Magnetic Particle Imaging (MPI)

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Tomographic imaging using the nonlinear response of magnetic particles

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The use of contrast agents and tracers in medical imaging has a long history. They provide important information for diagnosis and therapy, but for some desired applications, a higher resolution is required than can be obtained using the currently available medical imaging techniques. Consider, for example, the use of magnetic tracers in magnetic resonance imaging: detection thresholds for in vitro and in vivo imaging are such that the background signal from the host tissue is a crucial limiting factor. A sensitive method for detecting the magnetic particles directly is to measure their magnetic fields using relaxometry; but this approach has the drawback that the inverse problem (associated with transforming the data into a spatial image) is ill posed and therefore yields low spatial resolution. Here we present a method for obtaining a high-resolution image of such tracers that takes advantage of the nonlinear magnetization curve of small magnetic particles. Initial ‘phantom’ experiments are reported that demonstrate the feasibility of the imaging method. The resolution that we achieve is already well below 1 mm. We evaluate the prospects for further improvement, and show that the method has the potential to be developed into an imaging method characterized by both high spatial resolution as well as high sensitivity.
Comparison of imaging modalities

<table>
<thead>
<tr>
<th></th>
<th>CT</th>
<th>MRI</th>
<th>PET</th>
<th>SPECT</th>
<th>MPI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spatial resolution</td>
<td>0.5 mm</td>
<td>1 mm</td>
<td>4 mm</td>
<td>10 mm</td>
<td>&lt; 1 mm</td>
</tr>
<tr>
<td>Acquisition time</td>
<td>1 s</td>
<td>1 s – 1 h</td>
<td>1 min</td>
<td>1 min</td>
<td>&lt; 0.1 s</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>Low</td>
<td>Low</td>
<td>High</td>
<td>High</td>
<td>High</td>
</tr>
<tr>
<td>Quantifiability</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Harmfulness</td>
<td>X-ray</td>
<td>heating</td>
<td>β, γ radiation</td>
<td>γ radiation</td>
<td>heating</td>
</tr>
</tbody>
</table>

Outline

- MPI basics
- Spatial encoding
- Spatial and time resolution
- Reconstruction
- Technical challenges – MPI system at TUBS
- Tracer materials for MPI
- MPI applications - examples
MPI Basics

Signal in MPI system without static background field \((H_{\text{ext}} = 0)\)
Signal in MPI system in static background field \((H_{ext} > 0)\)
How to get a spatial image?

- Gradient field provides field-free point (FFP), nanoparticles in FFP generate harmonics
- Sample is mechanically moved through FFP or FFP is driven through sample volume via drive-field coils
Mechanical movement of sample through FFP and detection of single harmonic

1D image of Vitrovac stripes

Model: \[ M = \phi M_S L \left[ \frac{\mu_0 m(H_{DC} + H_{AC} \sin(\omega_{ext} t))}{k_B T} \right] \]
Shift of FFP via drive field

X-Space Imaging

\[ \frac{d}{dt} \left( \frac{H}{H_{sat}} \right) = \frac{H}{H_{sat}} \]

\[ M / A m \]

\[ \frac{dL}{dH} (PSF) \]

\[ * \]

Signal / a.u.
Spatial encoding using complete harmonics spectrum

Harmonics spectrum provides characteristic fingerprint for given position!
System function (matrix): 1D

Log magnitude

Harmonic #

Position and static flux density, resp.
## Spatial encoding - Comparison

<table>
<thead>
<tr>
<th>Single harmonic</th>
<th>Many harmonics (frequency domain)</th>
<th>X space (time domain)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>narrow bandwidth (&lt; 100 Hz, resonant readout)</td>
<td>large bandwidth (&gt; 1 MHz)</td>
</tr>
<tr>
<td></td>
<td>high sensitivity</td>
<td>Sensitivity limited by amplifier noise</td>
</tr>
<tr>
<td></td>
<td>simple reconstruction (time domain)</td>
<td>complex reconstruction (frequency domain)</td>
</tr>
<tr>
<td></td>
<td>no reference scan required</td>
<td>time-consuming reference scan</td>
</tr>
<tr>
<td></td>
<td>slow (max. 1 image/s)</td>
<td>fast (&gt; 20 images/s, real time)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Sensitivity limited by amplifier noise</td>
</tr>
<tr>
<td></td>
<td></td>
<td>simpler reconstruction (time domain)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>no reference scan required</td>
</tr>
<tr>
<td></td>
<td></td>
<td>slower (better SNR needed for reconstruction)</td>
</tr>
</tbody>
</table>
Sampling scheme to cover multidimensional field-of-view

- Sampling with Cartesian trajectories most obvious
- Praxis: Lissajous trajectories

Example: 2D Lissajous trajectory with $f_x/f_y = 24/25$
Sampling scheme to cover multidimensional field-of-view

- Finite repetition time: excitation frequencies must be commensurable
- Base frequency: \( f_B = f_x \cdot K_x = f_y \cdot K_y = f_z \cdot K_z \)
- **Example:** \( f_B = 250 \text{ kHz} \), \( K_x = 25 \), \( K_y = 24 \), \( K_z = 26 \)
  \( \Rightarrow f_x = 10 \text{ kHz}, \ f_y \approx 10.4 \text{ kHz}, \ f_z \approx 9.6 \text{ kHz} \)
  \( \Rightarrow \) repetition time: \( T^R = \frac{K_y K_z}{f_x} = 62 \text{ ms} \)
- Spatial resolution is determined by steepness of M-H curve and gradient field strength \( G \)
- **But:** density of trajectories must be large enough
  
  - Density parameter \( N_D = K_x \)
  - **Example:** FOV = 24 mm \( \Rightarrow \) with \( N_D = 25 \), distance between points in \( x \) direction about 1 mm
Extension of scanning range

- FOV is limited by gradient field $G$ and amplitude of driving field $H_D$
- **Example:** $G = 5 \text{ T/m}$, $H_D = 30 \text{ mT}$ (at 10 kHz)

  $$ \Rightarrow \text{FOV is cuboid with side lengths: } l_z = 2 \frac{H_D}{G_z} \approx 12 \text{ mm}, l_x = l_y = 2 \frac{H_D}{G_y} \approx 24 \text{ mm} $$

- Extension of scanning volume by using so-called focus field (e.g., multistation approach)
Spatial resolution

$$\Delta \xi_{\text{FWHM}} = 4.16$$

with $$\xi = \frac{\mu_0 m H}{k_B T} = \beta H$$

$$\Rightarrow \Delta R_{\text{FWHM}} = 4.16 \frac{1}{\beta G}$$

Examples: $$M_s = 4 \cdot 10^5 \text{ A/m}$$

$$D_c = 20 \text{ nm}, G = 5 \text{ T/m}$$

$$\Rightarrow R_{\text{FWHM}} = 2 \text{ mm}$$

$$D_c = 30 \text{ nm}, G = 6 \text{ T/m}$$

$$\Rightarrow R_{\text{FWHM}} = 0.5 \text{ mm}$$

More sophisticated: inclusion of convolution and SNR in imaging process (Buzug 2008):

$$\Delta R_{\text{FWHM}} \approx \frac{2\pi}{\ln(SNR(0)) \beta G}$$
Reconstruction

- Voltage induced in receive coil is given by convolution of particle concentration \( c(\vec{r}) \) and derivative of Langevin function \( \dot{L}(\beta Gr) \) (PSF)

\[
u(t) = \int_{FOV(t)} s(\vec{r}) c(\vec{r}) d^3 r
\]

with system function in time space \( s(\vec{r}) = -\mu_0 \vec{p}^R(\vec{r}) \cdot \frac{\partial m(\vec{r}, t)}{\partial t} \)
and receive coil sensitivity \( \vec{p}^R(\vec{r}) \) (calculated with Biot-Savart law)

- \( n \)-th harmonic of induction signal if given by

\[
U_n = \int_{FOV} S_n(\vec{r}) c(\vec{r}) d\vec{r}
\]

with \( S_n(\vec{r}) \) – system function in frequency space
\( c(\vec{r}) \) - particle concentration at location \( \vec{r} \)

- System function \( S_n(\vec{r}) \) is generally obtained by performing a reference scan of a point-like sample through FOV
- Solution of linear equation system \( g = S \cdot c \) using Tikhonov regularization method
Technical challenges

- Homogeneous sinusoidal excitation field (frequency $f_{exc}$ of few 10 kHz, amplitude $H_0$ of $\geq 30$ mT) with very low THD
  - Resonant excitation
  - Filtering
  - No eddy currents and distortions by nearby objects (e.g., use of litz wire)
  - Cooling (oil, water)
- Separation of field from excitation and field from nanoparticles
  - Band-stop filtering
  - Gradiometric arrangements
- Low-noise amplifier with large bandwidth (> 1 MHz) for receive coils
- Shielding against electromagnetic disturbances (?)
- Determination of system matrix (time-consuming)
- Suitable magnetic markers
Diameter of bore: 30 mm
Field of view (FOV): 25x15x25 mm

Layout: FFP scanner

Gradient $G$: 3 T/m \textbf{NdFeB}
max. 4 T/m Maxwell coils
→ 3-7 T/m adjustable (z-direction)

Excitation/Drive field $H_D$: Helmholtz-type coil / Solenoid X / Y / Z
Amplitude max. 30(60) mT @ ~10 kHz
THD < 0.002% (> 94 dB$_C$)

Cooling: Water-cooled
Shielding: Single-layer copper
Gradient coils

- Gradient strength G: 3 T/m NdFeB
  max. 4 T/m Maxwell coils
  **3-7 T/m** (z-Direction)

- Cooling: Water-cooled (closed circuit)
Drive coils

- **Drive field** $H_D$: Helmholtz-type coil / Solenoid
  Amplitude max. 30(60) mT @ ~10 kHz
  THD < 0.002% (> 94 dB$_C$)

- **Cooling:** Water-cooled (closed circuit)

![Graph showing flux density](image_url)

- $X$: 31 mT ($\pm 0.07\%$) @ 15 A
- $Y$: 30 mT ($\pm 3.13\%$) @ 25 A
- $Z$: 62 mT ($\pm 0.09\%$) @ 20 A
Signal chain: Excitation

- **D/A excitation:** NI PCIe-6733 (3x 16-bit, 1 MS/s)
- **Power amplifier:** img StageLine STA-3000
  3x 1.5 kW @ 4 ohms (20-20000 Hz)
  Hybrid Series-Parallel Resonating Circuit
- **A/D controller:** NI PCIe-6320 (3x 16-bit, 250 kS/s)

Power Amplifier (PA)
Resonating Band Pass Filter (BPF)
Transmit Coils (TxC)
Signal chain: Detection

- **Filter:** Passive Resonating Band Stop Filter
  - HighPass-Filter \( f_{\text{Low}} = 12 \text{ kHz} \)
- **Pre-Amplifier:** UltraLowNoise-Amplifier (ULNA)
  - \( e_N = 0.9 \text{ nV/} \sqrt{\text{Hz}}, \) Differential Input Stage
  - LowPass-Filter* \( f_{\text{High}} = 500 \text{ kHz} \)
  - Gain \( f_{10\text{kHz}} = 250, \) Gain \( f_{500\text{kHz}} = 1000 \)
- **A/D acquisition:** NI PCI-6133 (3x 14-bit, 2.5 MS/s)

![Diagram](image)

- Receive coils (RxC)
- Resonating Band Stop Filter (BSF)
- Low Noise Amplifier (LNA)

* Filter DLF \( f_C = 756 \text{ kHz (AM)} \) → Copper Shielding
MPI equipment: Rack, coils and cooling

2D image of letter E
Tracer materials for MPI

- Naive Langevin model picture: particles with large moments yield steep $M-H$ curves
- *But:* Must be able to follow the fast sinusoidal excitation field $\Rightarrow$ contradiction (?)

- Current status: Resovist® and FeraSpin™ possess richest harmonics spectra despite small size of elementary crystallites (5-7 nm)
- Only small part of iron oxide contributes to MPI signal
Philips Research Labs Hamburg (Borgert, Gleich, Weizenecker):
• Mouse scanner (demonstration of 3D real-time in-vivo MPI)
• Small animal MPI scanner
• Development of human diagnostic system for cardiovascular
diseases (BMBF project MAPIT)

Bruker 2013 (?): 2 mice scanner will be provided funded by DFG

Lübeck (Buzug): 2 ½ D system in development
UC Berkeley (Conolly): X space MPI systems (quasi static 3D images)

Braunschweig: 3D-System for mice
Real-time in-vivo MPI on mice

- 40 µmol/L Fe (Resovist)
- Frame Speed: 46.4 Hz → 21.5 ms → Beating mouse heart (240 bpm)

- FOV: 34X20x28
- Voxel size: 0.6 mm³
Real-time in-vivo MPI on mice


- Standard technique: X-ray imaging using iodine or gadolinium contrast agent
- **But:** iodine and gadolinium often toxic for CKD patients’ weak kidneys
  ⇒ significant morbidity and mortality
- MPI may become safe substitute for angiography
- Having better tracer materials promises spatial resolution of 250 μm
  ⇒ major breakthrough
Berkeley X-Space MPI Scanners
(group of Steven Conolly)

2D Projection Scanner

First Projection MPI Scanner
2.4 T/m Gradient

3D Scanner

High Resolution MPI Scanner
7 T/m Gradient

University of California, Berkeley
Filtered Backprojection (FBP)

- 2D scanner, 60 projections, 20 min
- X-space + FBP for reconstruction
- No deconvolution
- 1:10 diluted Resovist tracer

*Justin Konkle

University of California, Berkeley
Filtered Backprojection (FBP)  *Justin Konkle

- 2D scanner, 60 projections, 20 min
- X-space + FBP for reconstruction
- No deconvolution
- 1:10 diluted Resovist tracer
- 0.8 mm ID tubing on polycarbonate former
High Resolution 3D MPI Imaging

- 3D scanner, 4.3 min/image
- X-space reconstruction, Wiener deconvolution
- 1:10 diluted Resovist

University of California, Berkeley
1. Injection of 1:3 Resovist into ureter highlights renal pelvis

2. Subsequent DI water injection washes tracer into renal medulla

- 3D scanner, 2 min/image, 4.5 cm x 5.5 cm
- X-space reconstruction, Wiener deconvolution
Summary and outlook

- Promising new imaging modality
- Potential of real-time imaging of 3D distribution of magnetic markers with high spatial resolution
- Image reconstruction either in frequency space or in time space (X-space MPI)
- Challenges:
  - Excitation with very low THD ($f_{exc}$ of typically 25 kHz, $H_{ac} > 30$ mT)
  - Low-noise wide-band amplifier
  - Separation of signal from excitation and from markers (fundamental frequency)
  - Availability of optimum markers
  - Upscaling
- Applications:
  - Philips: real-time MPI of blood flow in mice
  - Berkeley: X-space MPI system for CKD patients
- Outlook: Combination of MPI with MRI (?)
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