IEEE/CSC & ESAS SUPERCONDUCTIVITY NEWS FORUM (global edition), April 2015.
Tutorial presentation given at KRYO 2014, Berlin, September 21-23, 2014.

Ultra-Low-Field MR

Basic Principles and some Applications

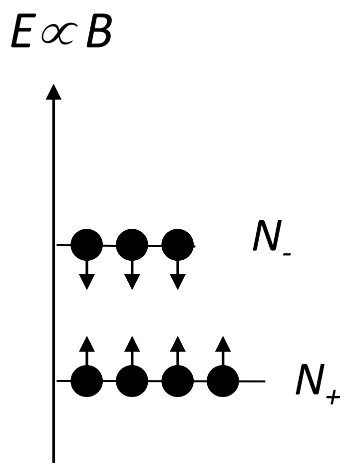
Rainer Körber

Magnicon GmbH
Division Berlin
and
PTB Berlin
Department of Biosignals

Fundamentals NMR

The basic pulsed NMR experiment

Sample containing nuclear moments ($N = N_+ + N_-$) at temperature T is exposed to magnetic field B.
→ Zeeman energy splitting governed by Boltzman distribution.



$$\frac{N_-}{N_+} = e^{-\gamma\hbar B/kT}$$

Zeeman splitting for spin-half system

N_-: spin population higher energy
N_+: spin population lower energy
γ: gyromagnetic ratio

if $\gamma\hbar B << k_B T$

$$\frac{N_+ - N_-}{N_+ + N_-} \approx \frac{\hbar\gamma B}{2k_B T}$$

^{1}H, 300 K, 3 T: 10 ppm

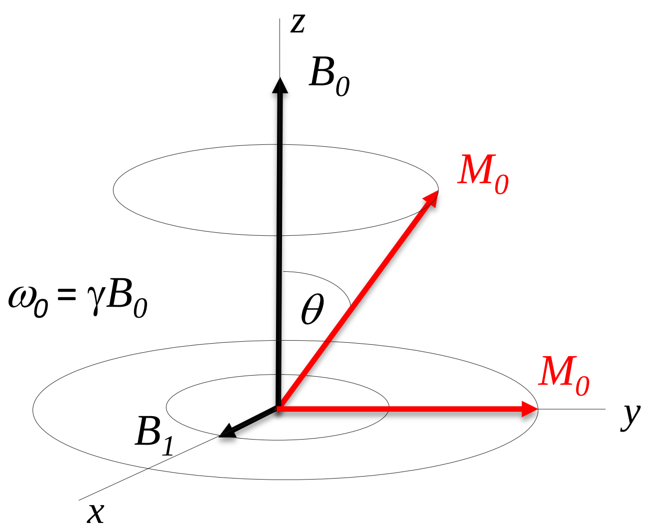
Very small polarisation even in modern MRI scanners with 3T.

In NMR also use magnetisation M: magnetic moment per unit volume

Curie Law $$M = N\frac{\gamma^2\hbar^2}{4kT}B$$

Fundamentals NMR

To manipulate equilibrium magnetisation M_0 in static field B_0:
apply rf field B_1 rotating at $\omega_0 = \gamma B_0$.



1. Measure M_z

Spin-lattice relaxation time T_1
Relaxation towards M_0 along B_0,
requires energy exchange with the lattice.

2. Measure M_y (free precession with ω_0)

Spin-spin relaxation time T_2
Relaxation in transverse plane,
dephasing of spins, no energy exchange.

Measurement of precessing magnetisation using Faraday detection,
i.e. measure dB/dt.

Signal $\propto M_0 \omega_0 \propto B_0^2$

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Fundamentals NMR

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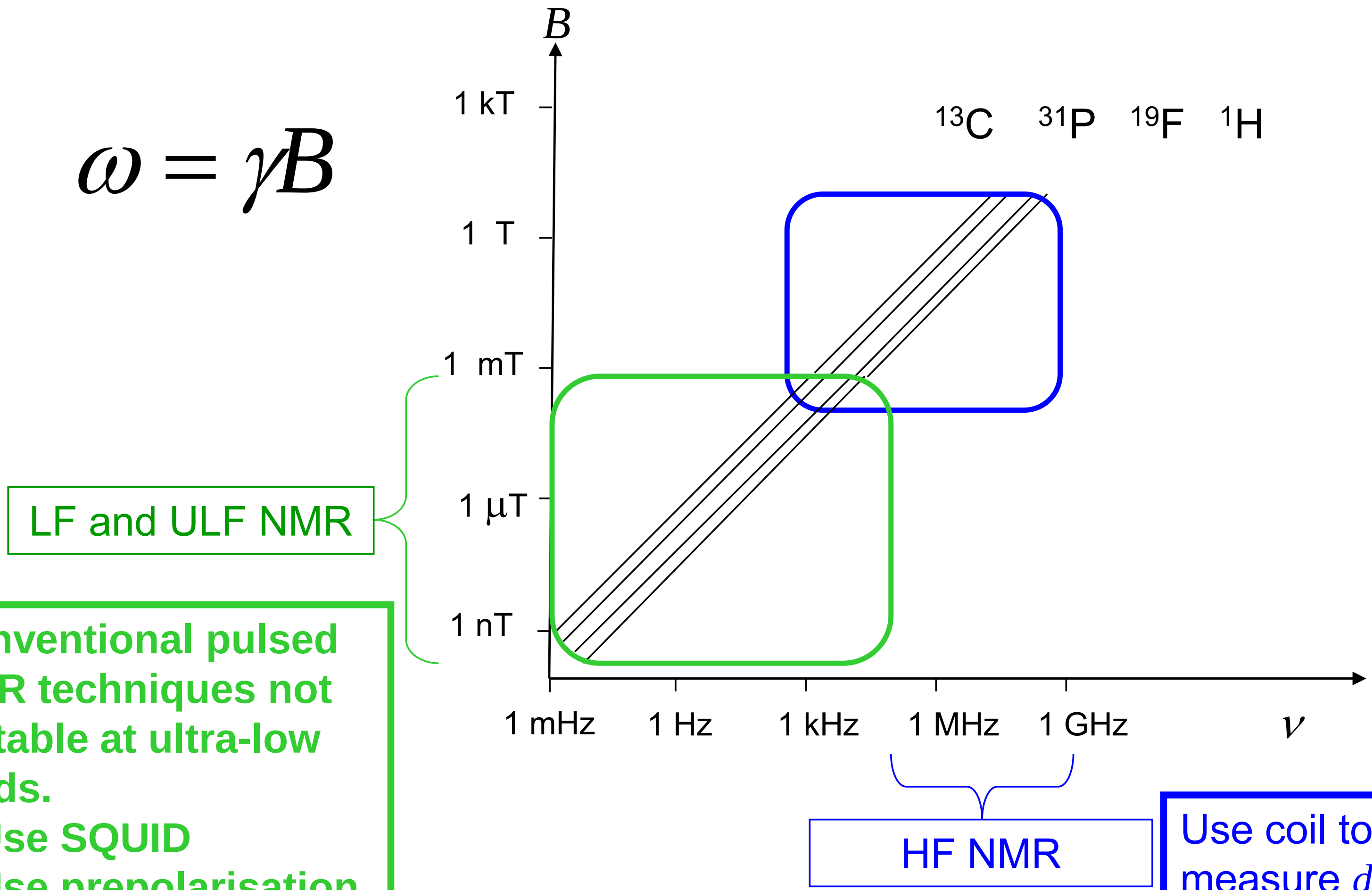
$$\omega = \gamma B$$



Conventional pulsed NMR techniques not suitable at ultra-low fields.
→Use SQUID
→Use prepolarisation

Use coil to measure *dB/dt*

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Basic ULF-NMR

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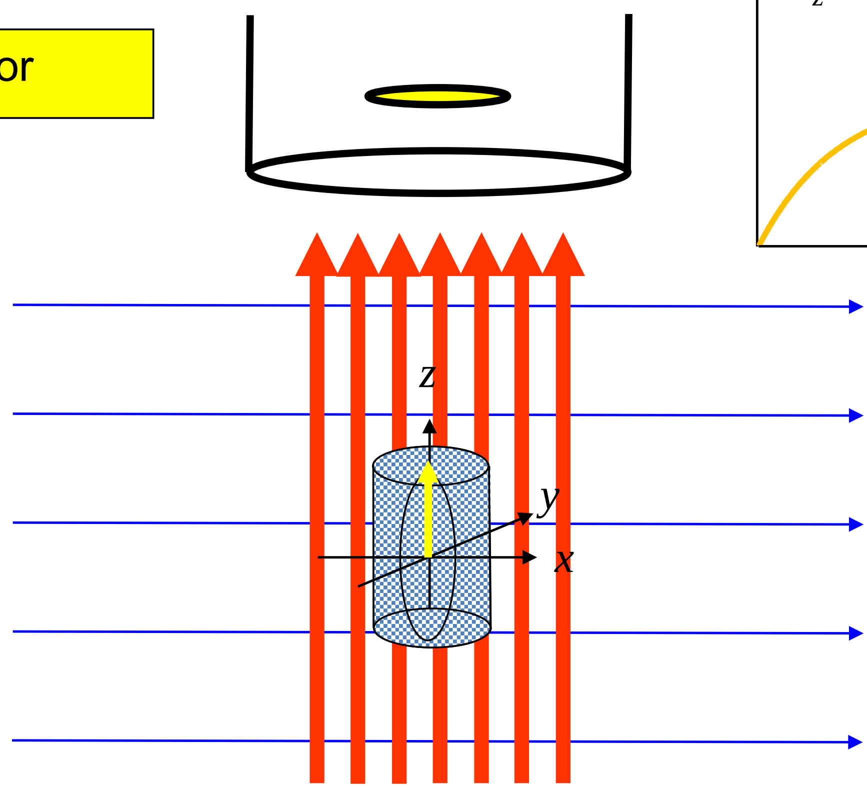
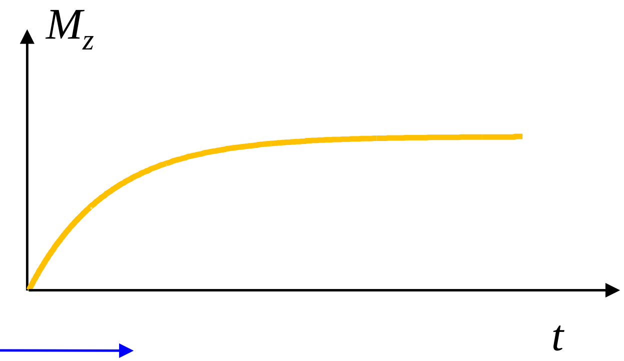
SQUID-Sensor





During polarisation magnetisation M_z grows with T_1.

B_{det}

Expose sample to detection field, ususally µT-range.

B_{pol}

To boost magnetisation of sample use prepolarisation, usually mT-range.

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Basic ULF-NMR

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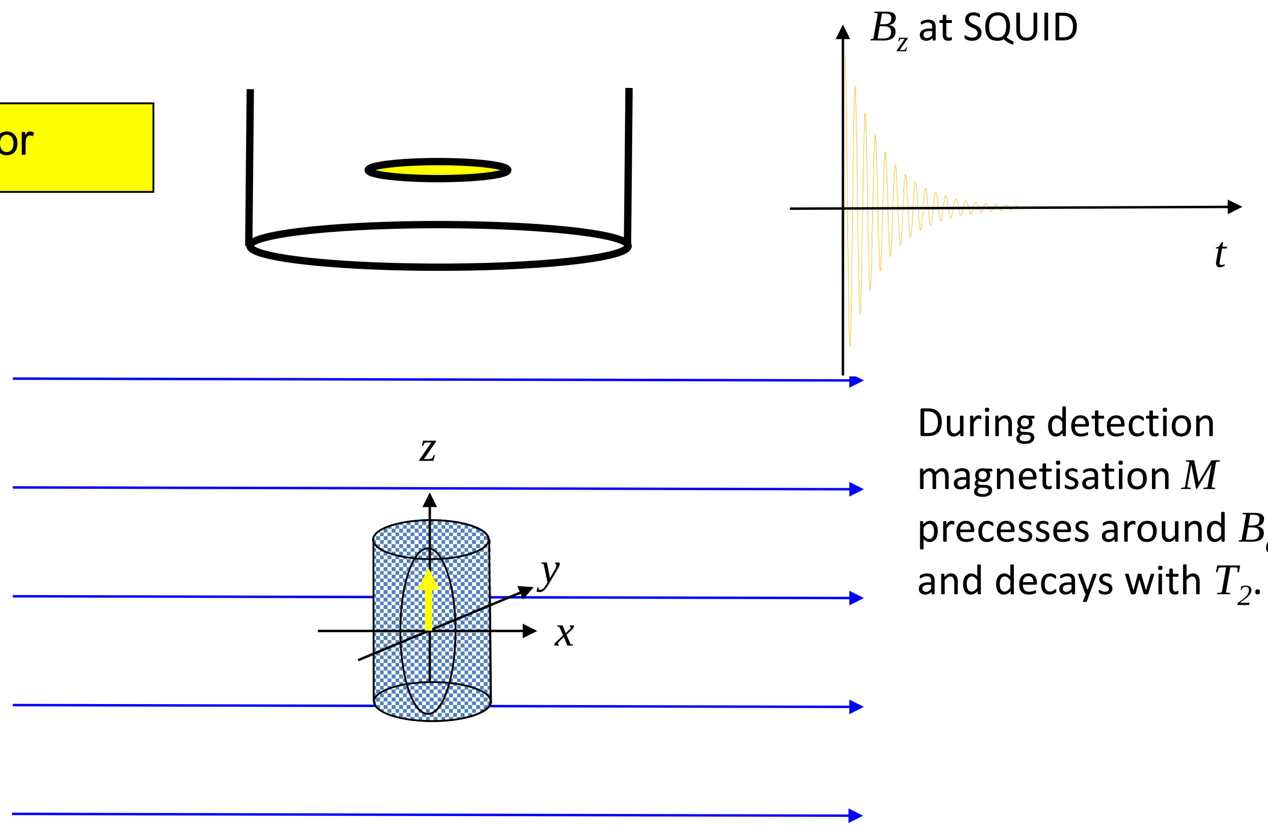
SQUID-Sensor



B_{det}

Expose sample to detection field, ususally μT-range.

During detection magnetisation M precesses around B_{det} and decays with T_2.

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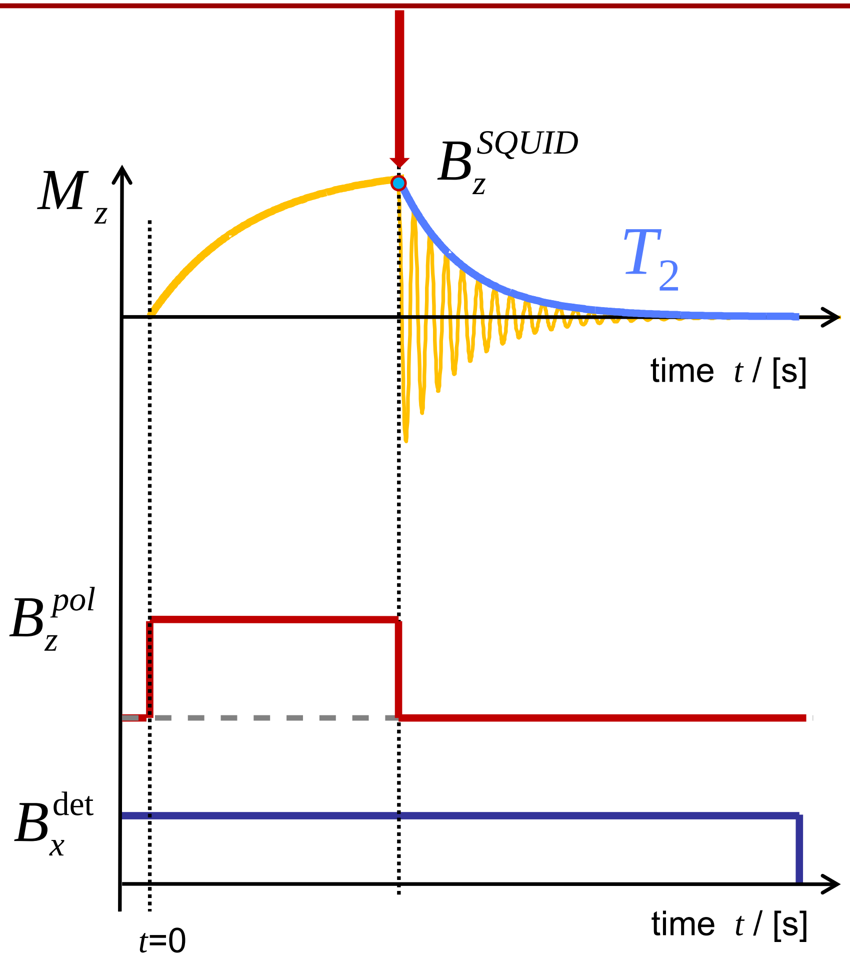
T_2 Relaxation

PTB



$M_0 \sim B_{pol}$

$\nu \sim B_{det}$

Signal $\propto M_0 \propto B_{pol}$

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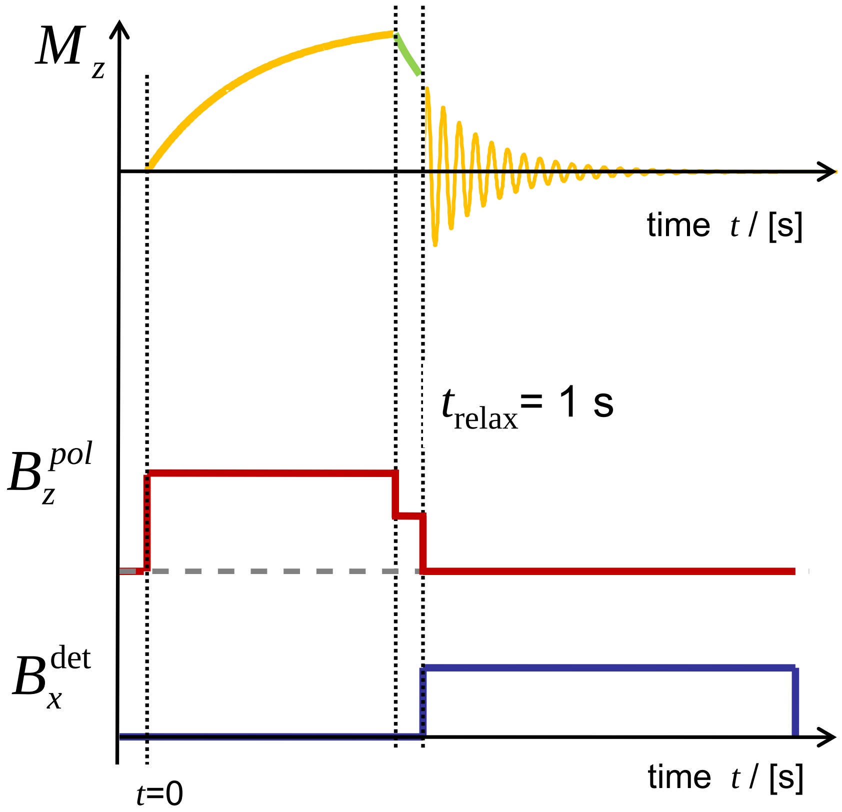
T_1 Relaxation

PTB



To measure T_1 at fields smaller than B_z^{pol}:

- Ramp down B_z^{pol} to relaxation field B_{relax}.
- Wait time t_{relax} for M_z to decay.

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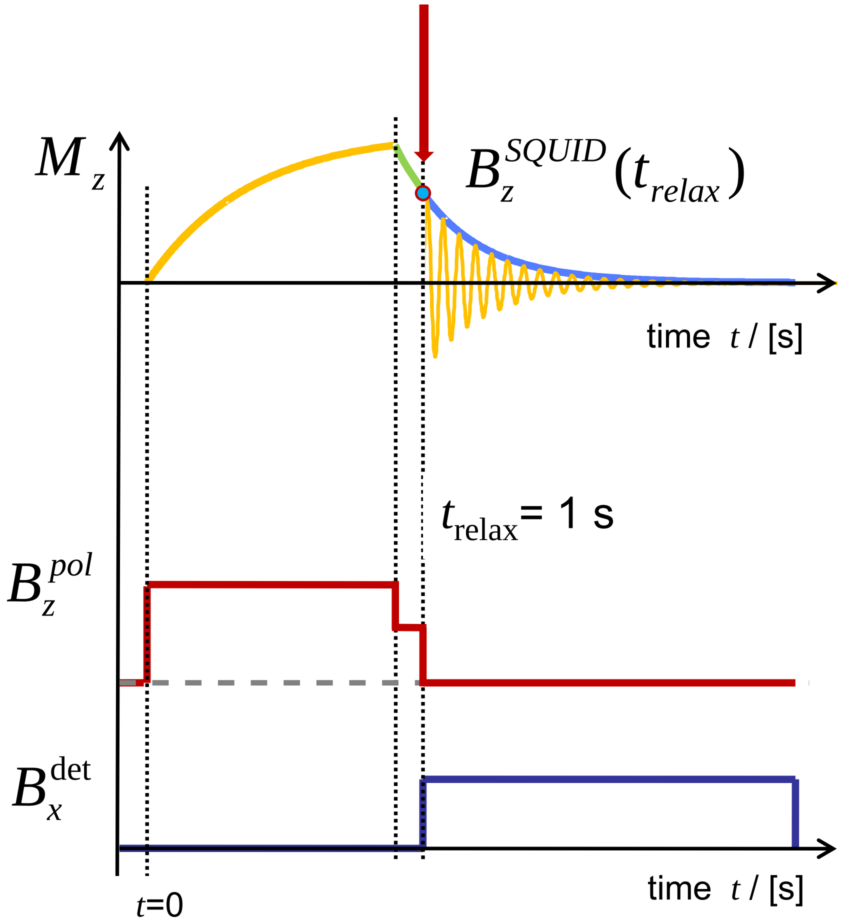
T_1 Relaxation

PTB



To measure T_1 at fields smaller than B_z^{pol}:

- Ramp down B_z^{pol} to relaxation field B_{relax}
- Wait time t_{relax} for M_z to decay.
- Induce precession by turning on B_x^{det} to read out B_z^{SQUID}.

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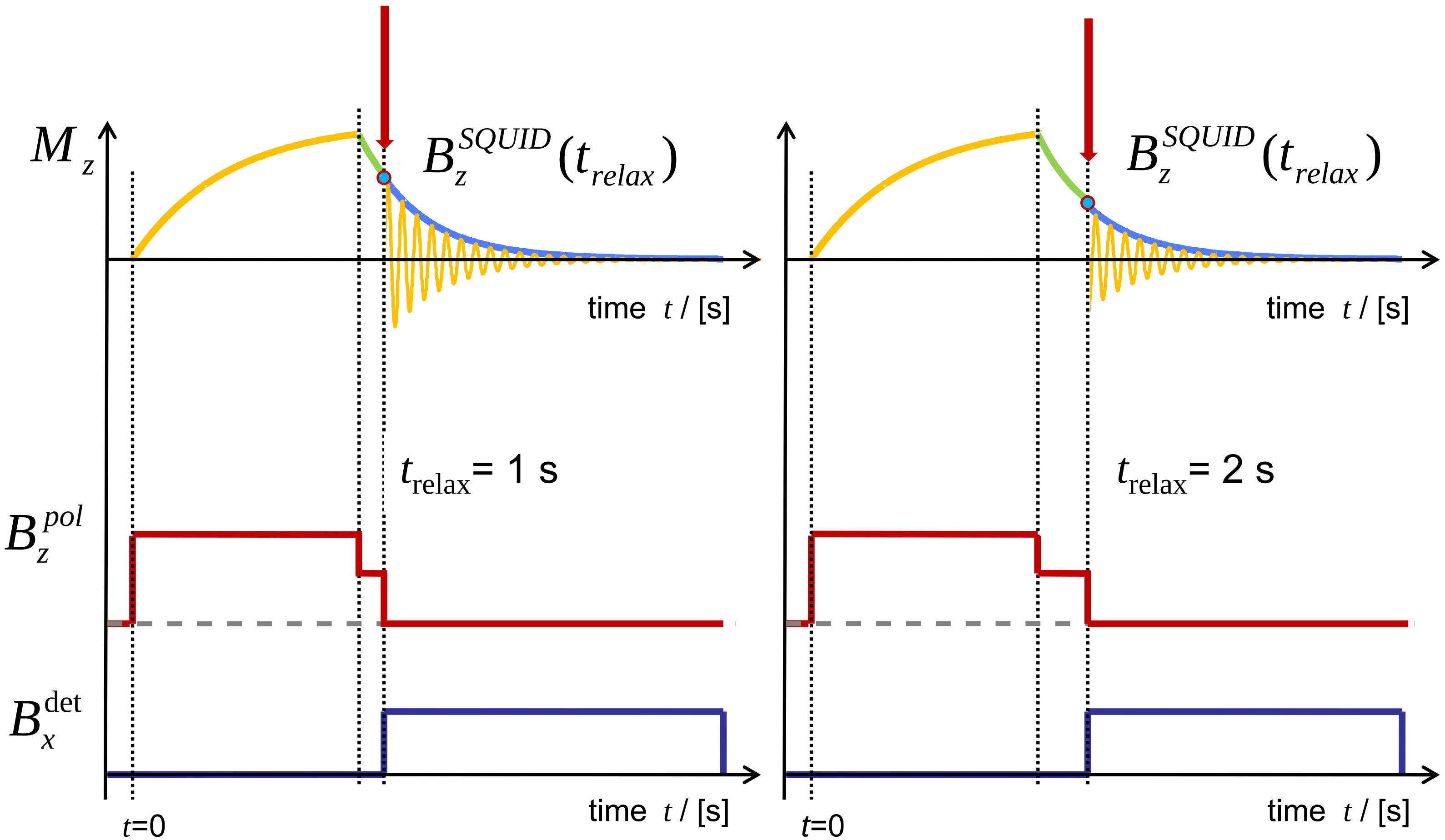
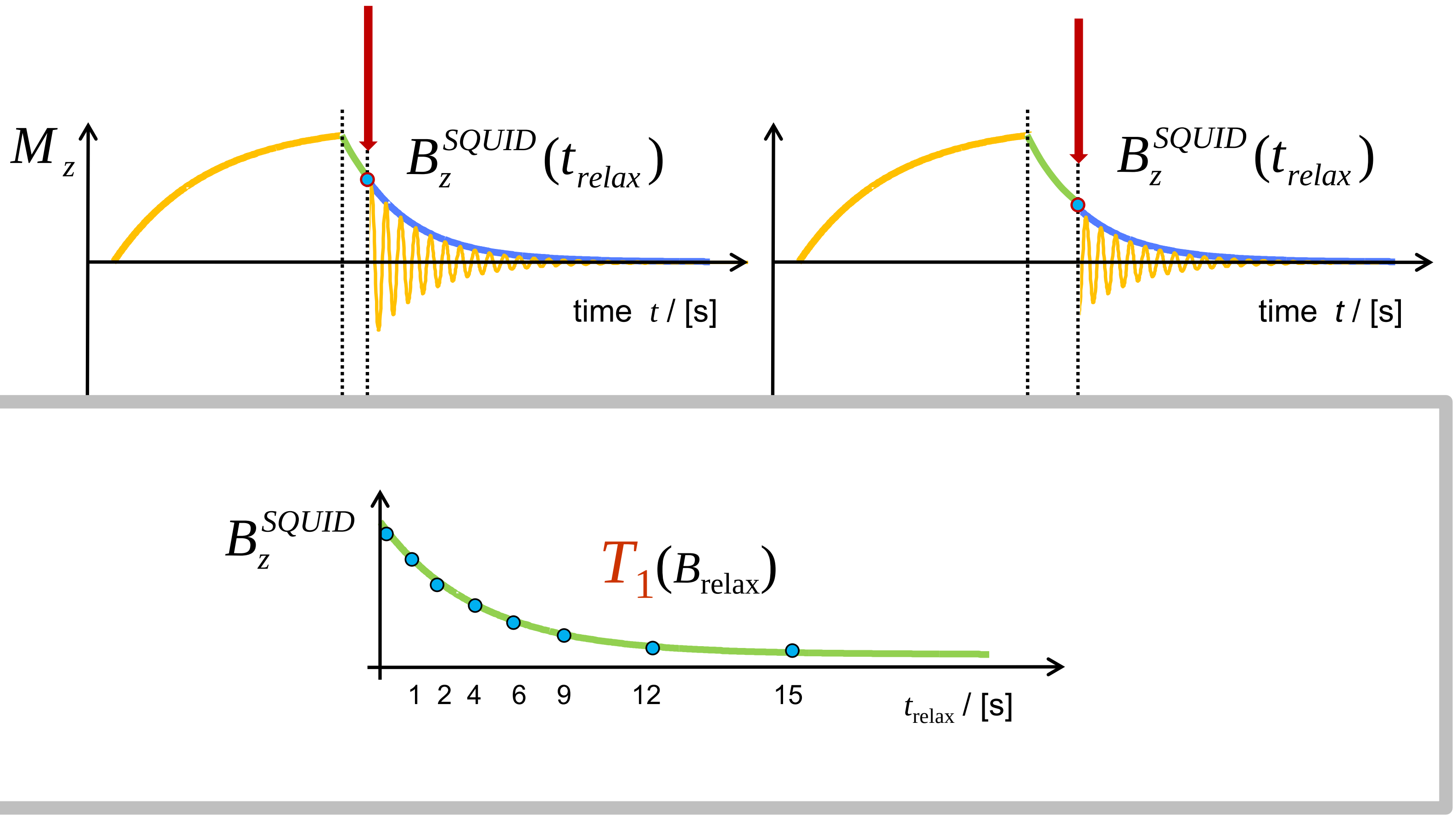
T_1 Relaxation

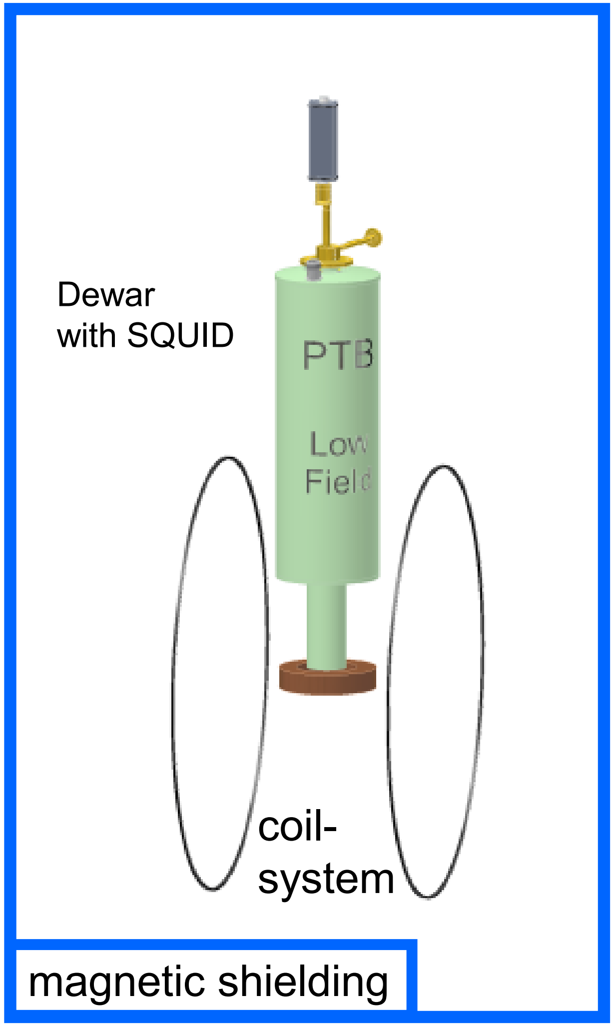
PTB



T_1 Relaxation

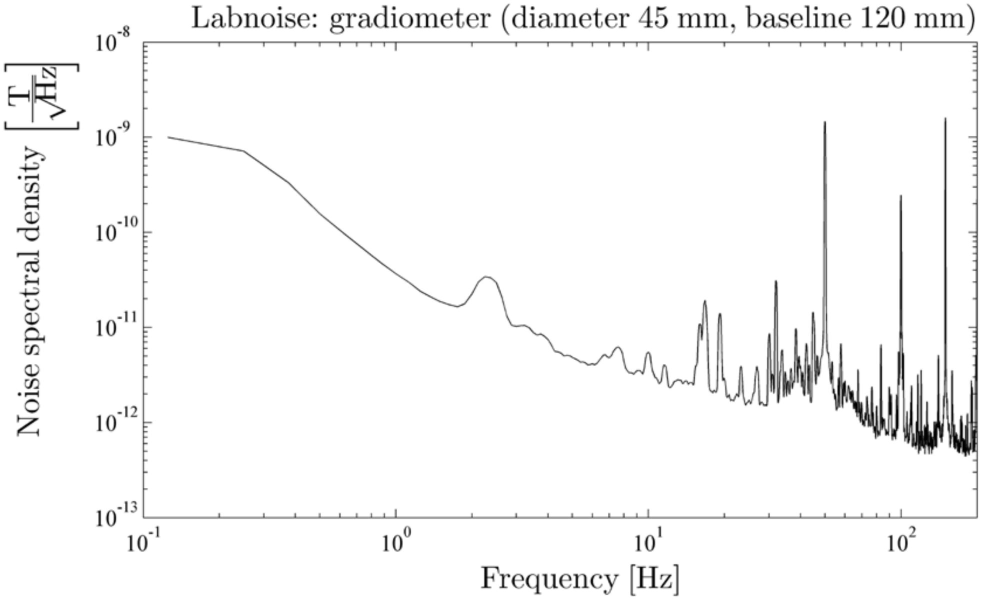


General Setup



To exploit sensitivity of SQUID:

Use magnetically shielded room



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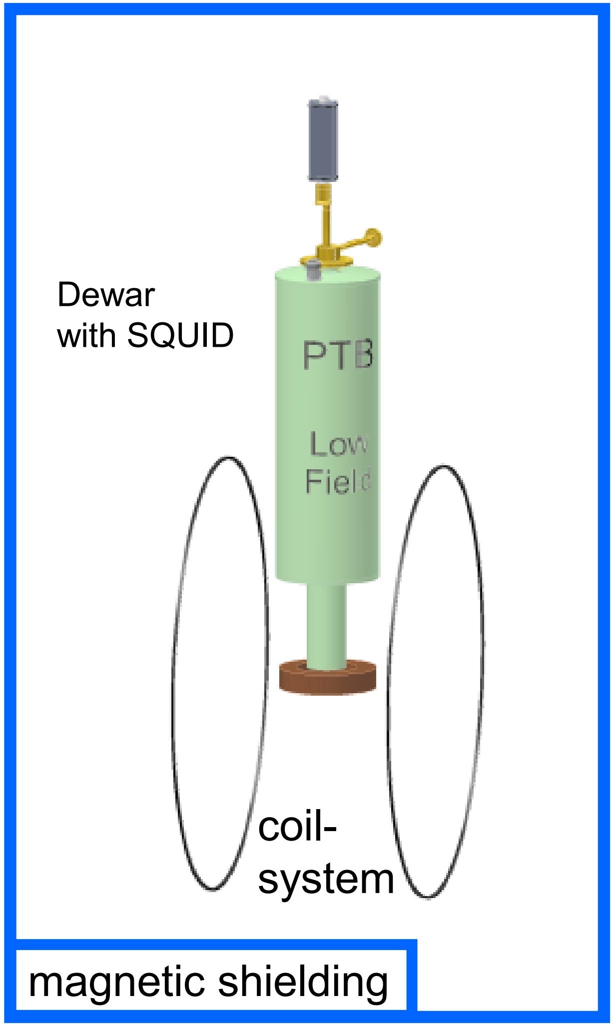
General Setup

PTB



To exploit sensitivity of SQUID:

Reduce Johnson noise

→ No large metallic surfaces in Dewar superinsulation and polarisation coil.

Seton et al. Cryogenics, 2005

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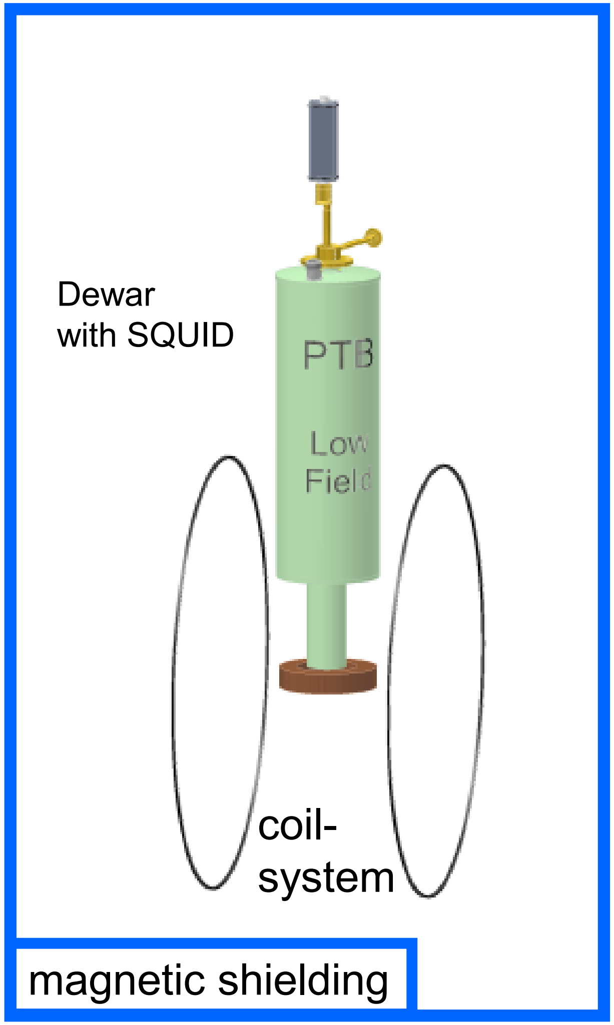
General Setup

PTB

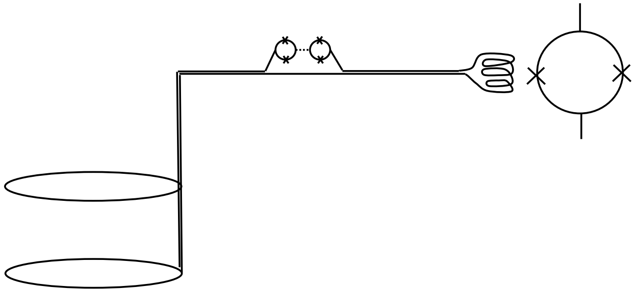


To operate SQUID:

- Protect from high fields (50 mT)

→ SQUID current sensor in superconducting shield connected to superconducting flux transformer

→ Current limiter in input circuit



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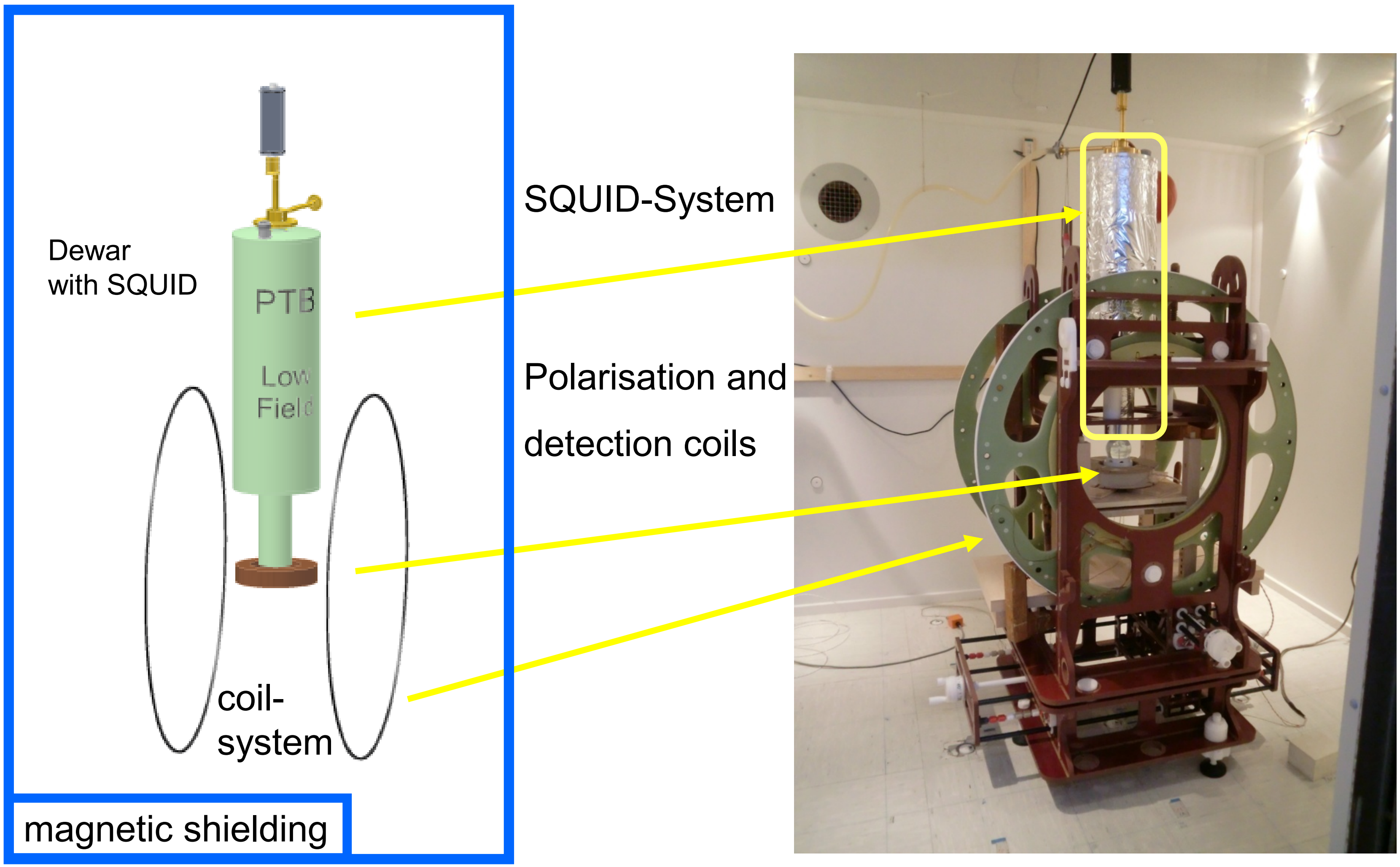
General Setup

PTB



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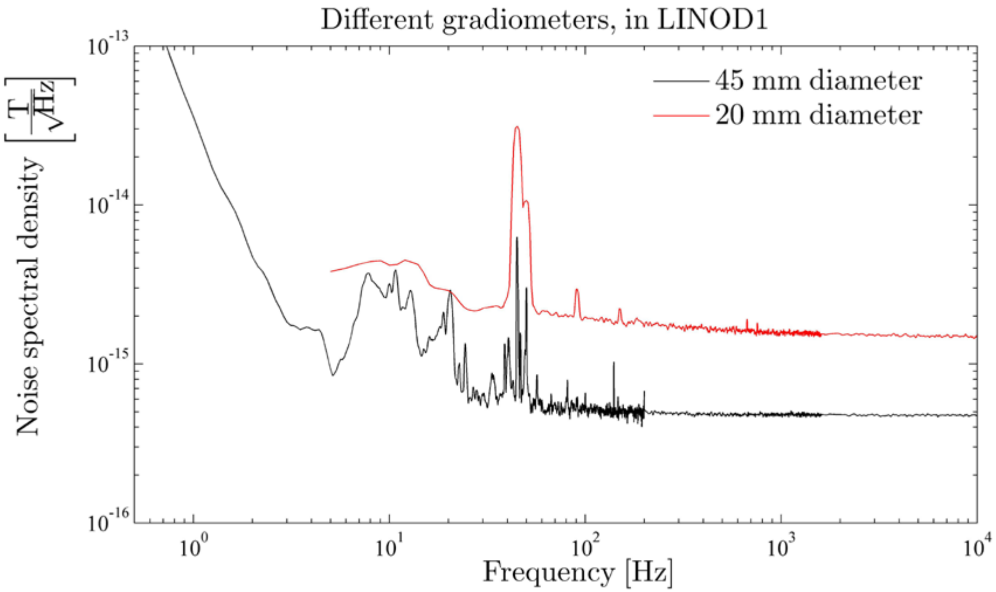
General Setup

PTB

Important parameters:

B_{det}: up to ~10 μT (400 Hz)

B_{pol}: up to 54 mT



Gradiometer 1st order
∅45 mm, 120 mm baseline
0.50 fT /√Hz

Gradiometer 1st order
∅20 mm, 120 mm baseline
1.57 fT /√Hz

Warm-cold distance Dewar: 9 mm (at RT)

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Applications

PTB

T_1 contrast at ultra-low fields

Difference in T_1 between materials (e.g. tissues)

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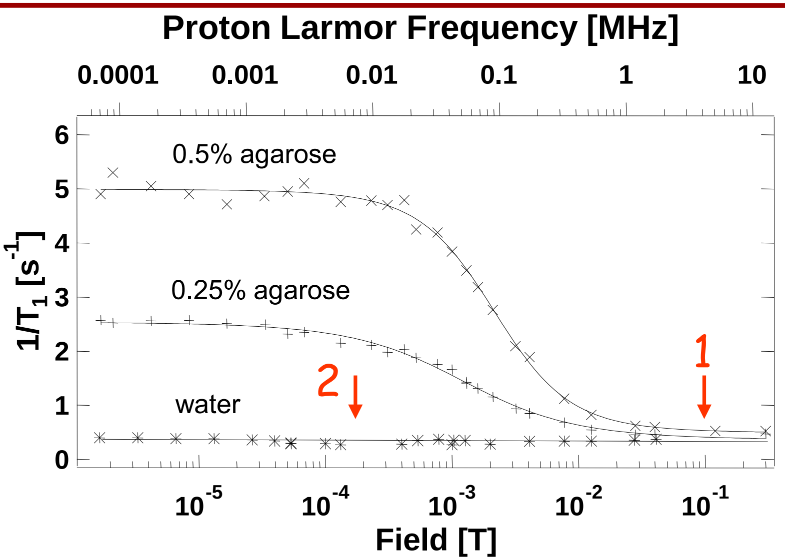
T_1 Contrast

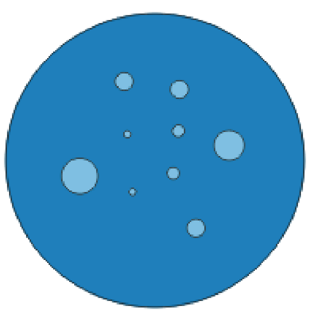
BERKELEY LAB

T_1 dispersion of water and agarose gel

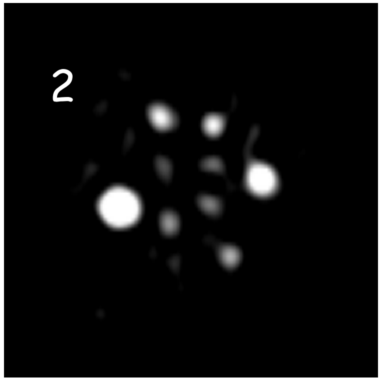


S-K. Lee *et al.*, Mag. Res. Med. **53,** 9 (2005)

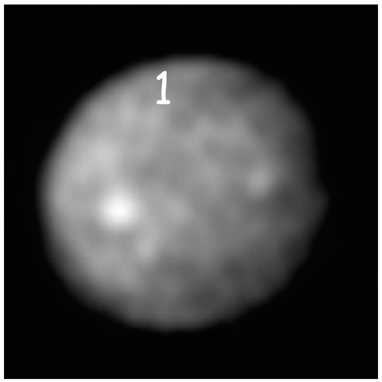
Phantom
Water columns in agarose gel, 1 – 6 mm diameter



T_1 contrast at 132 μT



T_1 contrast at 100 mT



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T_1 Contrast

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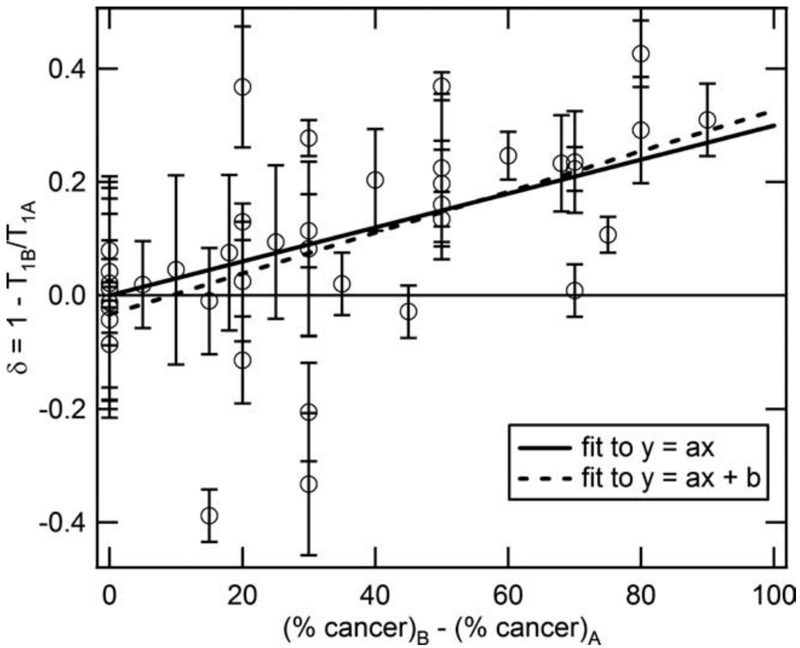
T_1 of *Ex Vivo* Prostate Tissue

Case #	% tumor	T_1 (ms)	δ
1 A 1 B	2 70	85 ± 6 66 ± 6	0.22
2 A 2 B	2 20	62 ± 9 57 ± 2	0.081
3 A 3 B	20 80	81 ± 6 52 ± 3	0.36
4 A 4 B	0 20	54 ± 6 51 ± 4	0.056
5 A 5 B	5 20	67 ± 4 68 ± 4	-0.015
6 A 6 B	0 40	62 ± 7 47 ± 4	0.24

- Use relative change:

$$\delta = 1 - T_{1B}/T_{1A}.$$



Busch *et al.* Mag Res Med, 67,1138-1145, (2012)

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T_1 Contrast

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Potential Applications for T_1 contrast

- Staging of prostate cancer prior to biopsy.
- T_1-weighted image of prostate to guide biopsy.
- Monitor cancer progression during active surveillance or radiation therapy.
- Imaging of other types of cancer, for example, brain and breast tumors.

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Applications

Imaging Brain Function

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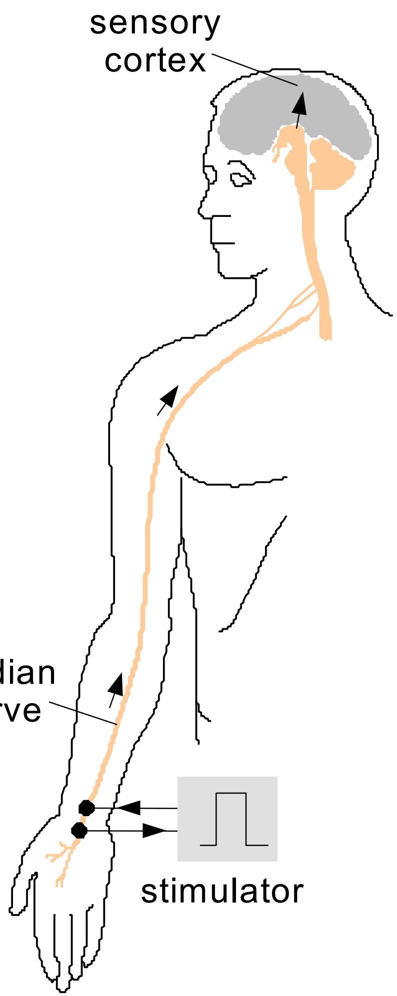
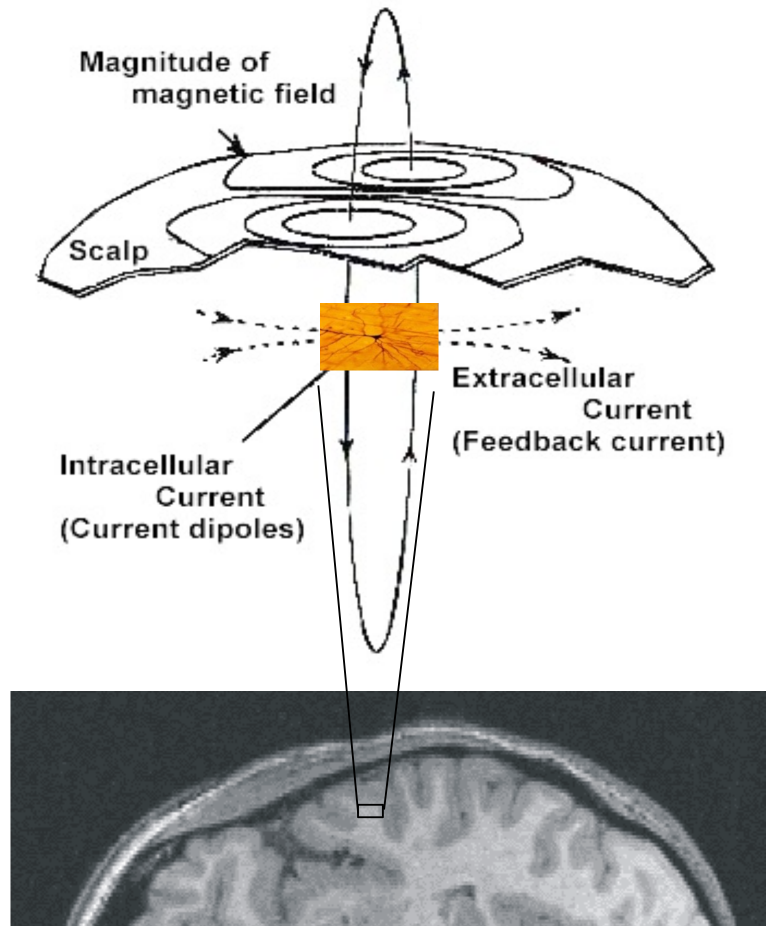
Brain Function

PTB





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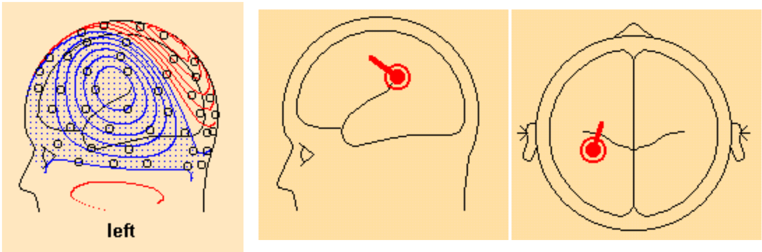
Brain Function

PTB

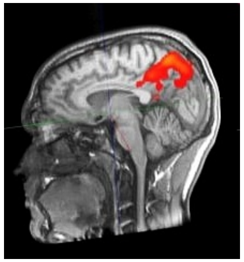
How to detect neuronal currents non-invasively?

Magnetoencephalography (MEG)



Direct, low localisation accuracy

Functional MRI (typ. 1.5 T)



Indirect, high spatial resolution

Approach I

Combine MEG with low field MRI.
→ Bias solution to inverse problem, minimise co-registration errors.

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MEG/MRI

Los Alamos NATIONAL LABORATORY EST. 1943

B_{pol} =30 mT
B_m = 46 μT
G_x=G_z= 140 μT/m
Δr = 3 · 3 mm^2

V. S. Zotev *et al*.“Microtesla MRI of the human brain combined with MEG“, J.Magn.Resonance,**194**,115,(2008)

MAGNICON

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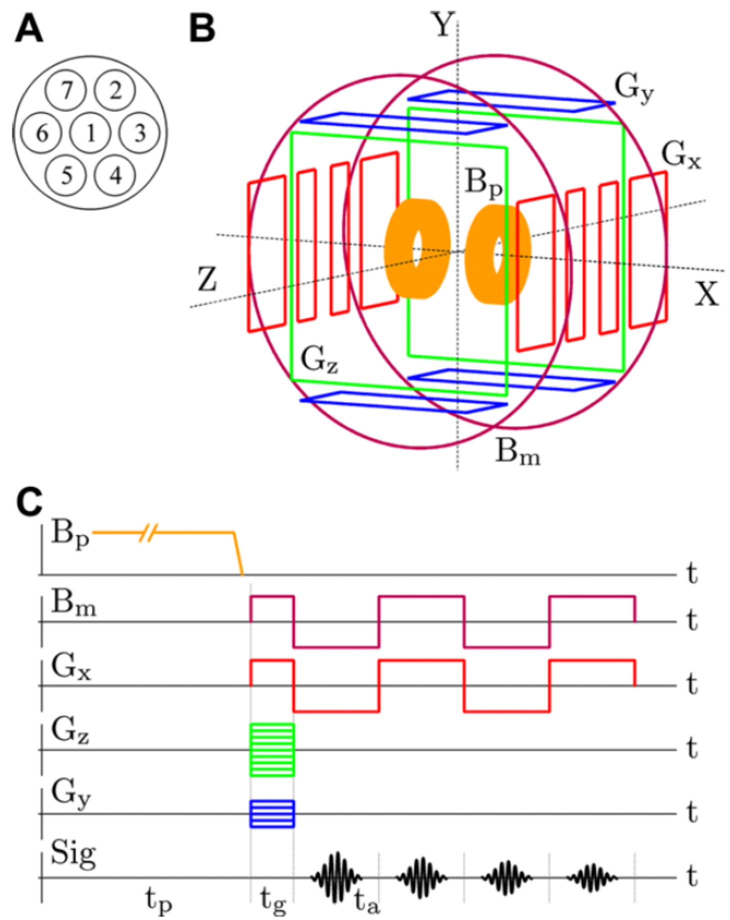
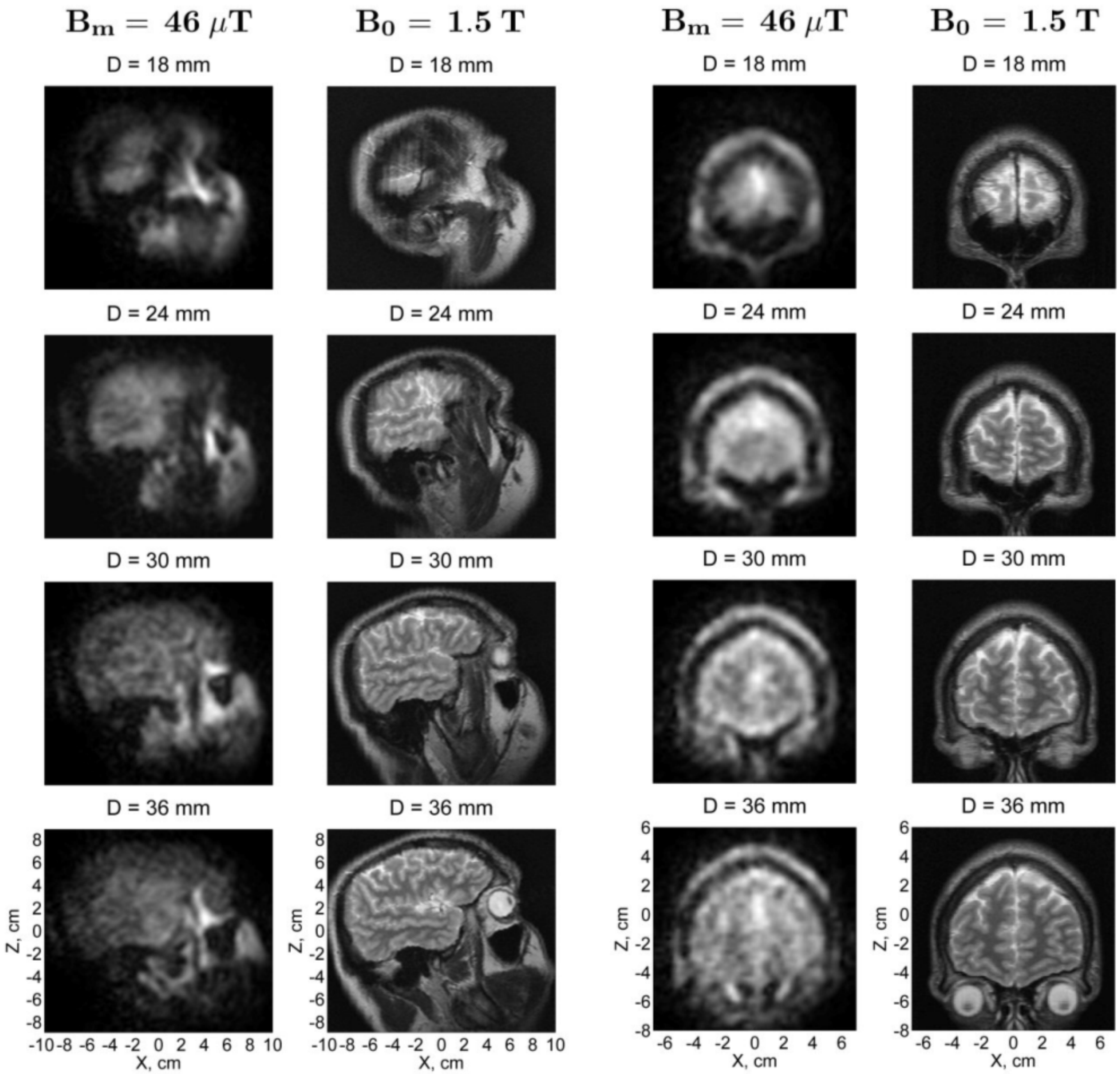


Los Alamos
NATIONAL LABORATORY
EST. 1943



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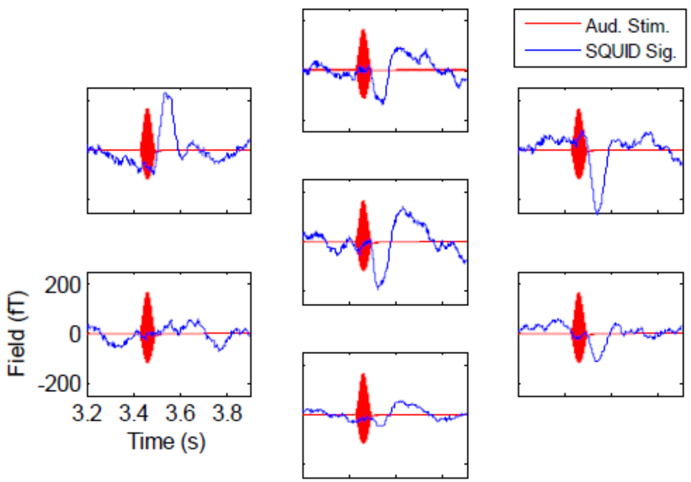

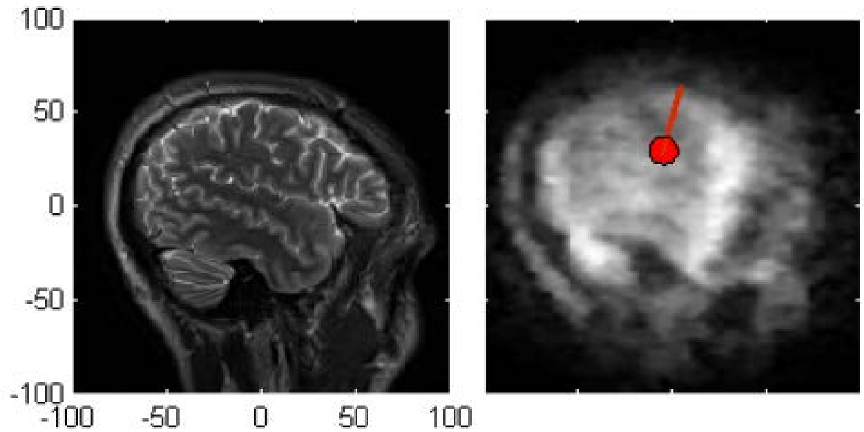

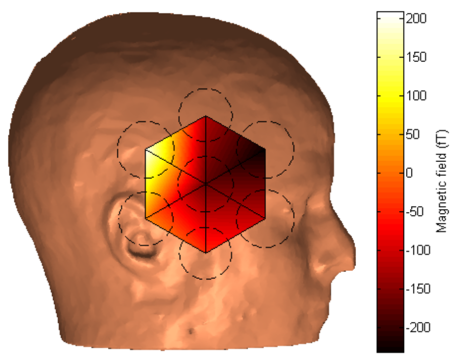

Interleaved MRI at 94 μT and MEG measurement

Co registration error ~ 3mm

P. Magnelind *et al.* “Co-registration of MEG and ULF MRI using a 7 channel Low T_c SQUID system” IEEE Trans. on Appl. Supuercon, **21**, 456-460 (2011)

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Brain Function

PTB

How to detect neuronal currents non-invasively?

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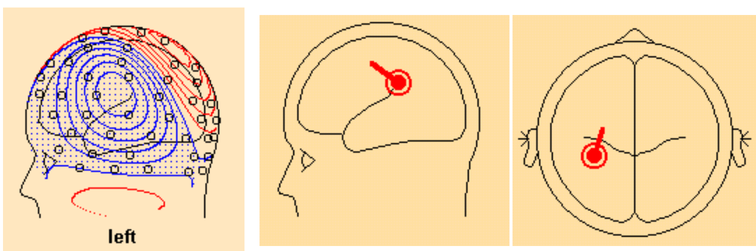

Direct, low localisation accuracy

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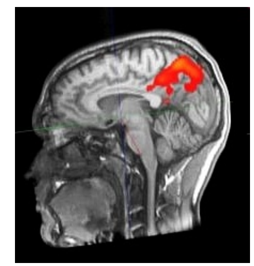

Indirect, high spatial resolution

Approach II

Combine direct detection of neuronal currents with imaging.
→Direct Neurocurrent Imaging (DNI)

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DNI

PTB

DC-Effect

• Based on sustained neuronal activity (~ s).

• Superposition of detection field and neuronal field leads to local change in precession frequency of protons near activity and to alteration of NMR line-shape.
• Utilize MR imaging techniques to localise activity.

Benefits

• Faster than fMRI: exploit influence of neuronal field rather than blood oxygenation (BOLD-effect).
• No artefacts due to BOLD-effect (negligible at ultra-low fields).
• No solution of inverse problem required as in MEG/EEG.

A.M. Cassara *et al.* “Neuronal current detection with low-field magnetic resonance: simulations and methods”, *Magn. Res. Imaging* **27**, 1131 – 1139, (2009)

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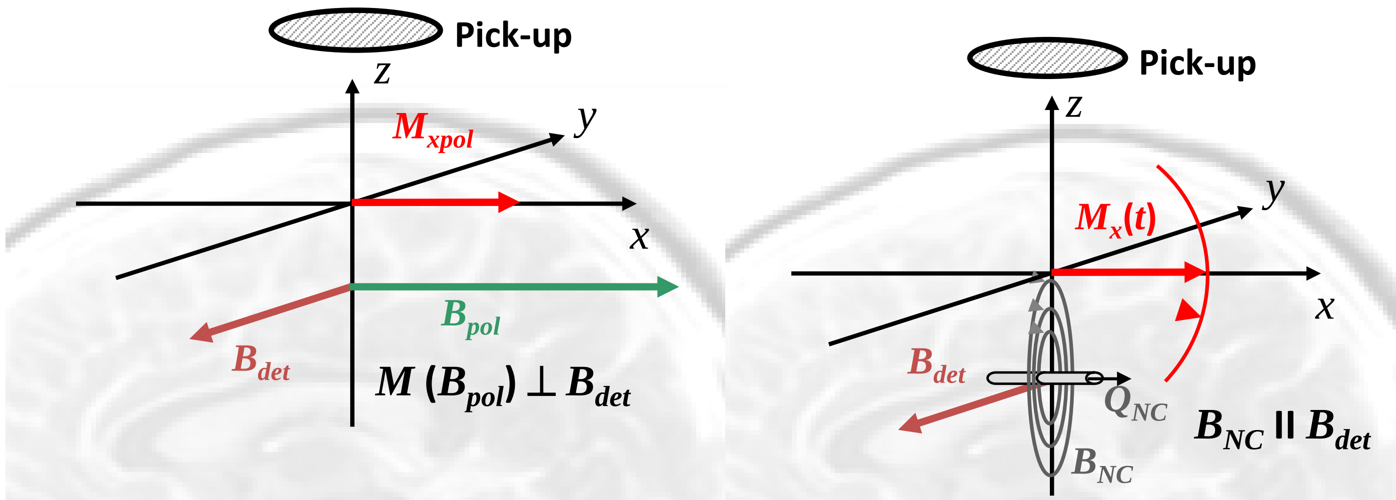
DNI

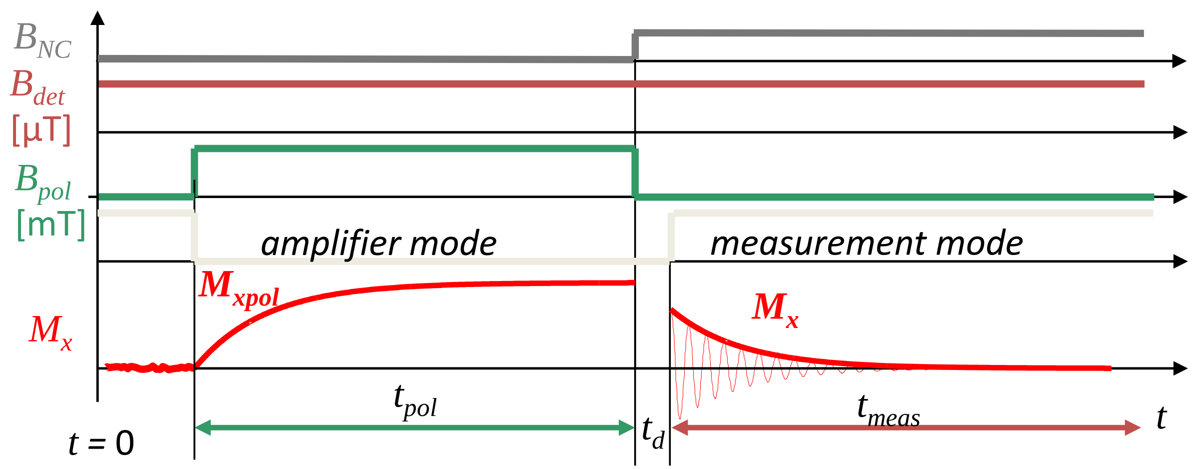
PTB

DC-Effect



Advantage over high field MR

increased influence of neuronal fields: Relative ~10 ppm



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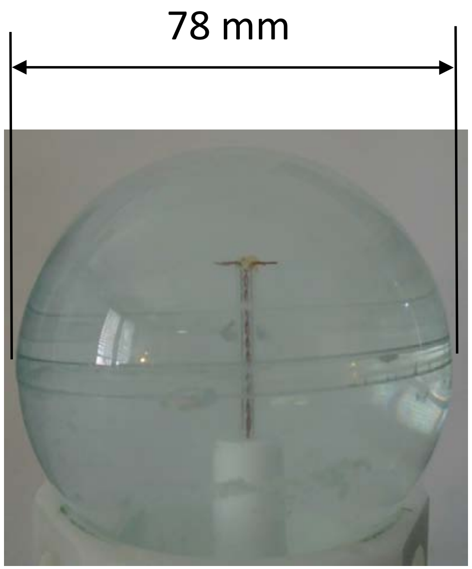
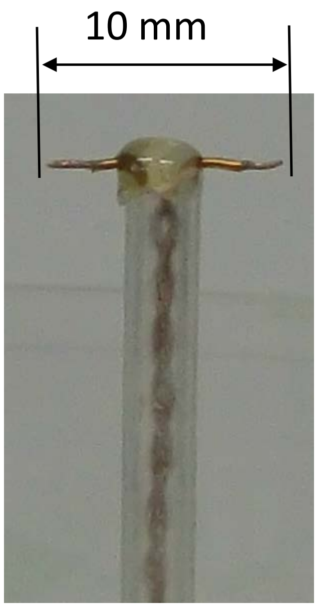
- Generation of current dipole moments of ~ 2 μAm.
- Depths 35 mm (from dewar bottom).





R. Körber et al. „An advanced phantom study assessing the feasibility of neuronal current imaging by ultra-low field NMR“ J. Mag. Res. **237**, 182-190 (2013)

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DNI

PTB

Phantom: $CuSO_4$-solution

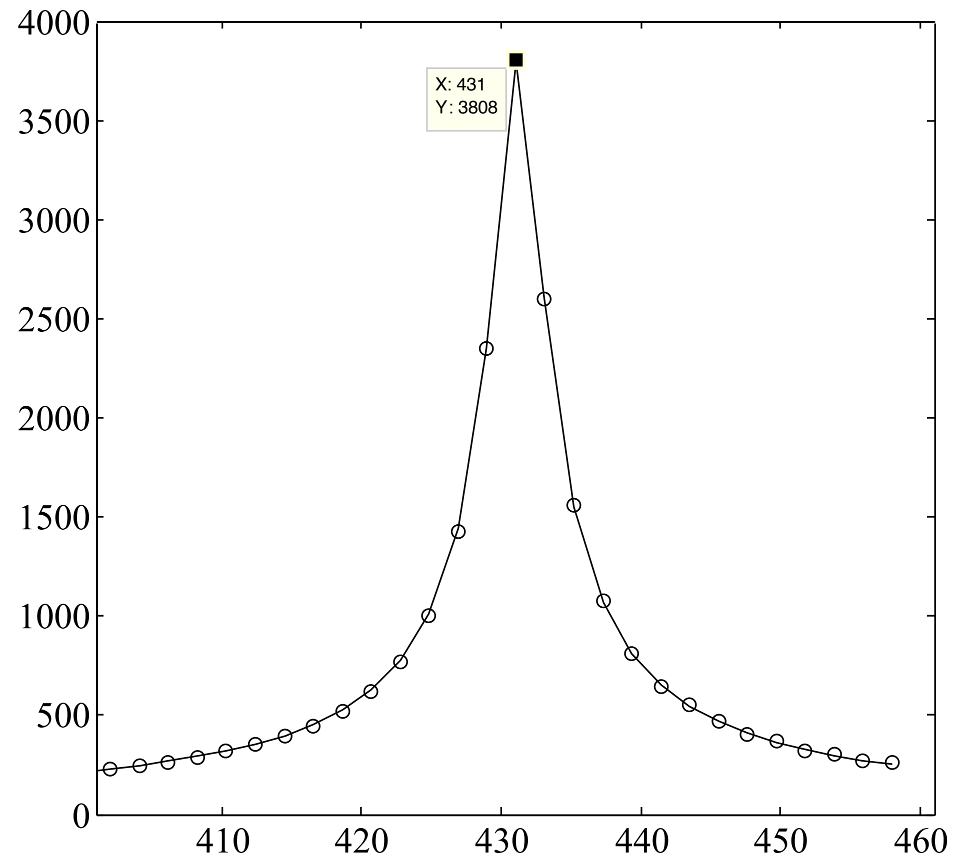
T_1 and T_2: 100 ms

Conductivity: 3.33 mS/cm

- Pre-polarisation

  50 mT

- Measurement time 30 min



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DNI

PTB

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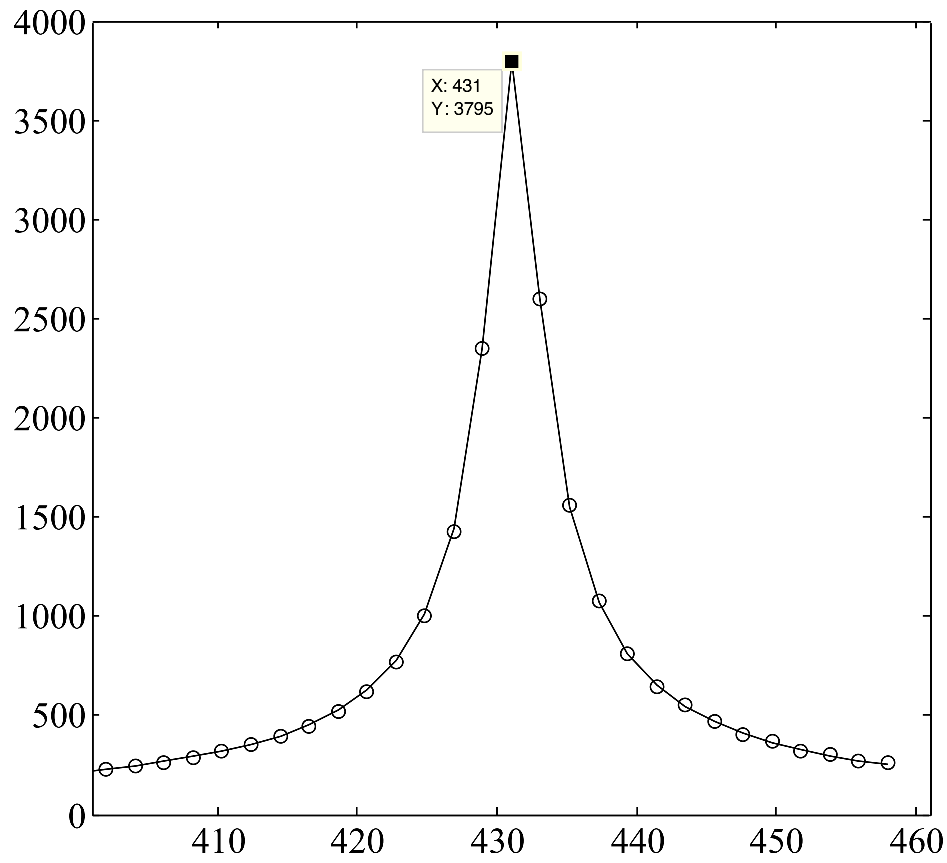
  50 mT

- Measurement time 30 min

Change in line-shape masked by signal from unaffected volume.



DNI

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T_1 and T_2: 100 ms

Conductivity: 3.33 mS/cm

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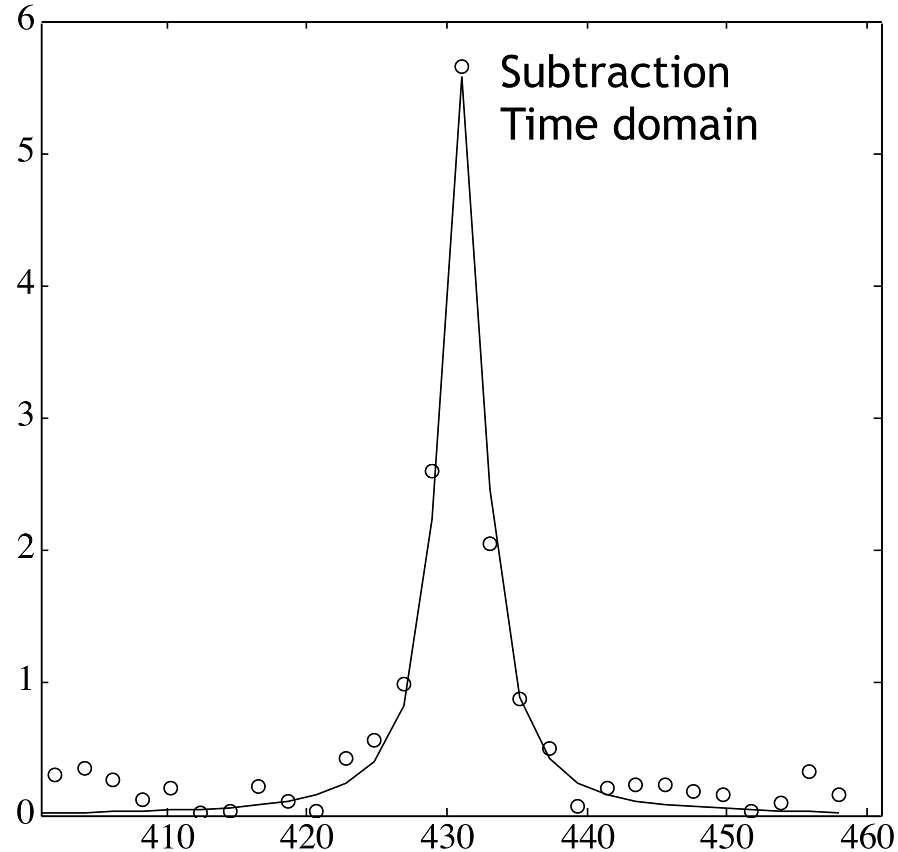
Change in line-shape masked by signal from unaffected volume.

Devise subtraction to reveal influence of dipole field.



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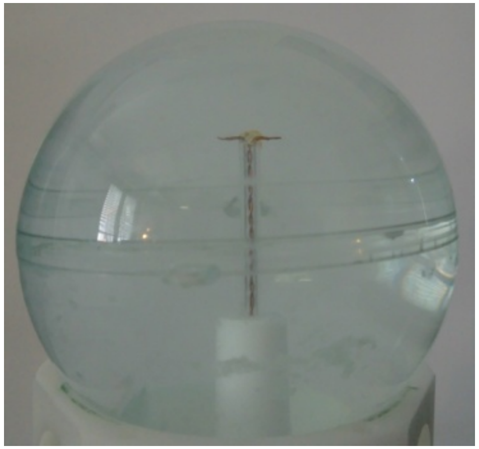
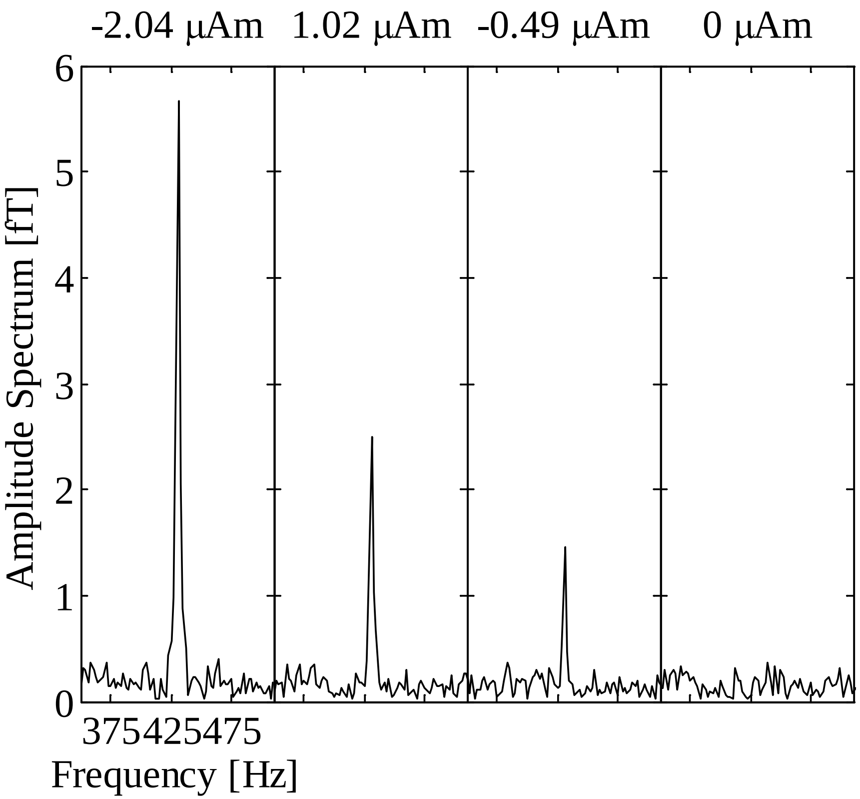
DNI

PTB



Depth dipole: 35 mm



- Symmetry of dipole field leads to partial cancellation effect after subtraction.
- Different sensor sensitivities of voxels around dipole prevent perfect cancellation.

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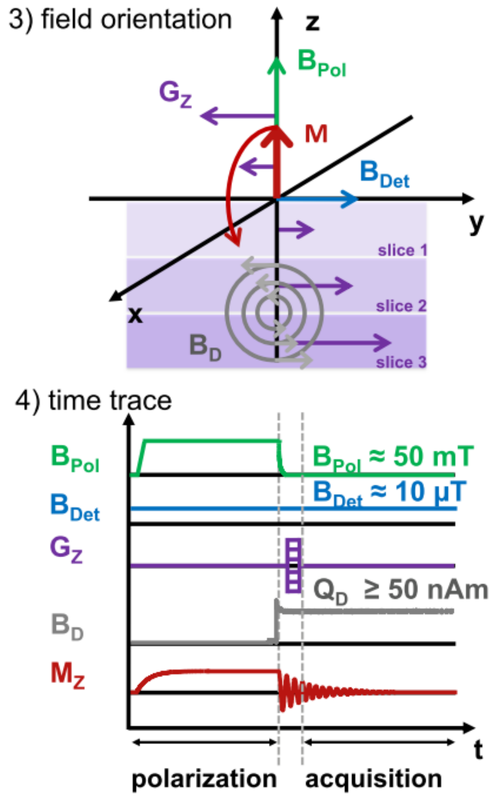
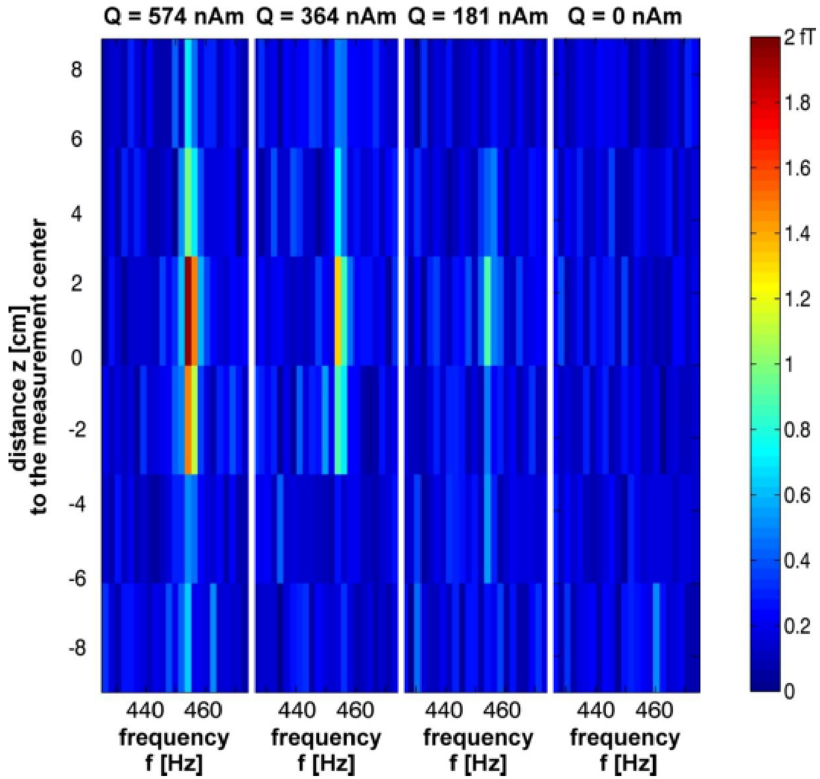
DNI

PTB





- Use 1-d encoding to overcome partial cancellation effect in simple NMR experiment.
- Devise subtraction to reveal influence of dipole field on ‘1-d image’.

→ Improvement of minimum detectable dipole strength by factor of ~ 2.8 to ~**180 nAm**.

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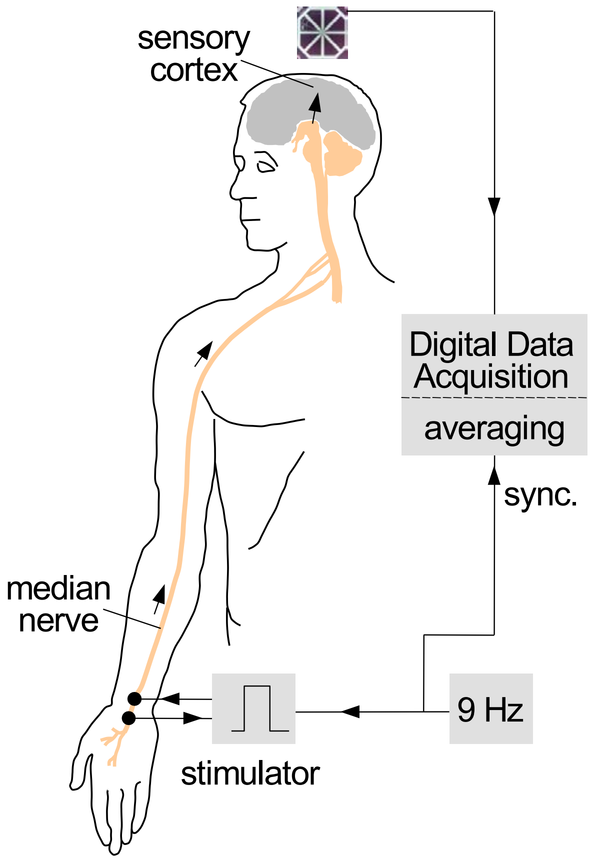
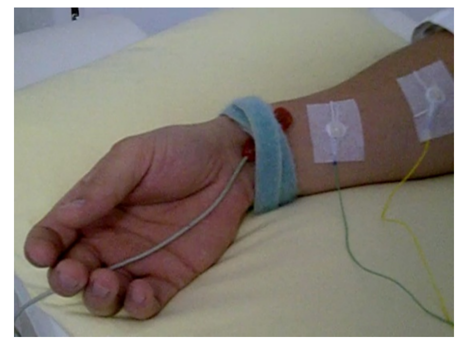
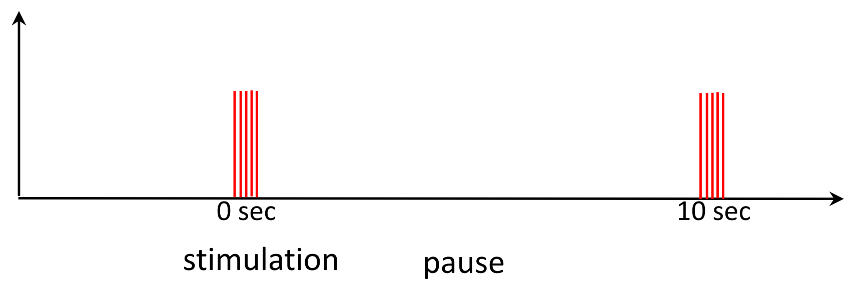
DNI

PTB

Generation of long-lived neuronal activity by electrostimulation of the median nerve.

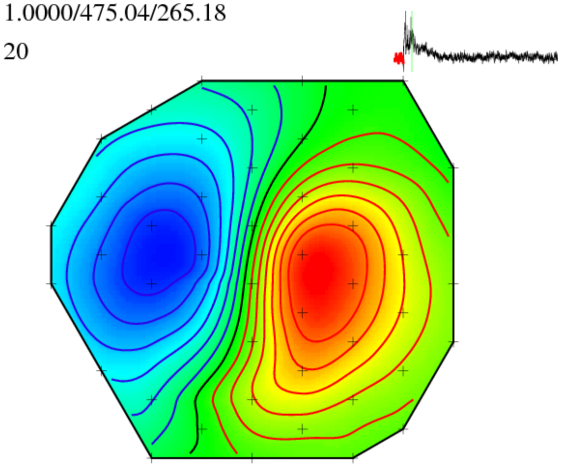


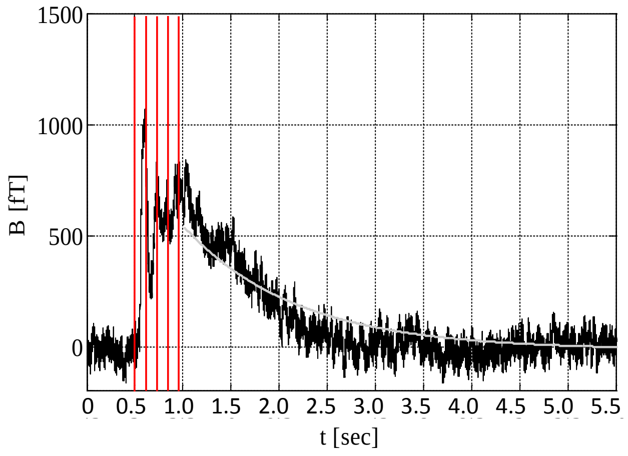




- Stimulate for 0.5 sec every 10 sec
- Current typ. 8 mA

DNI





Dipolar Field distribution:

- Localised source
- Max. Current dipole up to **50 nAm**
3.6 smaller than in phantom experiments
- depth ~ **35 mm**

R. Körber, *et al.* “Simultaneous measurements of somatosensory evoked AC and near-DC MEG signals”, Biomed. Tech, **56**, 91-97 (2011)

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Summary

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Different NMR techniques necessary for LF NMR/MRI:

- Prepolarization and SQUID detection.
- Be careful with noise sources.

Summary

A number of applications of LF NMR/MRI have potential for usage:

- T_1 contrast for instance for cancer detection.
- Combination of ULF MRI and MEG.
  Improve localization accuracy of MEG by biasing solution to inverse problem from anatomical knowledge, but still two separate modalities.
- Direct detection of neuronal currents: DNI
  Obtain 'true' image of brain function by detecting influence of neuronal fields on MR image, single modality.

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