Ultra-Low-Field MR

Basic Principles and some Applications

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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 Boltzmann distribution.

\[ E \propto B \]

Zeeman splitting for spin-half system

\[ \frac{N_-}{N_+} = e^{-\gamma_B B/kT} \]

\(N_-\): spin population higher energy
\(N_+\): spin population lower energy
\(\gamma\): gyromagnetic ratio

\[ \text{if } \gamma_B B \ll k_B T \]

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

\(^1\text{H}, 300 \text{ K}, 3 \text{ T}: 10 \text{ ppm}\)

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

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

\[ M = N \frac{\gamma^2 \hbar^2}{4kT} B \]

Curie Law
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 $\omega_0$)

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 $\propto M_0 \omega_0 \propto B_0^2$
Conventional pulsed NMR techniques not suitable at ultra-low fields.
- Use SQUID
- Use prepolarisation

Use coil to measure $dB/dt$
To boost magnetisation of sample use prepolarisation, usually mT-range.

Expose sample to detection field, usually µT-range.

During polarisation magnetisation $M_z$ grows with $T_1$. 

To boost magnetisation of sample use prepolarisation, usually mT-range.
Expose sample to detection field, usually μT-range.

During detection magnetisation $M$ precesses around $B_{\text{det}}$ and decays with $T_2$. 
$T_2$ Relaxation

$B_z^{SQUID}$

$M_z$ vs. time $t / [s]$

$M_0 \sim B_{pol}$

$\nu \sim B_{det}$

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

$B_{z}^{pol}$

$B_{x}^{det}$

$t=0$ vs. time $t / [s]$
$T_1$ Relaxation

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.
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 $B_z^{SQUID}$. 

$$t_{relax} = 1 \, \text{s}$$
$T_1$ Relaxation

$B_{z}^{SQUID}(t_{\text{relax}})$

$t_{\text{relax}} = 1 \text{ s}$

$t_{\text{relax}} = 2 \text{ s}$
$T_1$ Relaxation

$M_z$ vs. time $t$ / [s]

$B_z^{SQUID}(t_{\text{relax}})$

$B_z^{SQUID}(t_{\text{relax}})$

$T_1(B_{\text{relax}})$

$t_{\text{relax}}$ / [s]
General Setup

To exploit sensitivity of SQUID:

Use magnetically shielded room

Dewar with SQUID

coil-system

magnetic shielding

Labnoise: gradiometer (diameter 45 mm, baseline 120 mm)
General Setup

To exploit sensitivity of SQUID:

- Reduce Johnson noise

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

Seton et al. Cryogenics, 2005
General Setup

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
General Setup

SQUID-System

Polarisation and detection coils

magnetic shielding

Dewar with SQUID

coil-system

magnetic shielding

General Setup

Important parameters:

- $B_{det}$: up to ~10 µT (400 Hz)
- $B_{pol}$: up to 54 mT

Different gradiometers, in LINOD1

Gradiometer 1\textsuperscript{st} order
- ∅45 mm, 120 mm baseline
  - 0.50 fT /√Hz
Gradiometer 1\textsuperscript{st} order
- ∅20 mm, 120 mm baseline
  - 1.57 fT /√Hz

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

$T_1$ contrast at ultra-low fields

Difference in $T_1$ between materials (e.g. tissues)
$T_1$ contrast at 132 µT  $T_1$ contrast at 100 mT

$T_1$ dispersion of water and agarose gel

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

$T_1$ Contrast

$T_1$ of Ex Vivo Prostate Tissue

- Use relative change:
  \[ \delta = 1 - \frac{T_{1B}}{T_{1A}}. \]

<table>
<thead>
<tr>
<th>Case #</th>
<th>% tumor</th>
<th>$T_1$ (ms)</th>
<th>$\delta$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 A</td>
<td>2</td>
<td>85 ± 6</td>
<td>0.22</td>
</tr>
<tr>
<td>1 B</td>
<td>70</td>
<td>66 ± 6</td>
<td></td>
</tr>
<tr>
<td>2 A</td>
<td>2</td>
<td>62 ± 9</td>
<td>0.081</td>
</tr>
<tr>
<td>2 B</td>
<td>20</td>
<td>57 ± 2</td>
<td></td>
</tr>
<tr>
<td>3 A</td>
<td>20</td>
<td>81 ± 6</td>
<td>0.36</td>
</tr>
<tr>
<td>3 B</td>
<td>80</td>
<td>52 ± 3</td>
<td></td>
</tr>
<tr>
<td>4 A</td>
<td>0</td>
<td>54 ± 6</td>
<td>0.056</td>
</tr>
<tr>
<td>4 B</td>
<td>20</td>
<td>51 ± 4</td>
<td></td>
</tr>
<tr>
<td>5 A</td>
<td>5</td>
<td>67 ± 4</td>
<td>-0.015</td>
</tr>
<tr>
<td>5 B</td>
<td>20</td>
<td>68 ± 4</td>
<td></td>
</tr>
<tr>
<td>6 A</td>
<td>0</td>
<td>62 ± 7</td>
<td>0.24</td>
</tr>
<tr>
<td>6 B</td>
<td>40</td>
<td>47 ± 4</td>
<td></td>
</tr>
</tbody>
</table>

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.
Applications

Imaging Brain Function
Brain Function

Sensory cortex

Median nerve

Stimulator

Magnitude of magnetic field

Extracellular Current (Feedback current)

Intracellular Current (Current dipoles)
Brain Function

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.
$B_{pol} = 30 \text{ mT}$
$B_m = 46 \mu\text{T}$
$G_x = G_z = 140 \mu\text{T/m}$
$\Delta r = 3 \cdot 3 \text{ mm}^2$

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Interleaved MRI at 94 µT and MEG measurement

Co registration error ~ 3mm

How to detect neuronal currents non-invasively?

**Magnetoencephalography (MEG)**

- Direct, low localisation accuracy

**Functional MRI (typ. 1.5 T)**

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**Approach II**

Combine direct detection of neuronal currents with imaging.

→ Direct Neurocurrent Imaging (DNI)
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.

DC-Effect

\[ M_x(t) \]

Advantage over high field MR
increased influence of neuronal fields:
Relative \(~10\) ppm

• Generation of current dipole moments of ~ 2 µAm.

• Depths 35 mm (from dewar bottom).

Phantom: CuSO$_4$-solution

$T_1$ and $T_2$: 100 ms

Conductivity: 3.33 mS/cm

• Pre-polarisation
  50 mT

• Measurement time 30 min
Phantom: CuSO$_4$-solution

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Change in line-shape masked by signal from unaffected volume.
Phantom: CuSO$_4$-solution

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Conductivity: 3.33 mS/cm

- Pre-polarisation
  50 mT
- Measurement time 30 min

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

Devise subtraction to reveal influence of dipole field.
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.
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.
Generation of long-lived neuronal activity by electrostimulation of the median nerve.

- Stimulate for 0.5 sec every 10 sec
- Current typ. 8 mA
Dipolar Field distribution:

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

Different NMR techniques necessary for LF NMR/MRI:

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

Bernstein Focus Neurotechnology-Berlin
Grant numbers 08GQ0850 (B1) & 01GQ0852 (B2)