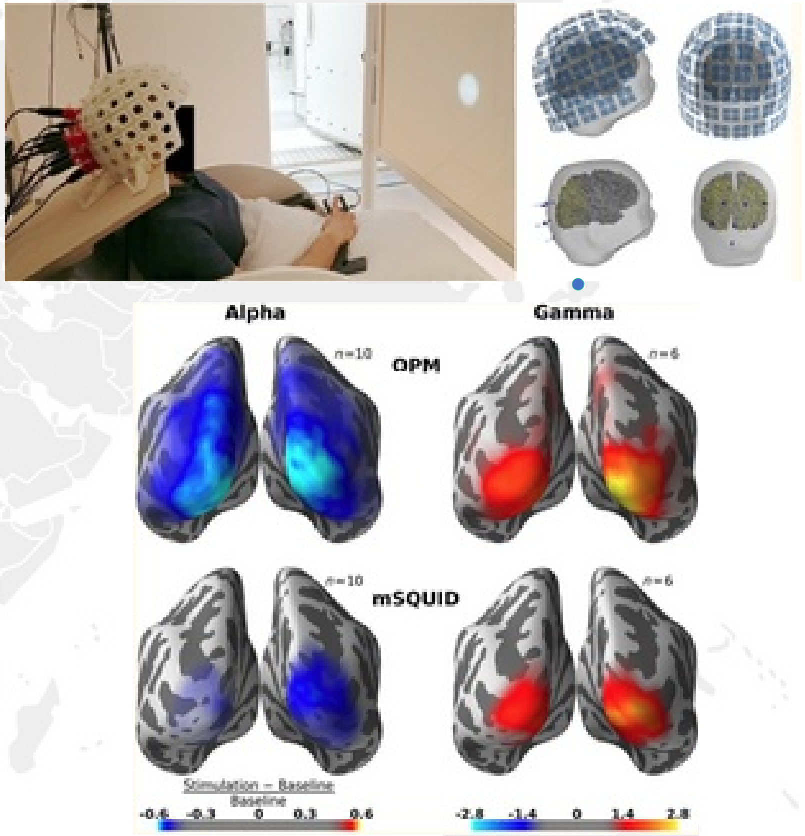
Applications

Evoked responses

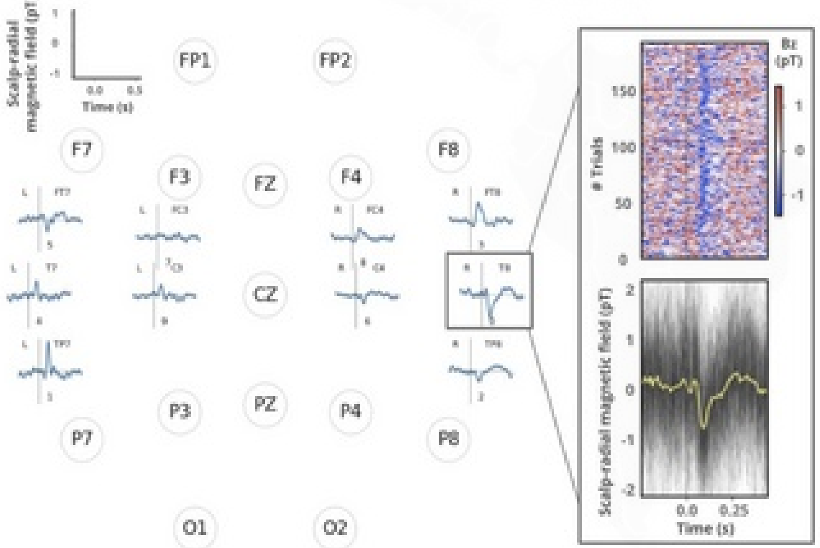
Nottingham Somatosensory evoked responses (Boto et al, 2017)



Aalto Visual evoked responses (Livanainen et al, 2020)



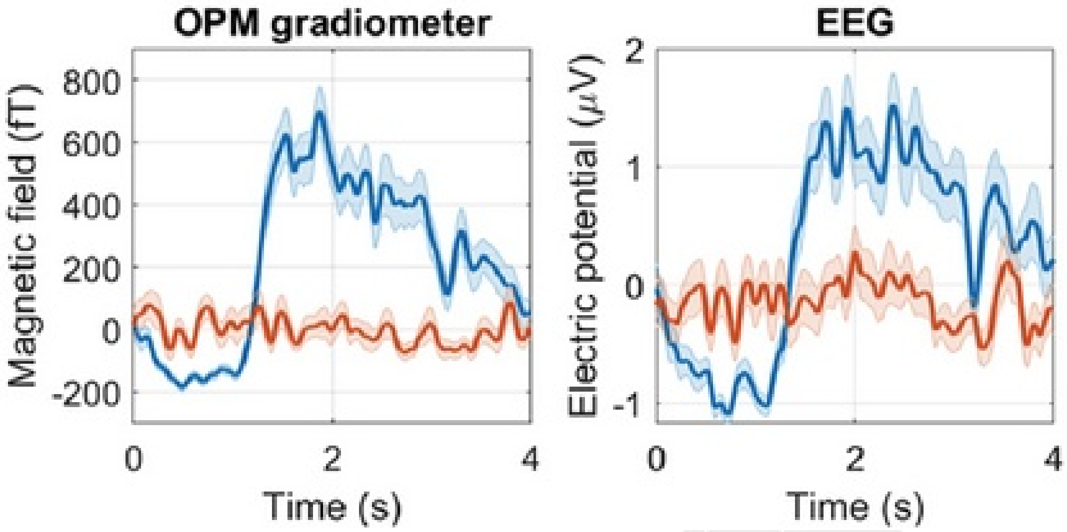
Kernel (LA) Auditory evoked responses (Pratt et al, 2021)



Applications Multi-modal imaging

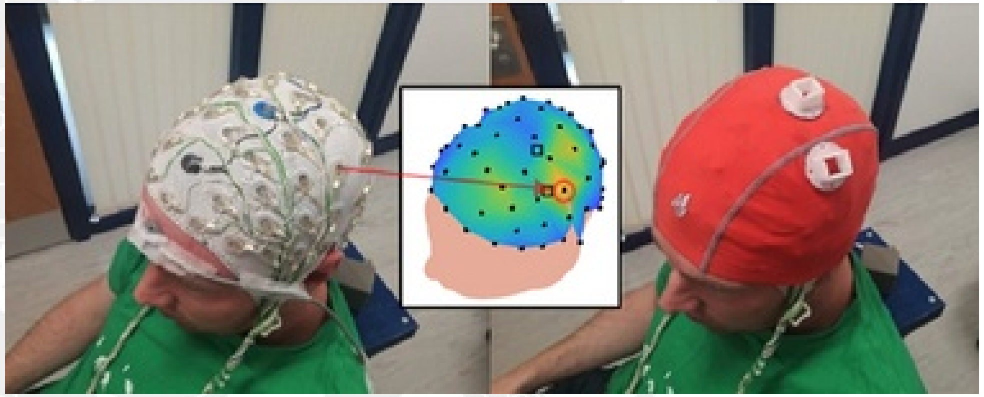
Nottingham

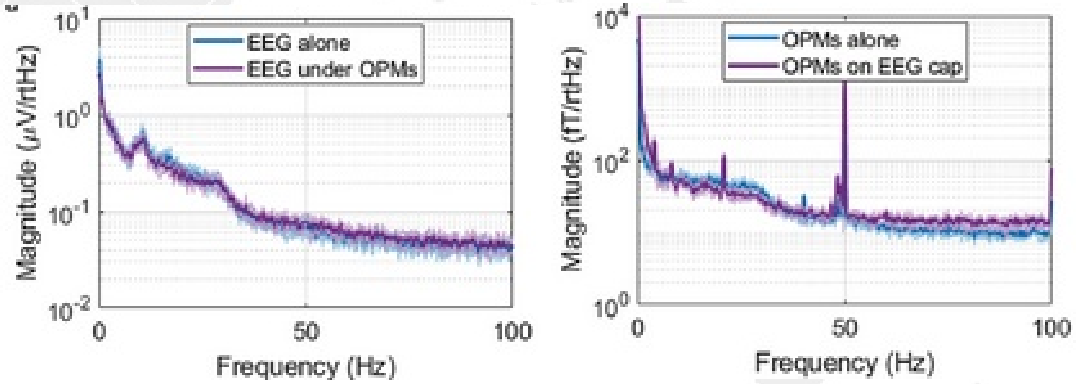
- Hyperscanning (Holmes et al, 2021)
- Connectivity (Boto et al, 2021)
- **Simultaneous EEG and OPMs (Boto et al, 2019)**
- Integration with virtual reality (Roberts et al, 2019)
- …



Birmingham (Jensen and Kowalczyk)

- Concurrent TMS-OPM setup





Applications

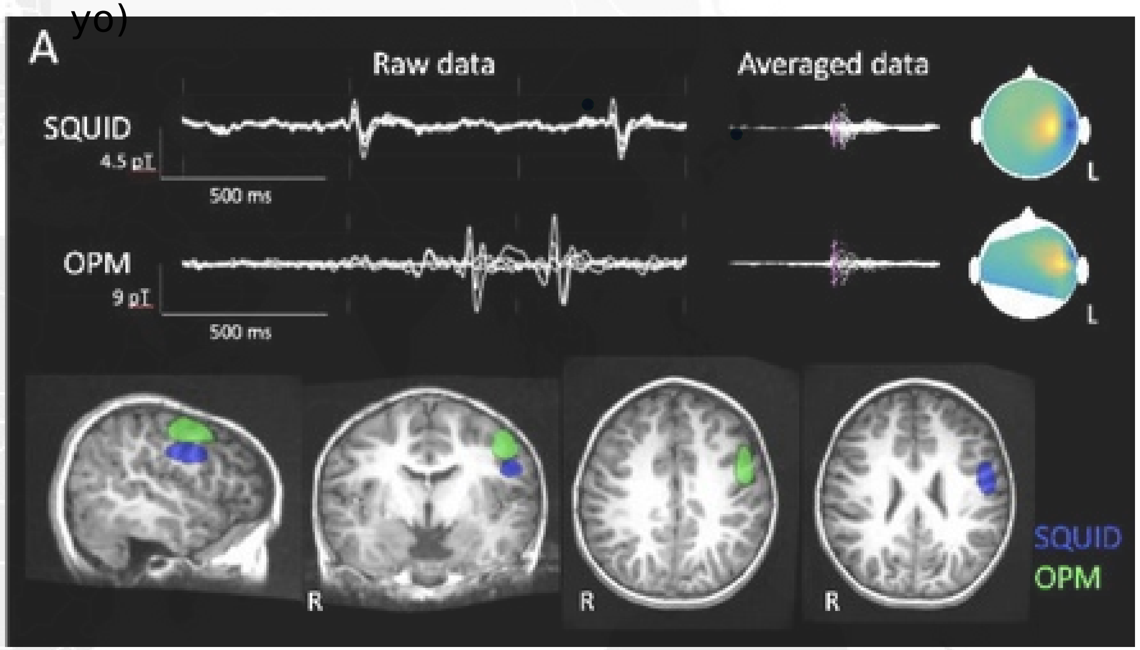
Children

Sickkids [Toronto]

- Autism

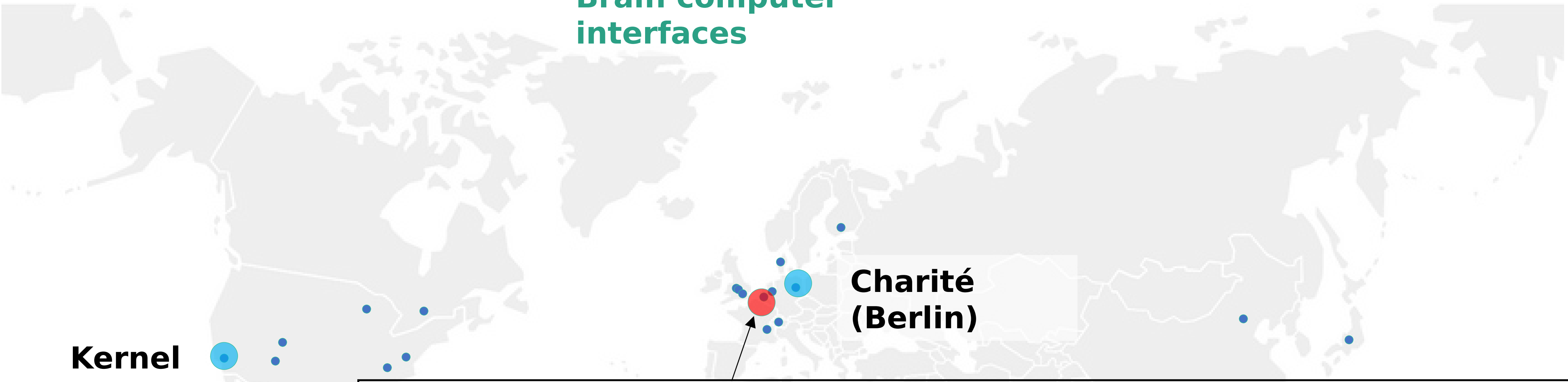
ULB [Brussels] (Feys et al, 2021)

- Interictal epileptiform discharges in children (5-11 yo)



Applications

Brain computer interfaces

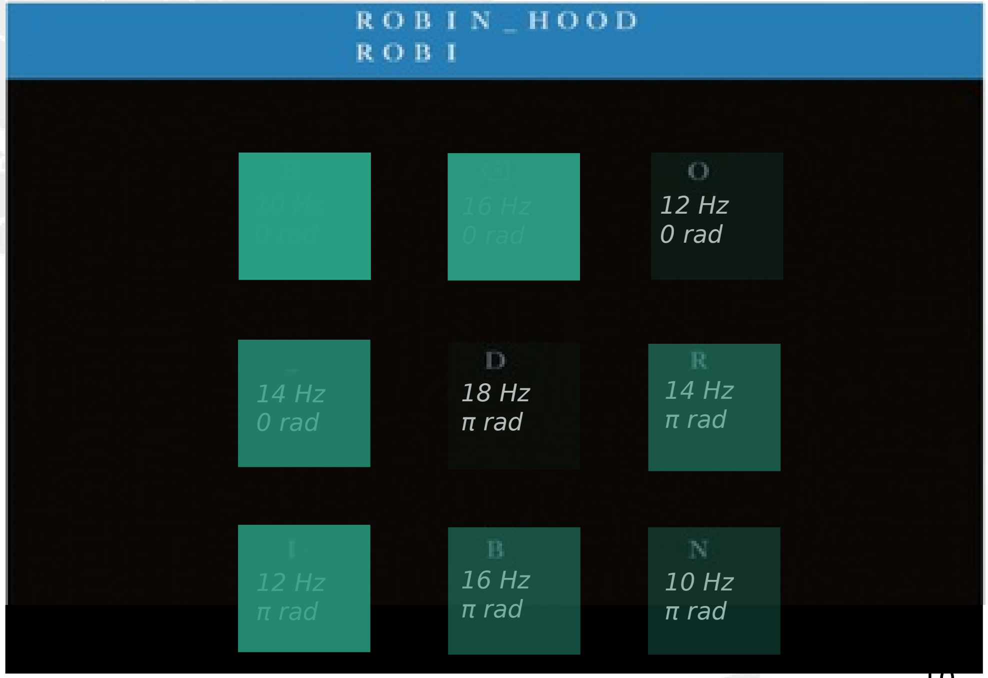


Kernel

Charité (Berlin)

KU Leuven-Notthingham
(Witte... et al, 2021)

	subject 1	subject 2	subject 3
correct / corrected / wrong	BRAIN KU_LEUVEN #QUANTUM ROBIN_HOOD CYBORG	BRAIN CYBORG KU_LEUVEN ROBIN_HOOD #QUANTUM	KU_LEUVEN ROBIN_HOOD BRAIN #QUANTUM CYBORG
accuracy	40/43 (93.0%)	38/38 (100%)	38/38 (100%)



From a wearable version of SQUID-MEG…

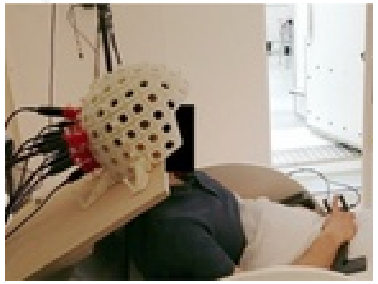
Wittevrongel et al, 2021

Kernel Flux

Hill et al, 2020

FieldLine Inc.

Cerca Magnetics

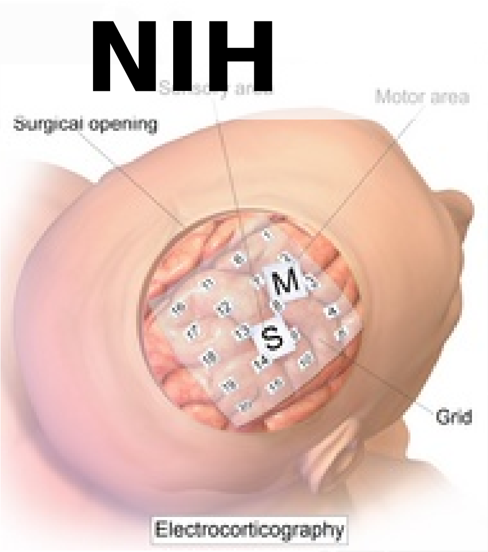


Livanainen et al, 2020

… to a non-invasive version of ECoG

OPMs at NIH

Magnetocorticography (MCoG)

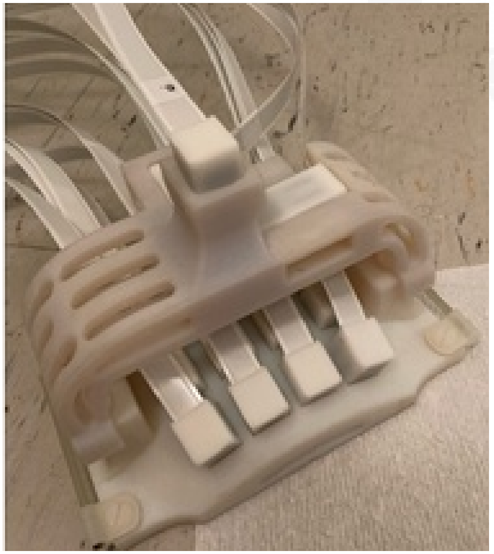


Wikipedia

ECoG
- gold standard for IED detection
- but invasive procedure + associated bleeding/infection risk
- “Limited” to epilepsy patients

SQUID-MEG
- Non-invasive
- Interictal spikes can be detected
- But <u>cannot</u> distinguish between closely-spaced sources of similar amplitude

MCoG [OPMs]
- Shares advantages of SQUID-MEG
- <u>Can</u> distinguish between closely-spaced sources of similar amplitude



Applications

- Identify the ictal onset zone in epilepsy
- Separate signals from cortical lamina
- Understand local cortical networks in language production
- Brain-computer and Brain-machine interface

OPMs at NIH

Initial setup: 16 sensors (+3 refs)

- Accurate

- FDM printer (Stratasys Objet 260 Connex 3)
- Rigur plastic, res: 0.001 inches
- Curvature r=80mm

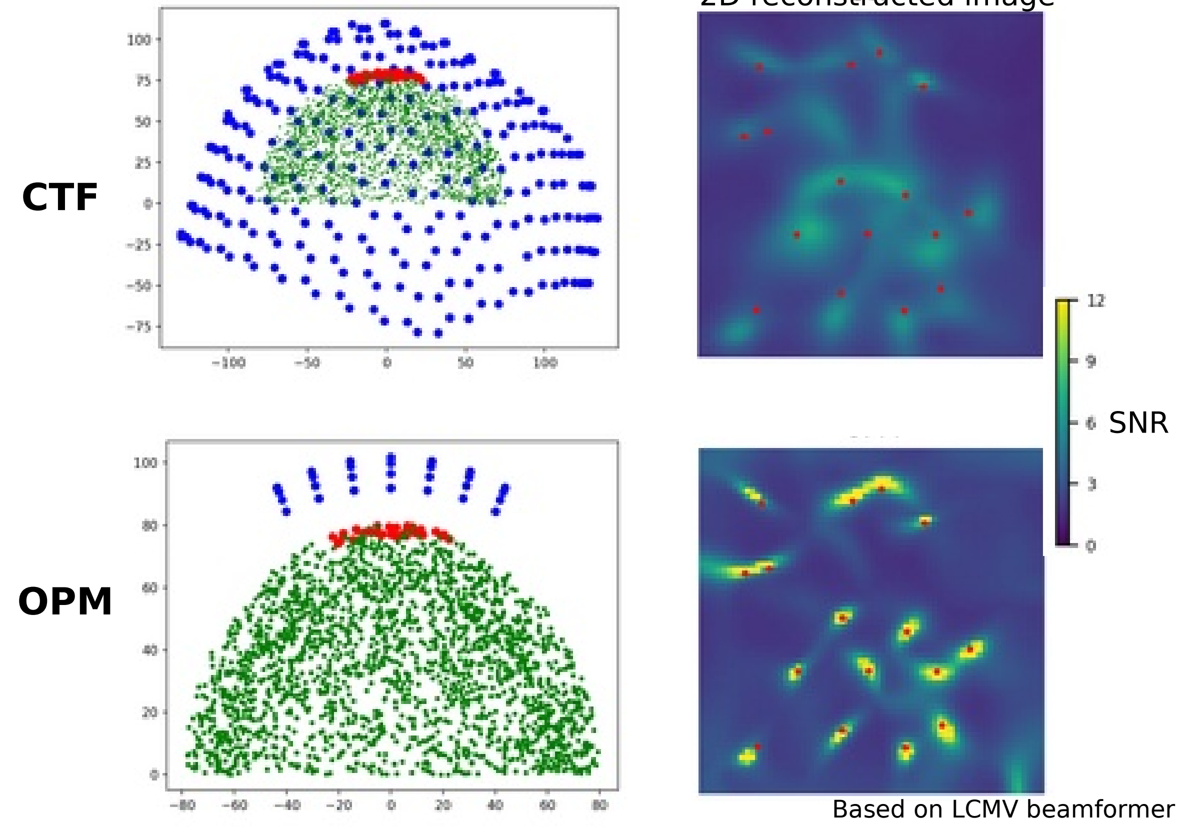
OPMs at NIH

Initial setup: 16 sensors (+3 refs)

- Accurate
- Keep sensors as tightly packed as possible

- FDM printer (Stratasys Objet 260 Connex 3)
- Rigur plastic, res: 0.001 inches
- Curvature r=80mm

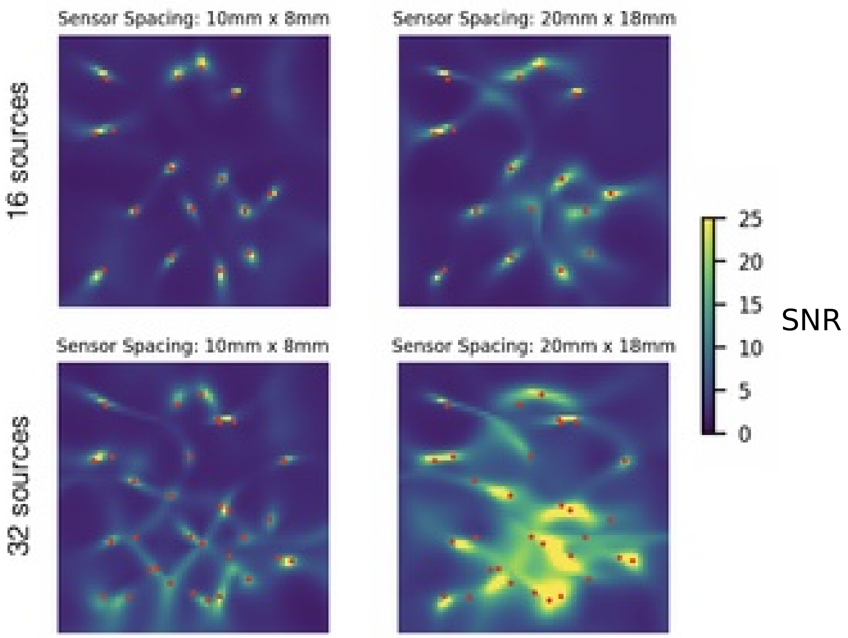
2D reconstructed image



Based on LCMV beamformer estimates of test sources

Nugent et al, under review

Spacing between OPMs



OPMs at NIH

Initial setup: 16 sensors (+3 refs)

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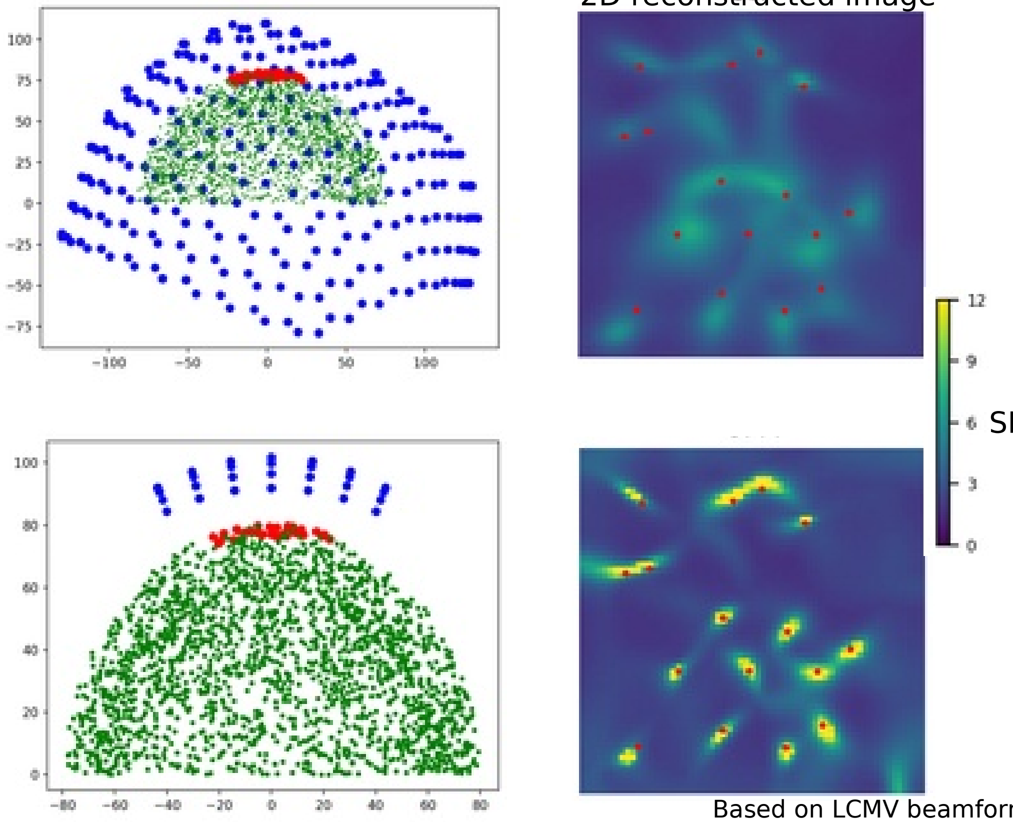
- Keep sensors as tightly packed as possible
- Reference array

- FDM printer (Stratasys Objet 260 Connex 3)
- Rigur plastic, res: 0.001 inches
- Curvature r=80mm

2D reconstructed image

CTF

OPM



SNR

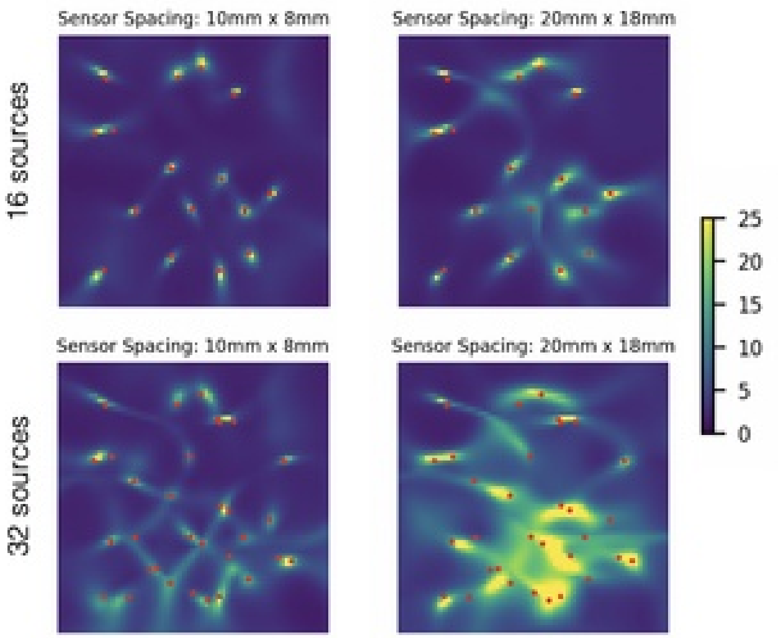
Based on LCMV beamformer estimates of test sources

Nugent et al, under review

Spacing between OPMs

Packed

Not Packed



SNR

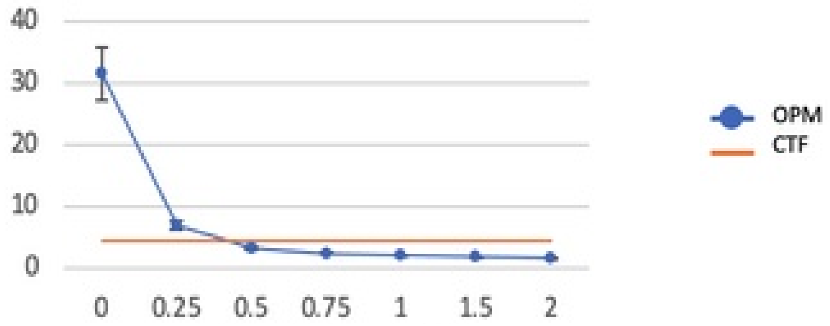
OPMs at NIH

Initial setup: 16 sensors (+3 refs)

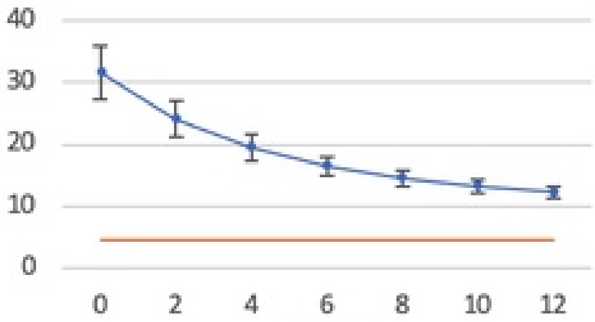
- Accurate
- Keep sensors as tightly packed as possible
- Reference array
- Fixed

SNR

Localization error (mm) of sensor position



Gap (mm) between sensor and scalp



56 sensors (+3 refs)

OPMs at NIH

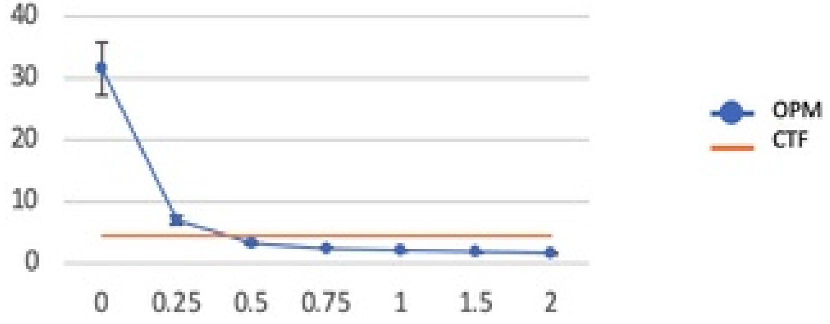
Challenges

- Sensors heat up
- Crosstalk
- Calibration

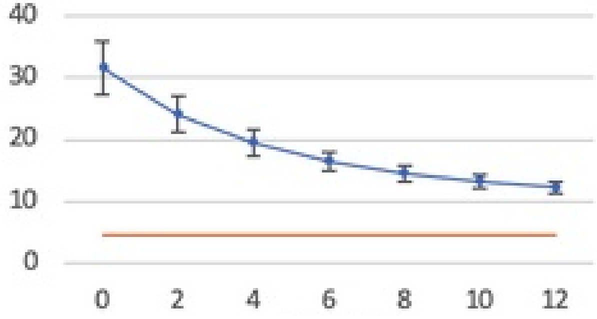
Initial setup: 16 sensors (+3 refs)

Localization error (mm) of sensor position

SNR



Gap (mm) between sensor and scalp



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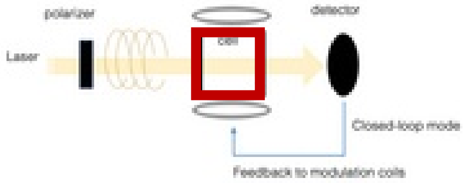


Graphite foil

Air

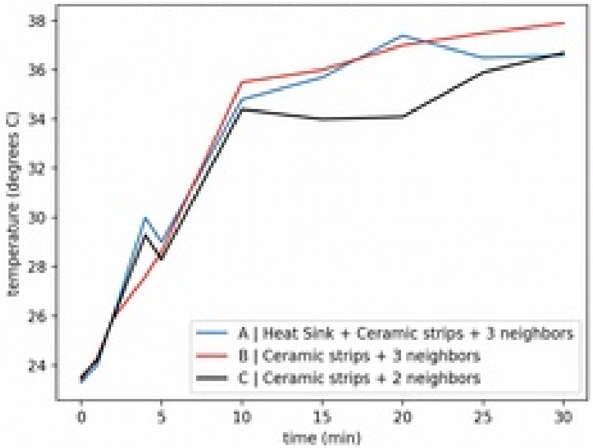
Heat Sink

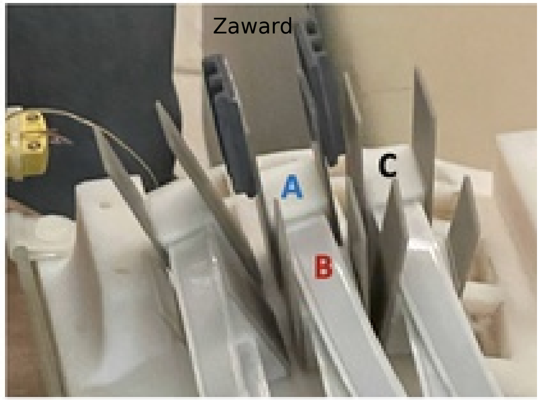
Cooling cap

Ceramic strips

Thermal mitigation strategies over time

7x8 sensor fixture
With ceramic strips + heat sinks

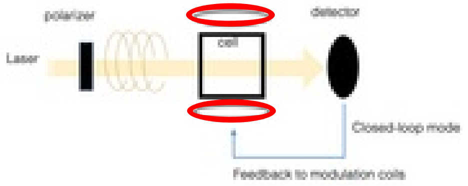




OPMs at NIH

Challenges

- Sensors heat up
- **Crosstalk**
- Calibration

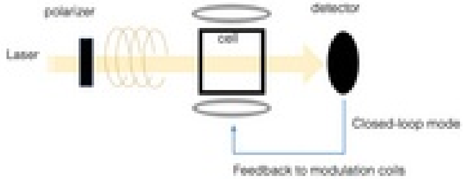


- In dense arrays, modulation and negative feedback fields are sensed by neighboring sensors
- Can affect the orientation of a sensor's sensitive axis

OPMs at NIH

Challenges

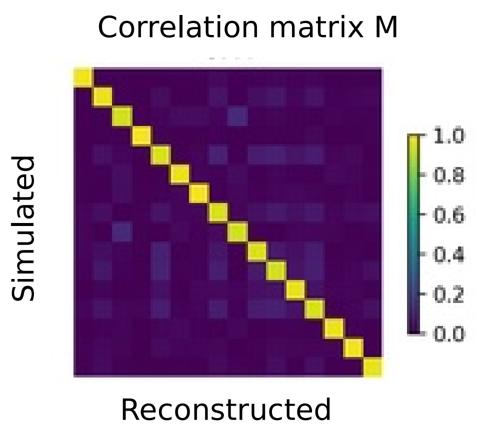
- Sensors heat up
- **Crosstalk**
- **Calibration**



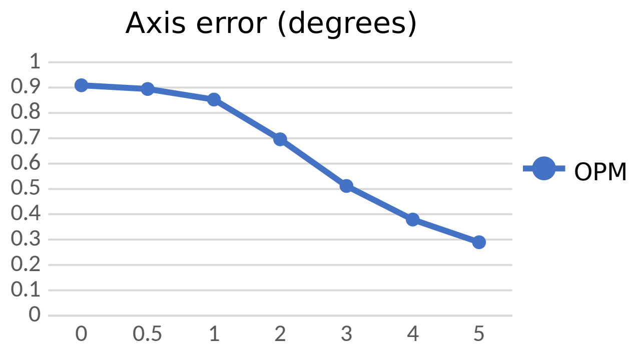
- For maximum accuracy of source localization/ discrimination
- To calibrate gain and axis of each sensor

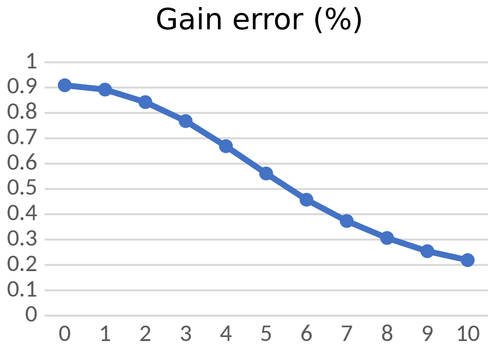
- In dense arrays, modulation and negative feedback fields are sensed by neighboring sensors
- Can affect the orientation of a sensor's sensitive axis

Independent source resolution (ISR)



ISR= mean(diag(M))-mean(off-diag(M))





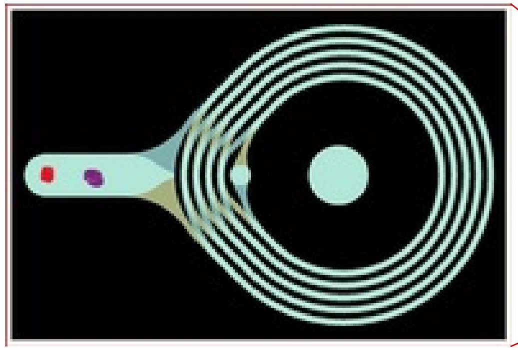
Nugent et al, under review

OPMs at NIH

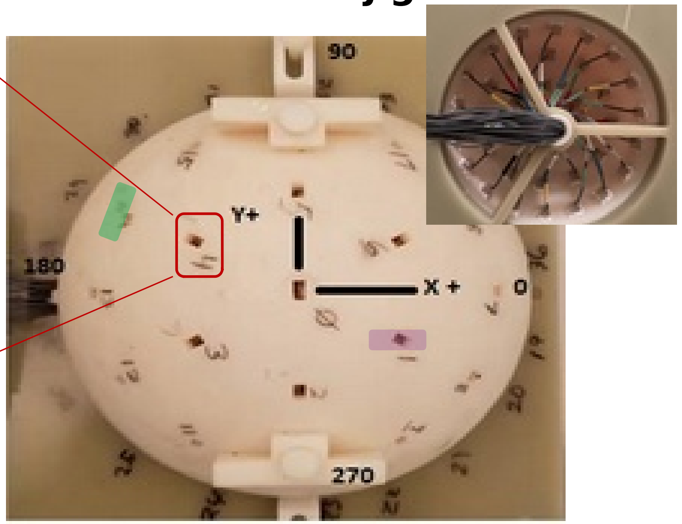
Challenges

- Sensors heat up
- Crosstalk
- **Calibration**

Coil geometry

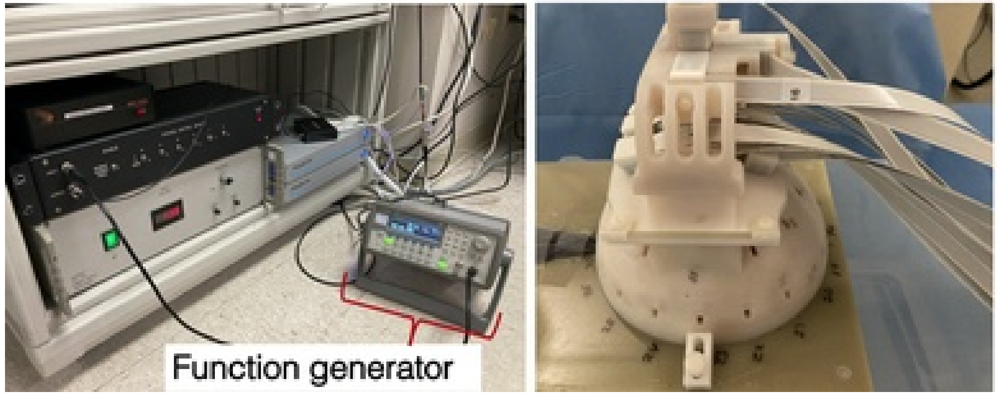


Calibration jig

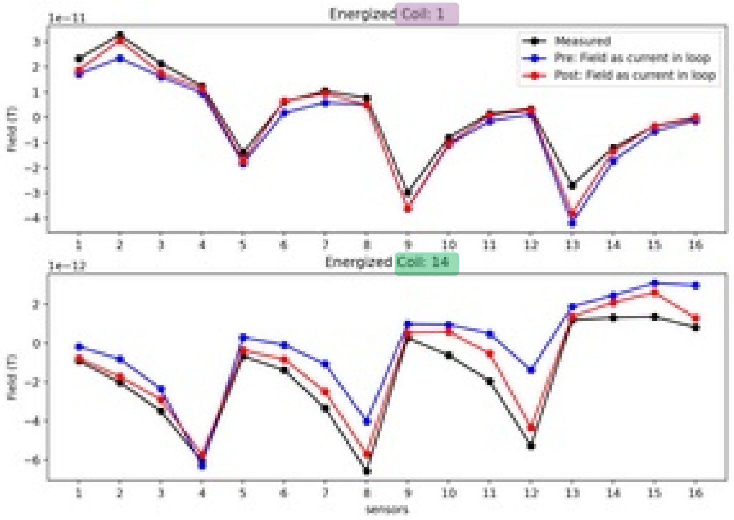


A hollow semi-sphere with 37 coils in it
Coils are arranged in different “rings”
They are energized one at a time

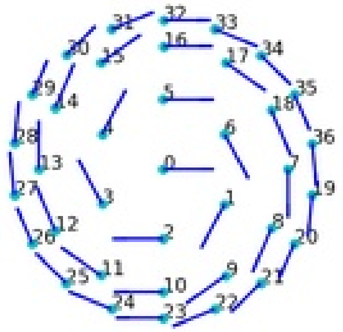
Setup



- Coils energized sequentially with function generator
- Recorded by sensors placed on calibrator
- Field modeling is performed



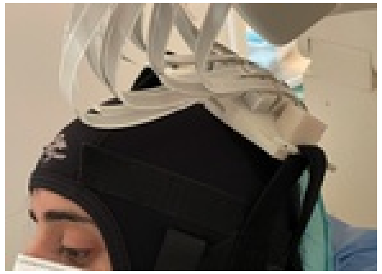
Coil orientation in jig

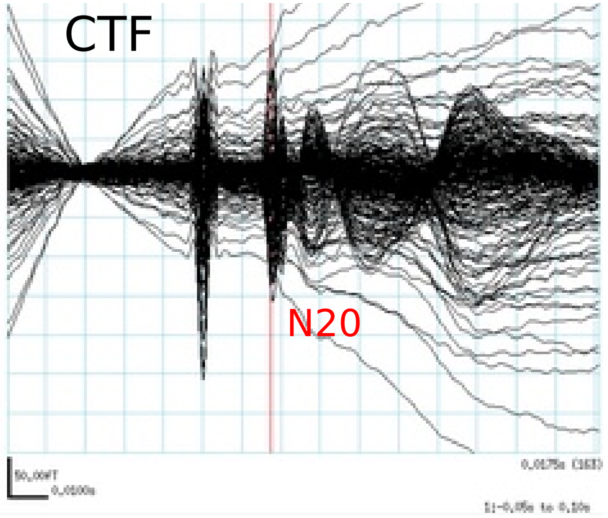


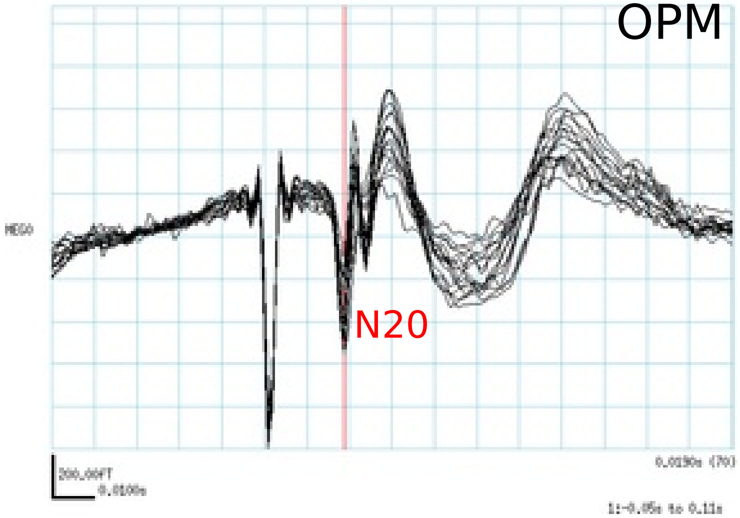
Schematic view of the known coil positions & orientations

OPMs at NIH

In parallel…







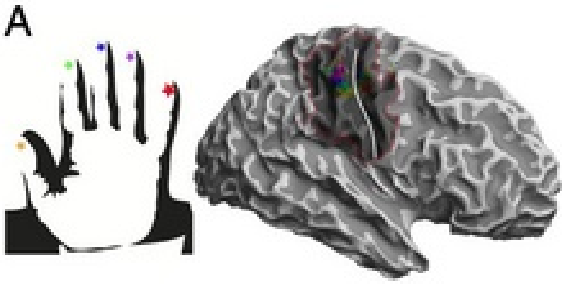
- Right median nerve stimulation
- 500 us pulse duration, 0.35s ISI
- 400s duration

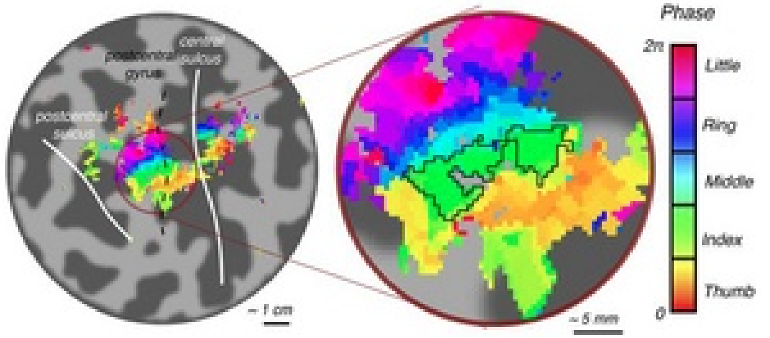
- DC removal + 300Hz low pass filter
- ~1140 trials

Next

Digit representation in somatosensory cortex

Galileo tactile stimulation system





Sanchez-Panchuelo et al, 2012

Solve current challenges:

- Fine-tune calibration algorithm
- Assess thermal mitigation strategy in 7x8 array
- Weight relief mechanism for sensor fixture
- Keep ambient fields at zero
  (Mu Coils: from static to dynamic zeroing)

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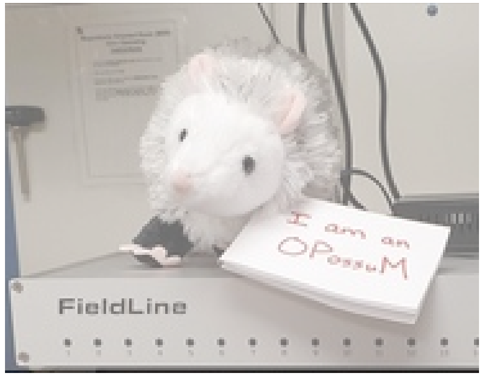
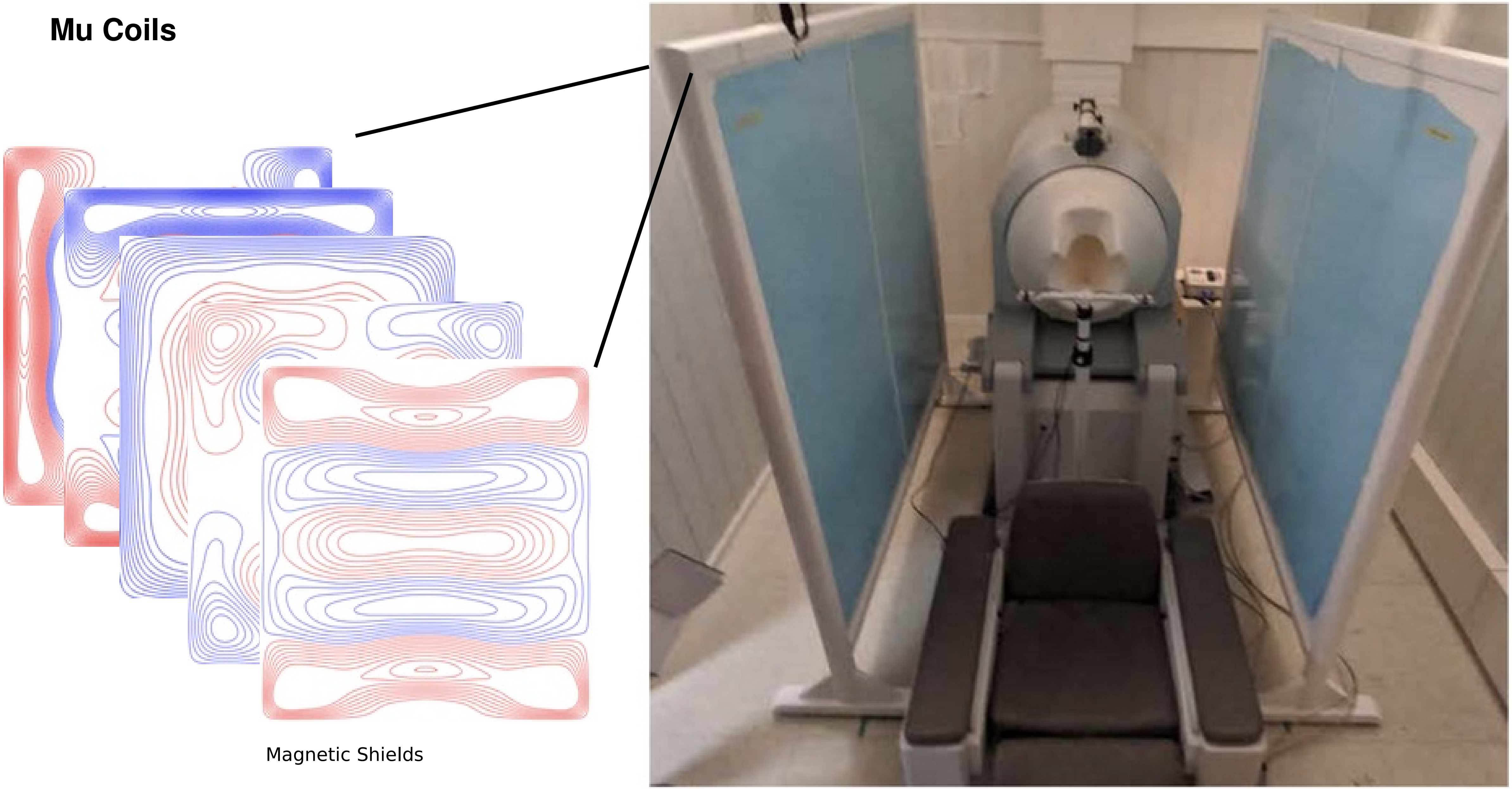


Mu Coils



Magnetic Shields

The remnant field inside most MSRs can be several tens of nT with a spatial variation of several nT over 10 cm
Even small head movements and rotations can result in complete loss of data, or data which is corrupted by motion artefacts

Applications

Nottingham

- Hyperscanning (Holmes et al, 2021)
- Connectivity (Boto et al, 2021)
- Simultaneous EEG and OPMs (Boto et al, 2021)
- Integration with virtual reality (Roberts et al, 2019)
- …

Birmingham (Jensen and Kowalczyk)

- Concurrent TMS-OPM setup

UCL

- **Hippocampal measurements** (Barry et al, 2019)
- Magnetospinography (Bestmann lab)