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At the intersection of microengineering and magnetic resonance: challenges and opportunities

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Dr. Mazin Jouda, Dr. Neil MacKinnon, Dr. Sören Lehmkuhl, Prof. Jürgen Brandner

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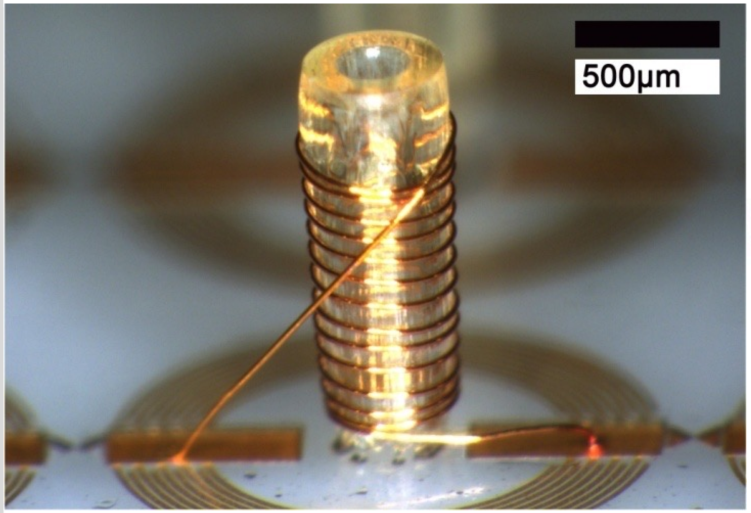
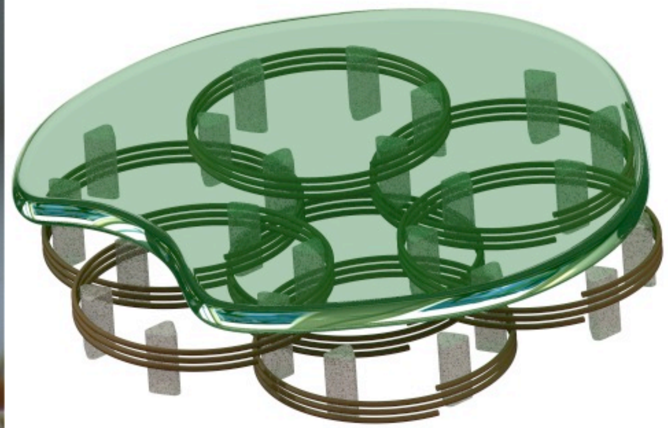
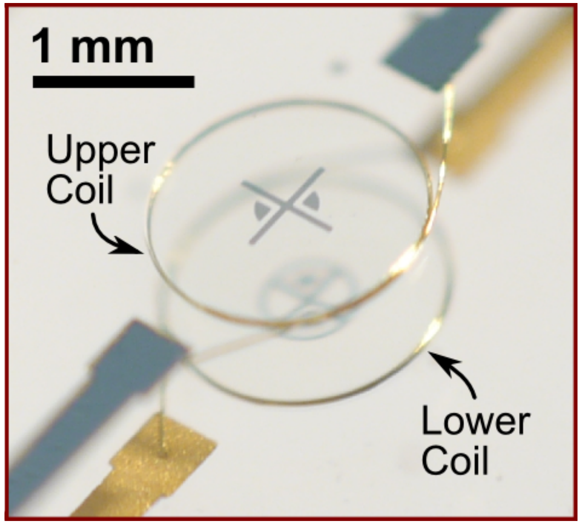
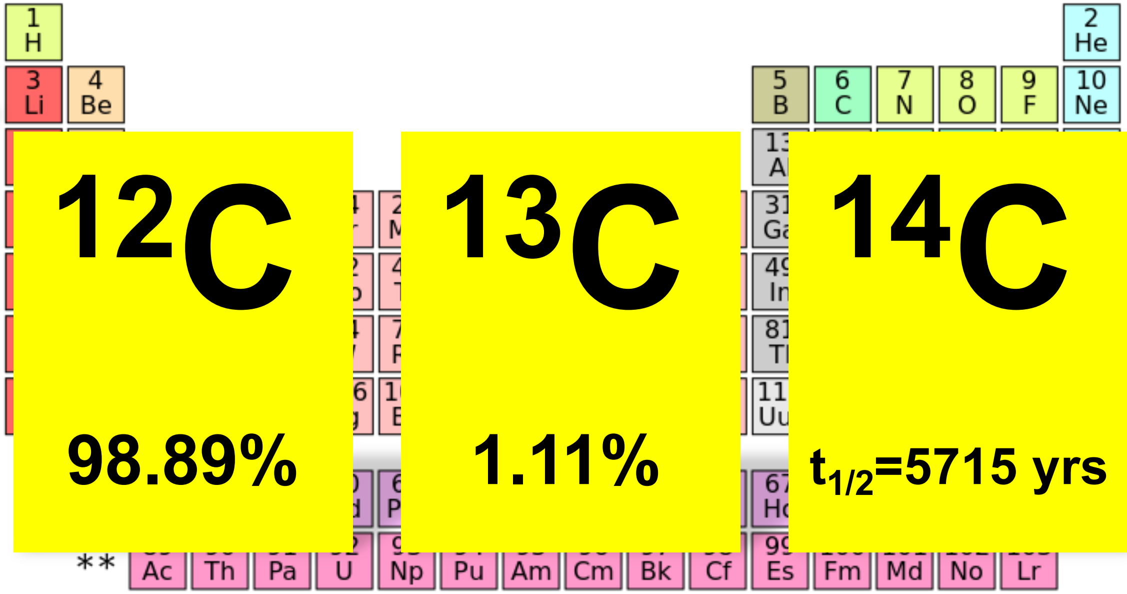






Why μ-MR?

- Small amounts of sample – typically **< 1 μl**
  - isotopically labelled biological molecules
  - synthesis of advanced materials
  - pharmaceutics: combinatorial analysis of large numbers of compounds
  - high-throughput screening of various samples



Σ (protons + neutrons)	# protons	I
Odd	-	1/2, 3/2, …
Even	Odd	1, 2, …
Even	**Even**	**0**

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Small samples – (even) less signal

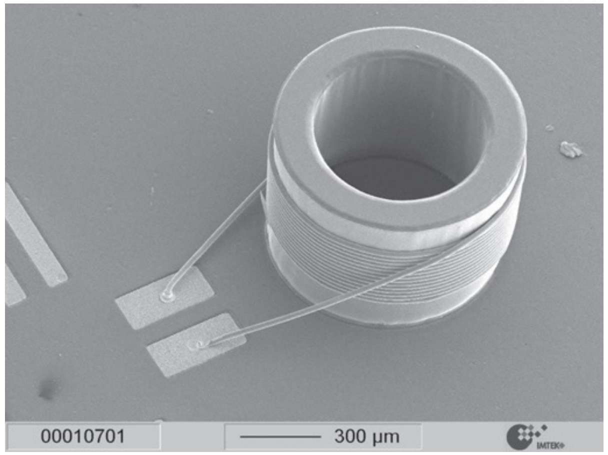
https://www.healthcare.siemens.com/magnetic-resonance-imaging/options-and-upgrades/coils/cp-head-array-coil

- high B_0 fields
- miniaturized RF receiver coils
- superconducting receiver coils
- hyperpolarisation techniques

10^{-6}
signal reduction

signal-to-noise recovery

JMM, 20 (2010) 015021 (11pp)



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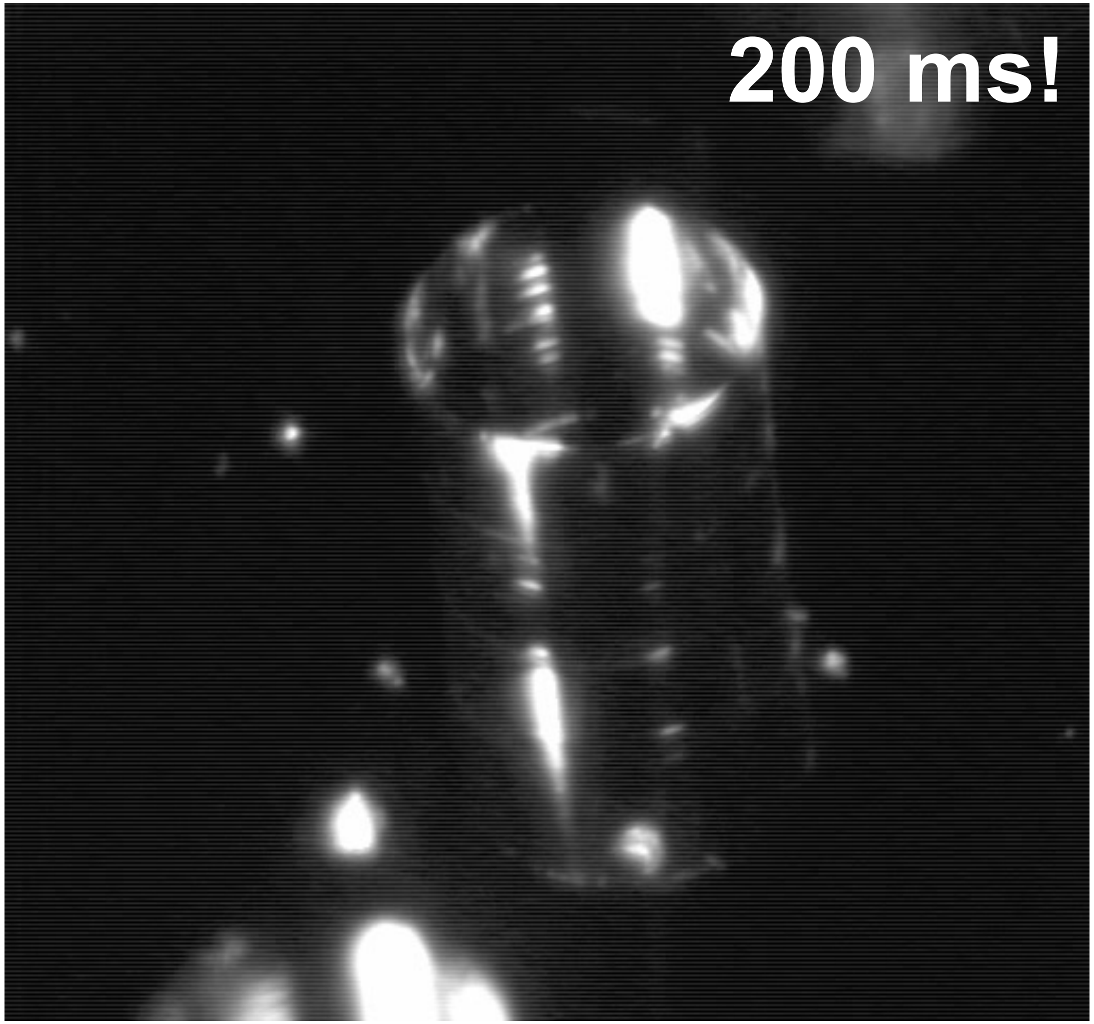
Small detectors – how to make them?

- MEMS techniques:
  - photolithography
  - metal/dielectric deposition
  - wet/dry etching
  - electroplating
- Printed Circuit Boards (PCB)
- hybrid techniques:
  - MEMS + wirebonding



Reading list – microcoils by wirebonding

- K. Kratt et al., *J. Micromech. Microeng.* **20** (2010) 015021 (11pp)
- K. Kratt et al., *Sensors and Actuators* A **156** (2009) 328–333

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How much signal / how much noise? – SNR

detector quality | sample quantity | sample type | B_0 field

$$SNR \approx \frac{\left(B_1/i\right)\cdot N \cdot \gamma \cdot \hbar \cdot I\left(I+1\right)\cdot \omega_0^2}{\sqrt{4k_B T \cdot R_{noise} \cdot \Delta f}}$$

- (Mandatory) reference:
  - D.I. Hoult and R.I. Richards, *The Signal-to-Noise Ratio of the NMR Experiment*, **J. Magnetic Resonance, 24, 71-85 (1976)**

Why are microcoils good?

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- on axis sensitivity in the center of an ideal single-layer solenoid:

$$\left(\frac{B_1}{i}\right) = \frac{\mu_0 \cdot n}{d_{coil} \cdot \sqrt{1+\left(\frac{h}{d_{coil}}\right)^2}}$$

n = # of windings

d_{coil} = coil diameter

h = coil height

- when $h/d_{coil} = const.$ → sensitivity increases for smaller diameters

Noise

- at the microscale, the detector becomes the main source of noise in the system!

- (Mandatory) reference:
  - T.L. Peck, R.L. Magin, and P.C. Lauterbur, Design and Analysis of Microcoils for NMR Microscopy, **J. Magnetic Resonance, Series B 108, 114-124 (1995)**

Four micro-detectors today

- wirebonded solenoidal microcoil
    - imaging and spectroscopy
- on-chip *MACS* micro-resonator
    - for magic angle coil spinning applications
- planar array of micro-coils
    - for planar samples
- Helmholtz coil micro-detector
    - for lab-on-a-chip applications

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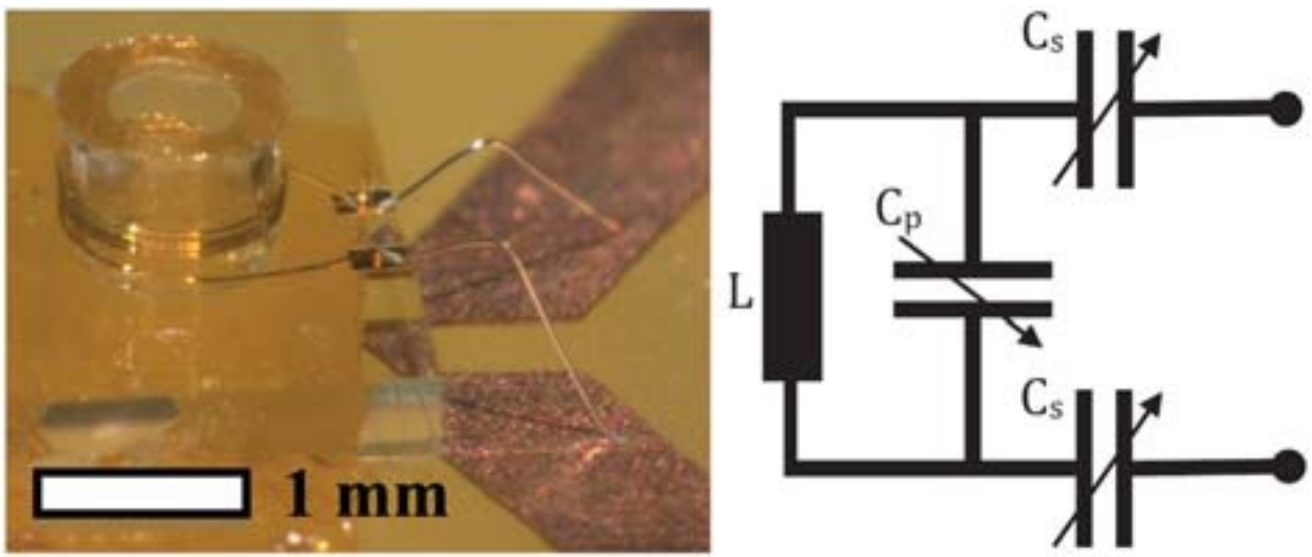
Experimental – MRI @ 9.4 T

- 9.4T MRI scanner – 1H Larmor frequency = 400 MHz
- coil connected with PCB tuning and matching circuit @ 400 MHz / 50 Ω
- signal transmitted via wires tethered at the terminals of the circuit



(a) (b)

Lab Chip, p. 1387 (2010)

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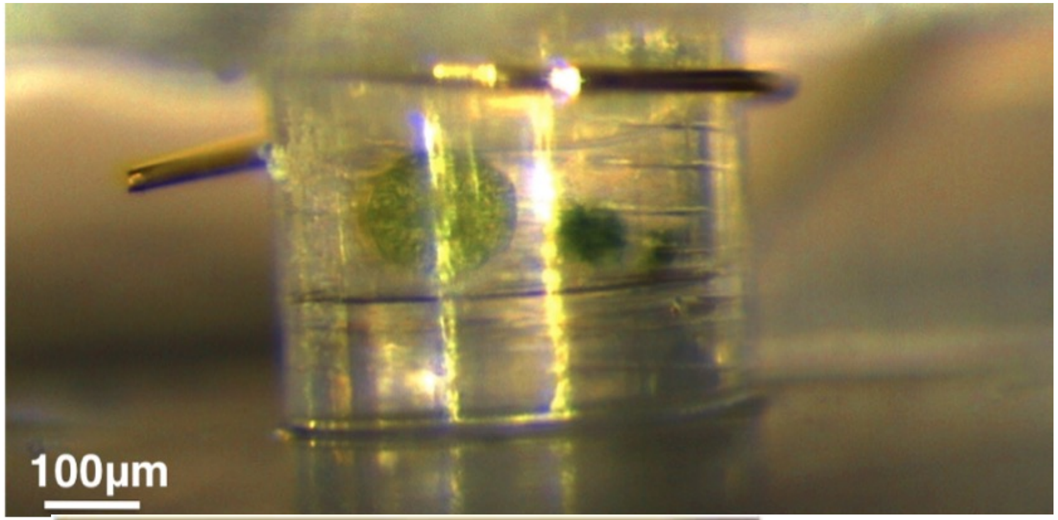
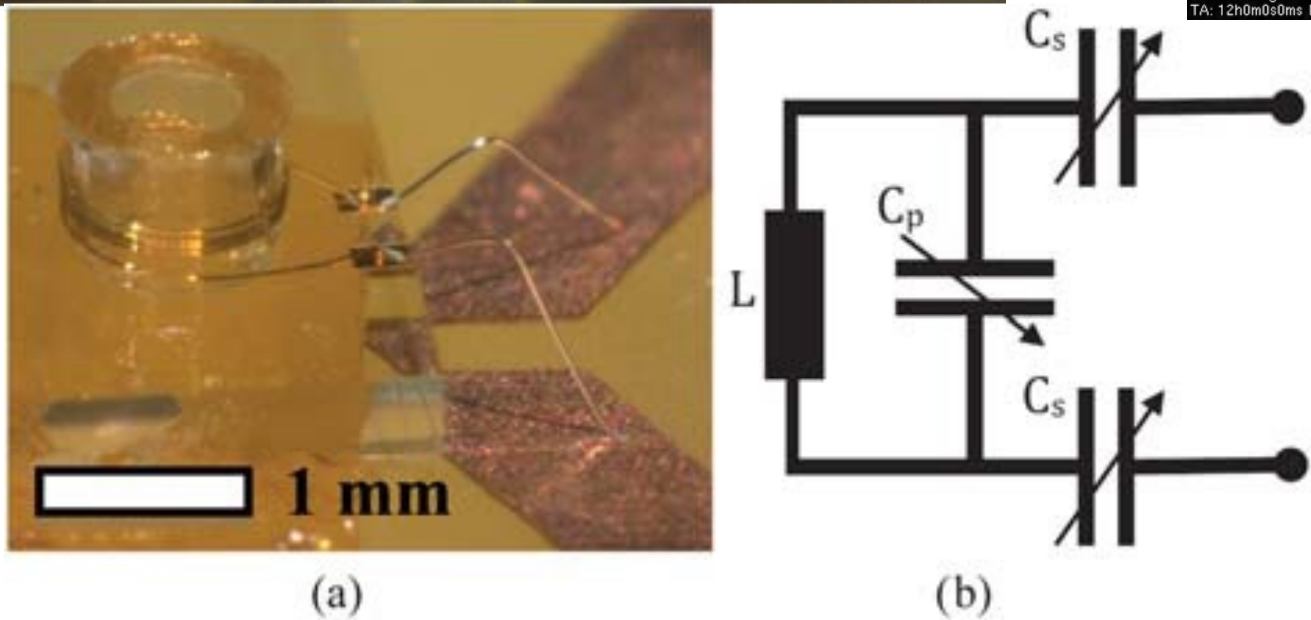
Imaging of algal cells





MEMS 2011, p. 809

Reading list – MRI with wirebonded microcoils

- V. Badilita et al., *Lab on a Chip* **10** (2010) 1387–1390
- M. Mohmmadzadeh et al., *J. Magnetic Resonance* **208** (2011) 20–26

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Magic Angle Spinning NMR spectroscopy

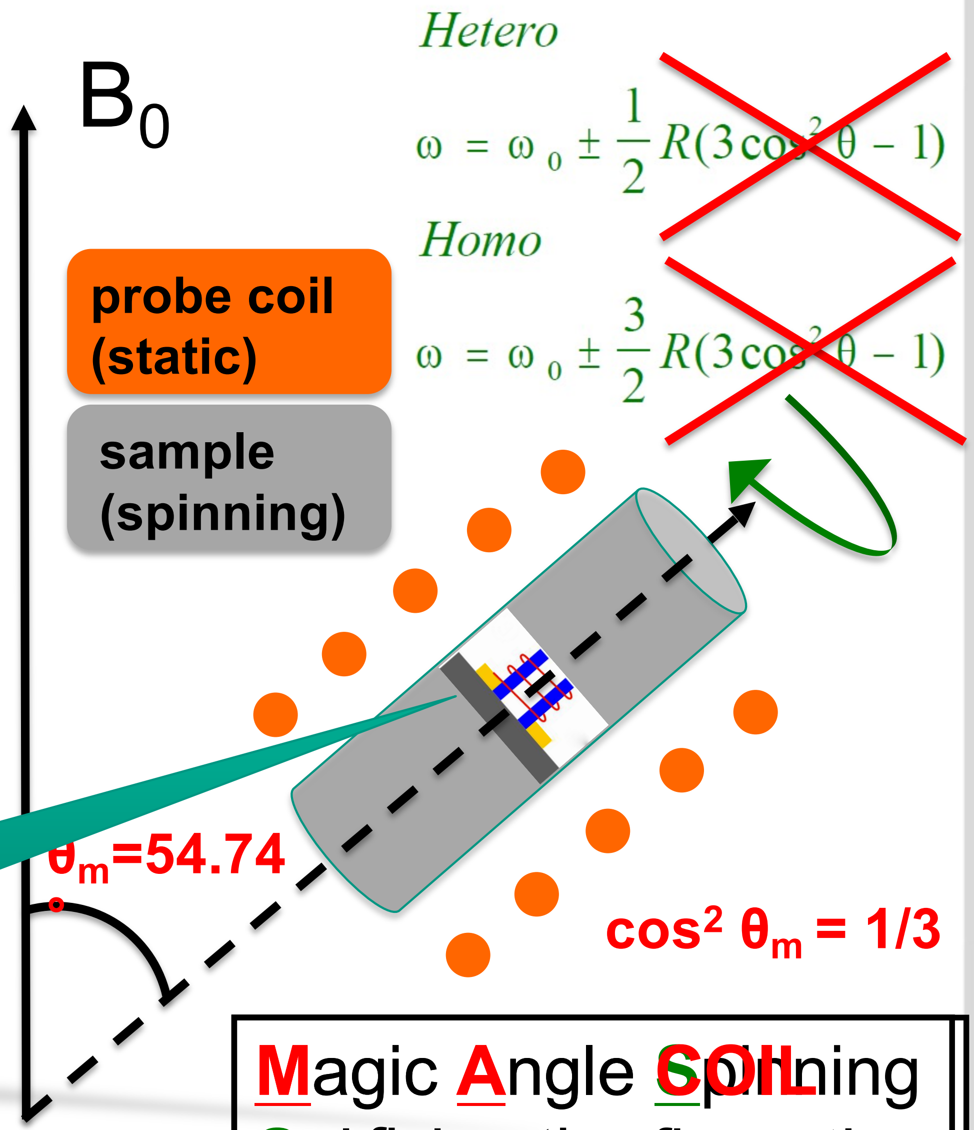
- nuclear spin interactions (dipolar, chemical shift anisotropy, quadrupolar) lead to broad and featureless lines

↓

- nuclear spin interactions are time dependent and can be averaged by magic angle spinning

↓

- high resolution spectra



simultaneous spinning of coil AND sample

wireless transmission of signal to probe coil

Magic Angle COIL Spinning configuration

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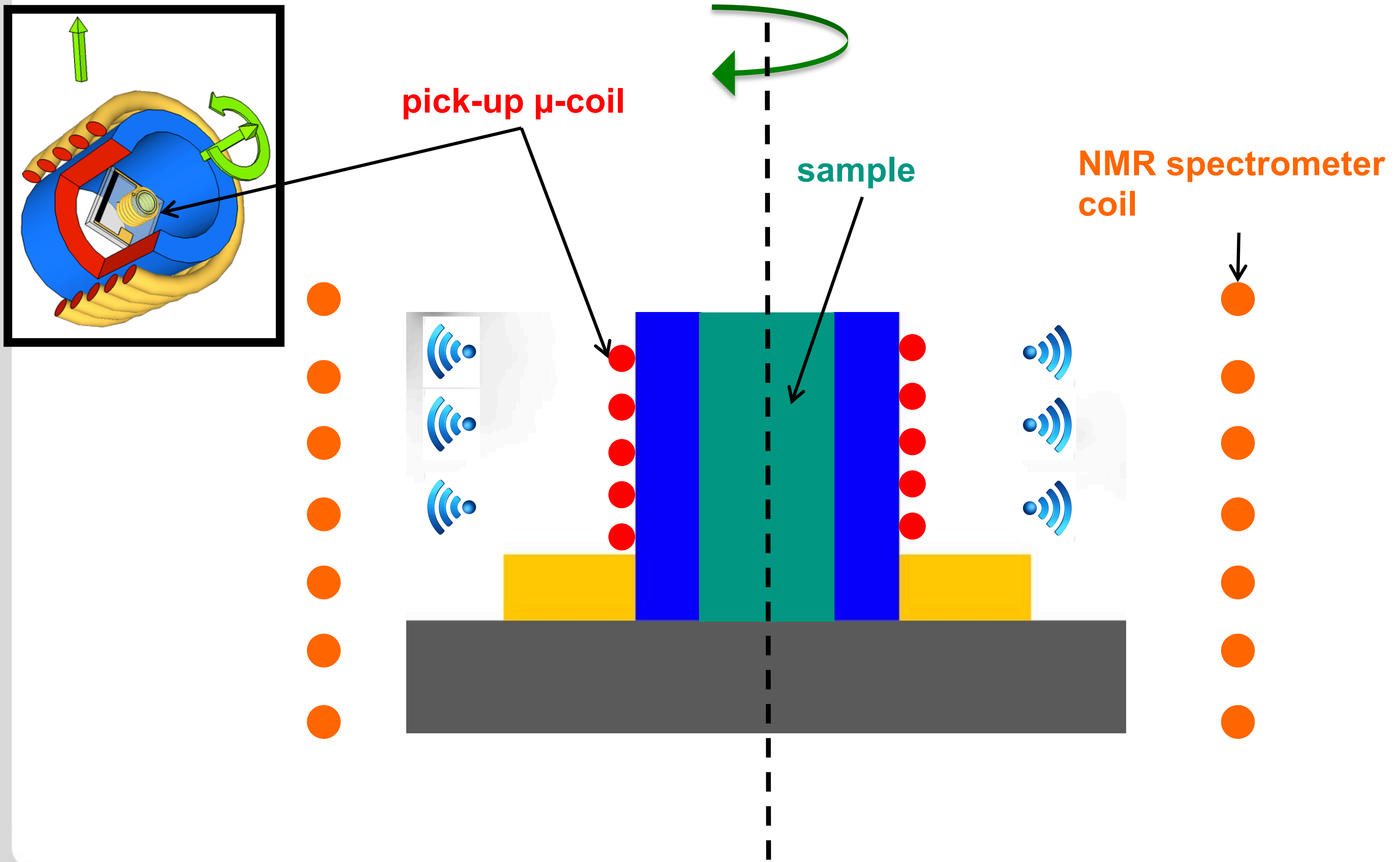
Why inductive coupling for NMR?



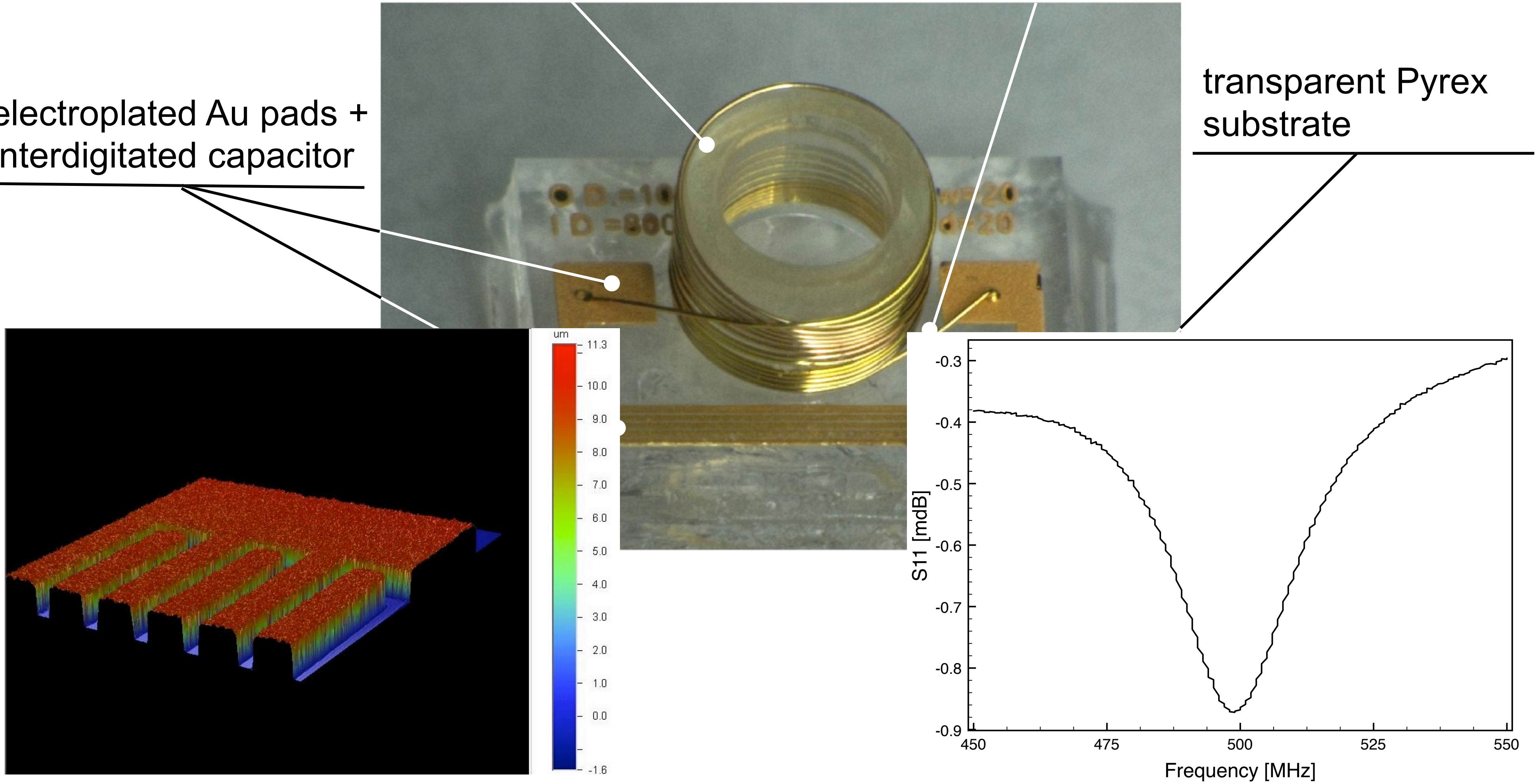
Wirebonded microcoil for wireless NMR

transparent SU-8 sample holder

insulated Au wire 25µm diameter

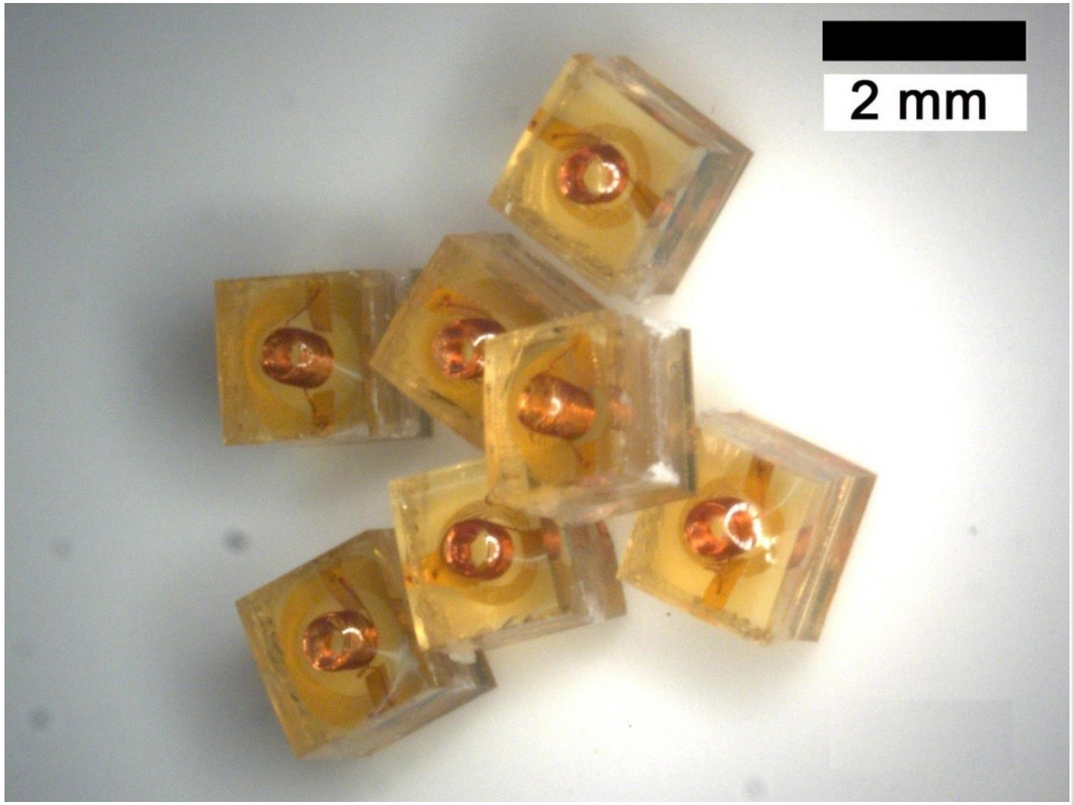
electroplated Au pads + interdigitated capacitor

transparent Pyrex substrate



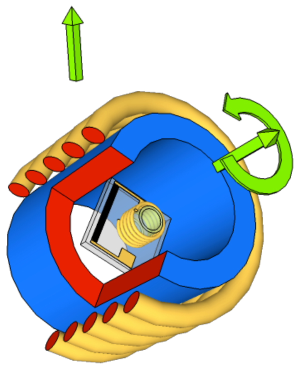
Low-cost microfabricated micro-detectors

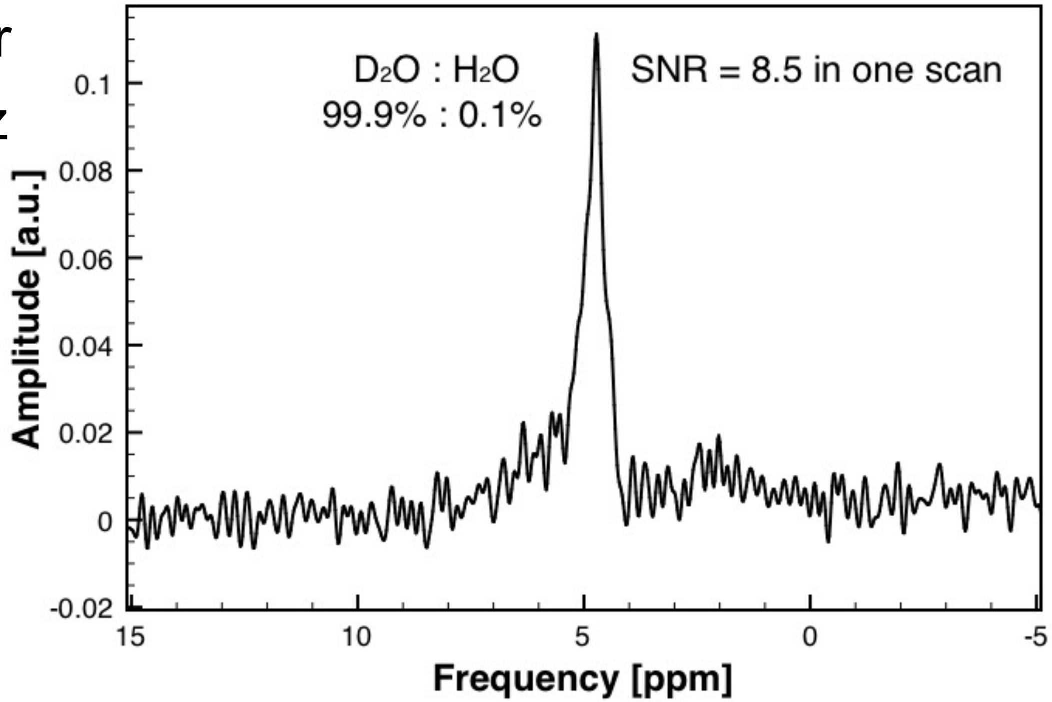
- Sample volume: 150 nl
- Coil outer diameter: 500 µm
- Coil inner diameter: 400 µm
- Coil length: 1000 µm
- Chip dimension: 2 x 2 mm^2
- Cost per chip: 2 – 3 €

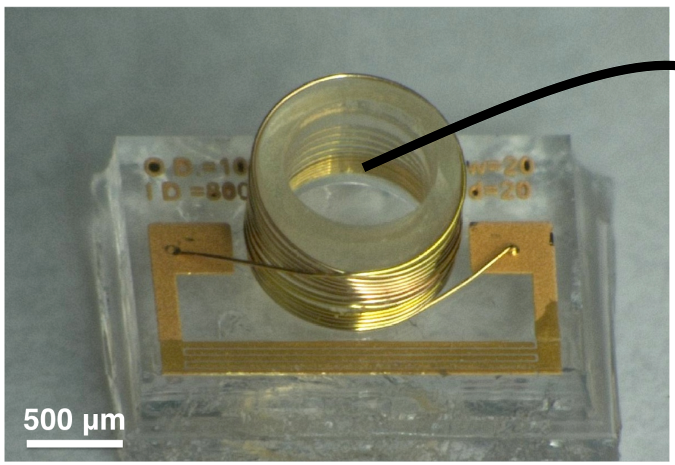


Inductive coupling – high sensitivity

- vertical bore 11.7 T spectrometer
- ^{1}H Larmor frequency = 500 MHz

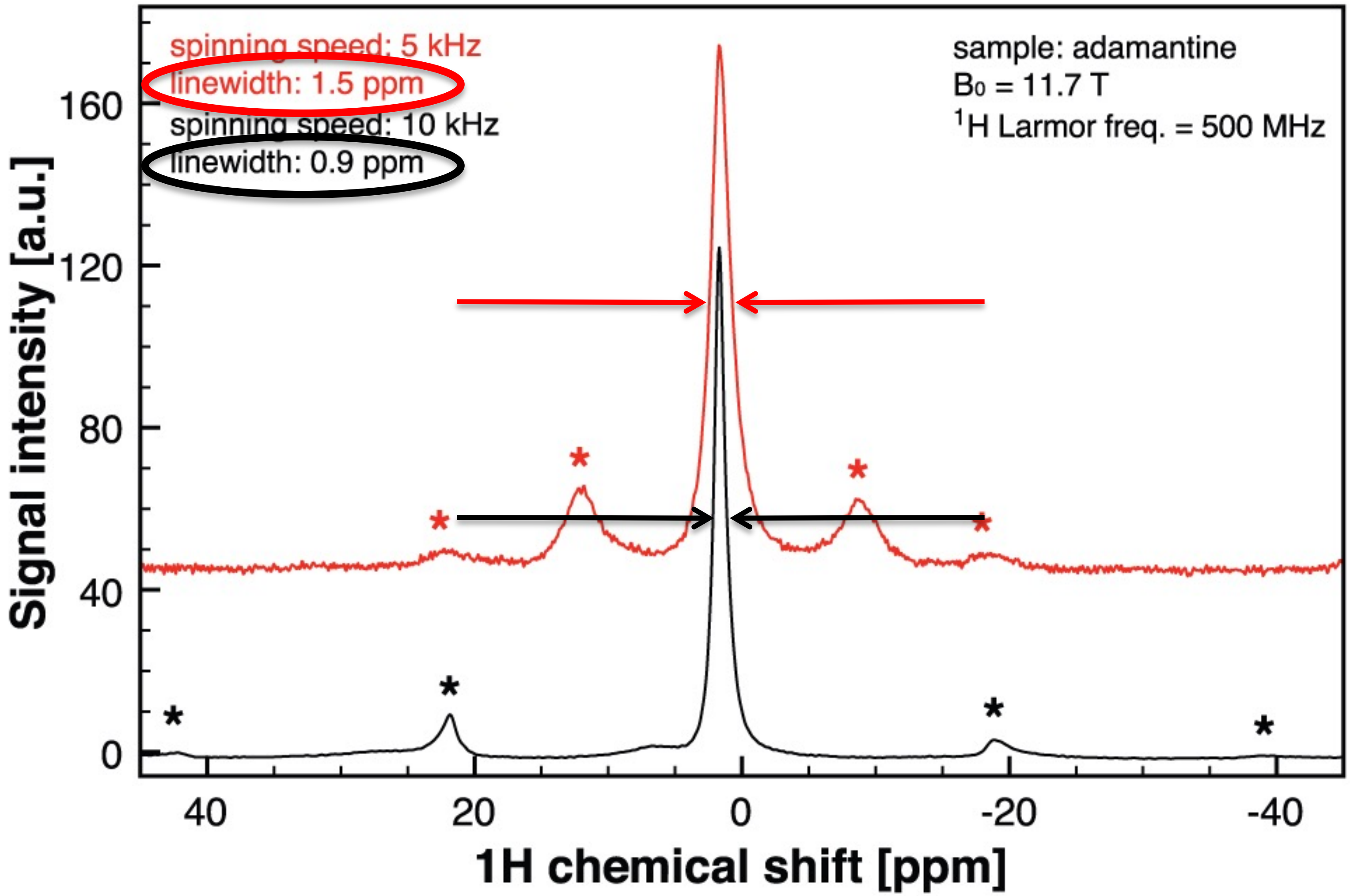




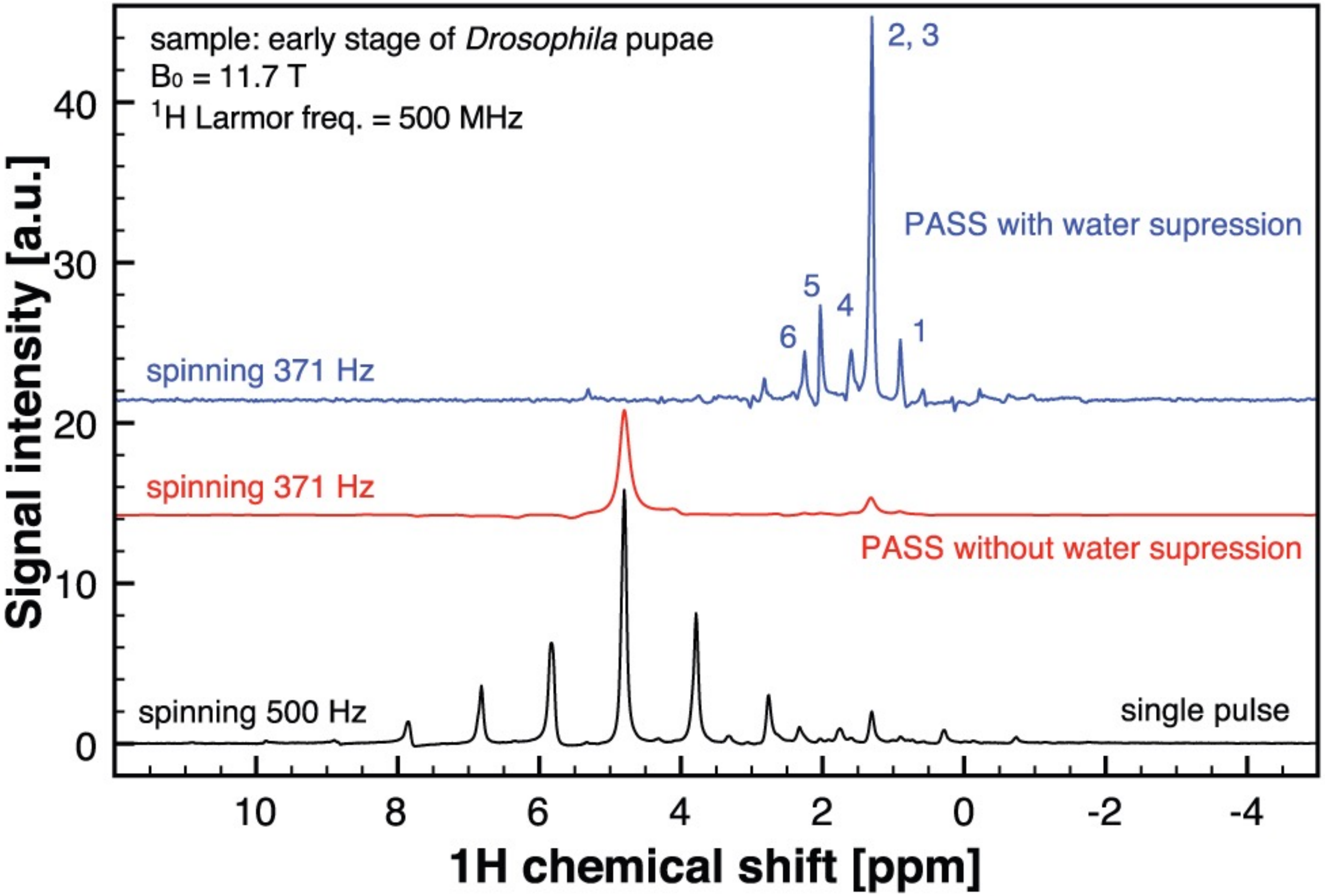


- mixture D_2O:H_2O 99.9 : 0.1%
- signal from 300 pl H_2O

Faster spinning – higher resolution



Slow spinning for biological samples



+ water supression

+ sideband supression

slow spinning sidebands

1 – Lipid – CH_3

2 – fatty acid – $(CH_2)_n$

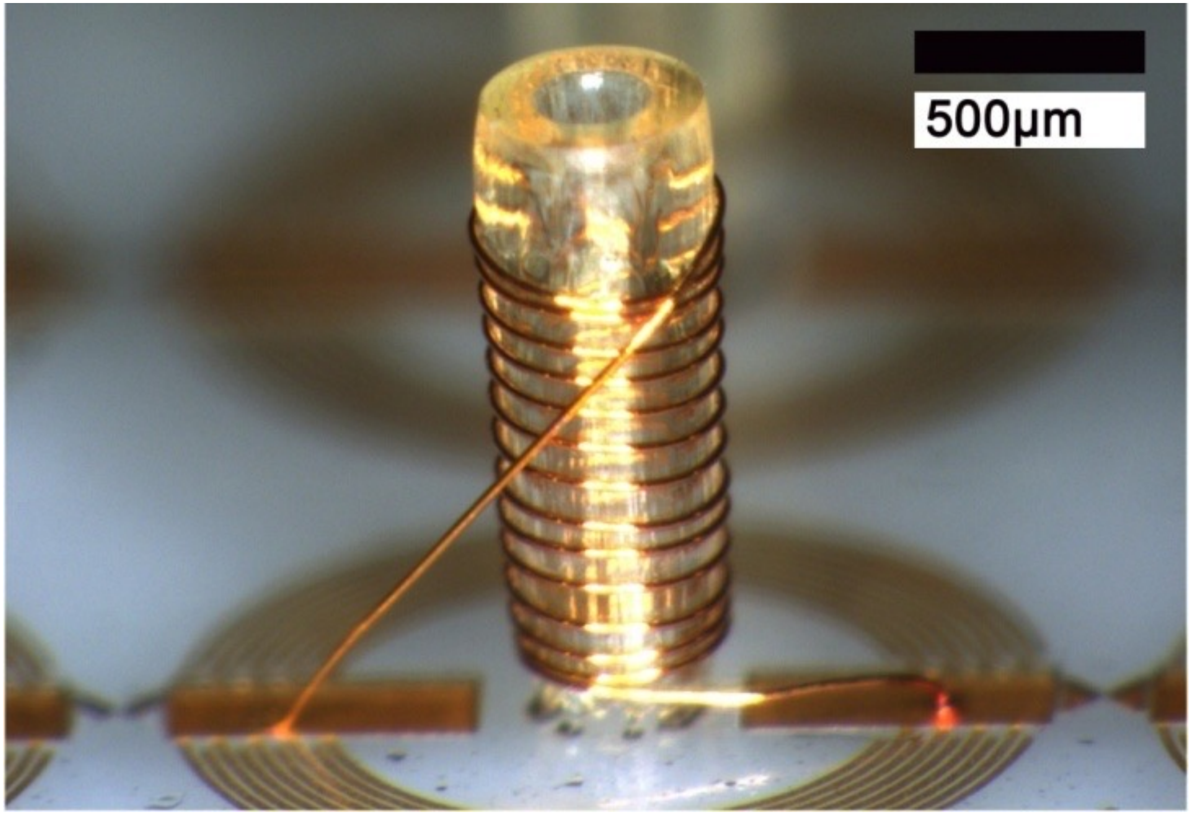
3 – lactate – CH

4 – lipid– CH_2–CH_2–CO–

5 – lipid– CH=CH–CH_2–CH_2–

6 – lipid–CH_2–CH_2–CO

MACS challenges



- fast spinning in high magnetic field (B_0)
  - eddy currents
    - heating
    - „magnetic brake“
- fast spinning (>100kHz)
  - huge centrifugal forces

Reading list – MACS

- D. Sakellariou et al., *Nature* **447** (2007) 694-698
- P.M. Aguiar et al., *J. Magnetic Resonance* **200** (2009) 6–14
- V. Badilita et al., *PLoS ONE* **7(8)** (2012) e42848

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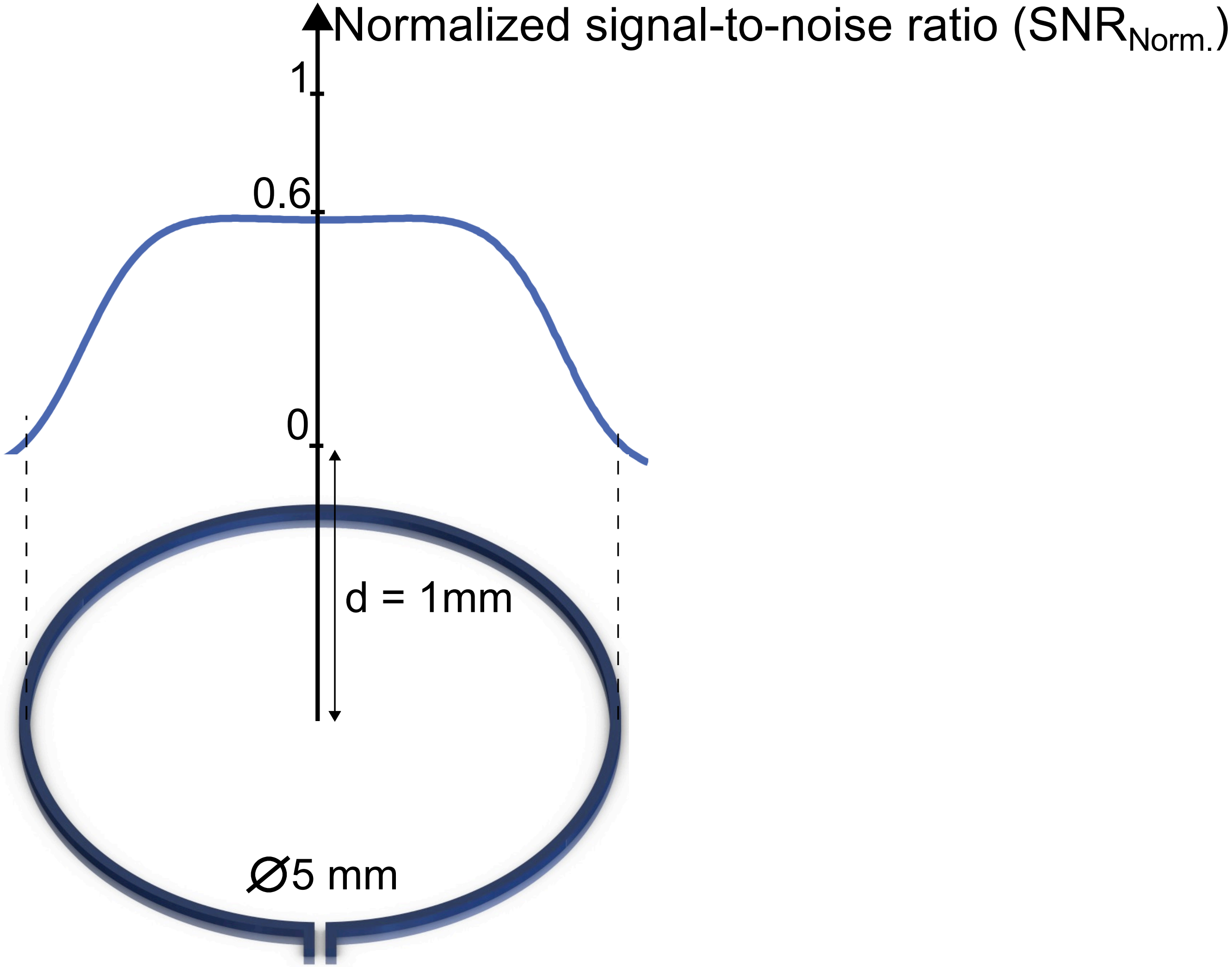
The sample determines the coil



Gruschke et al., Lab Chip, 2012, 495

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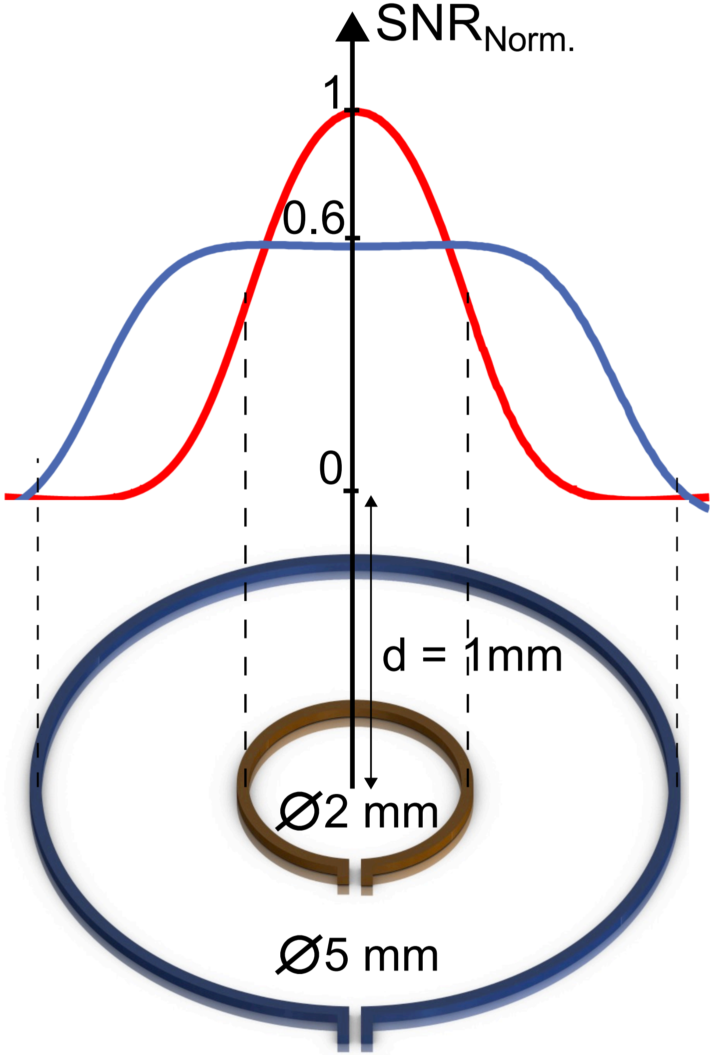

Gruschke et al., Lab Chip, 2012, 495

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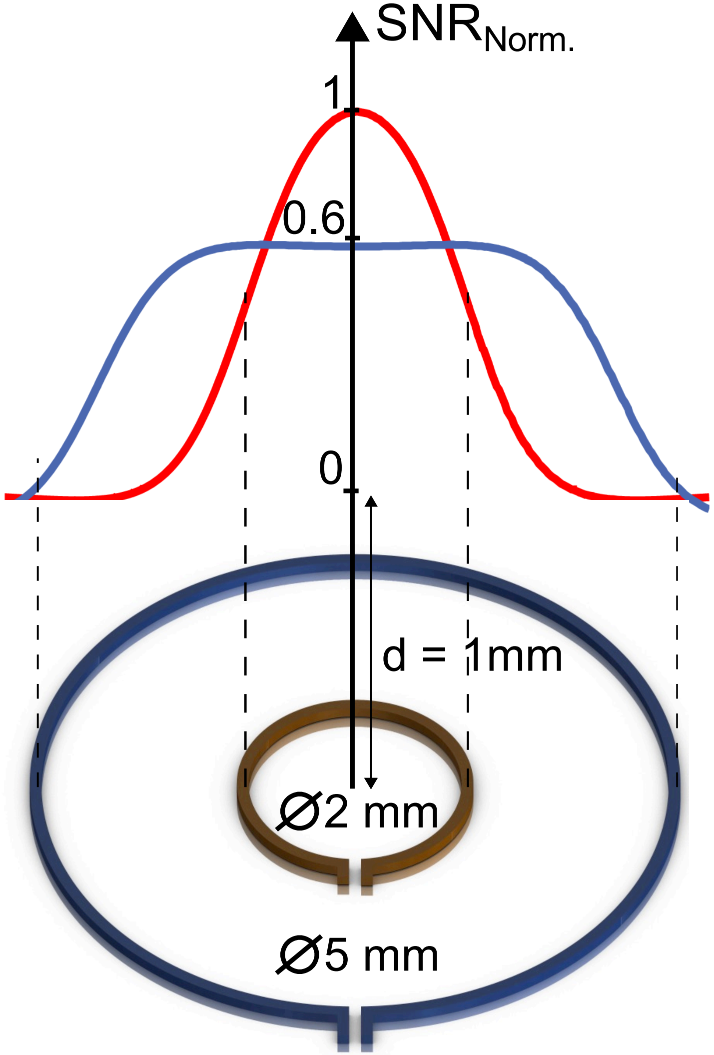

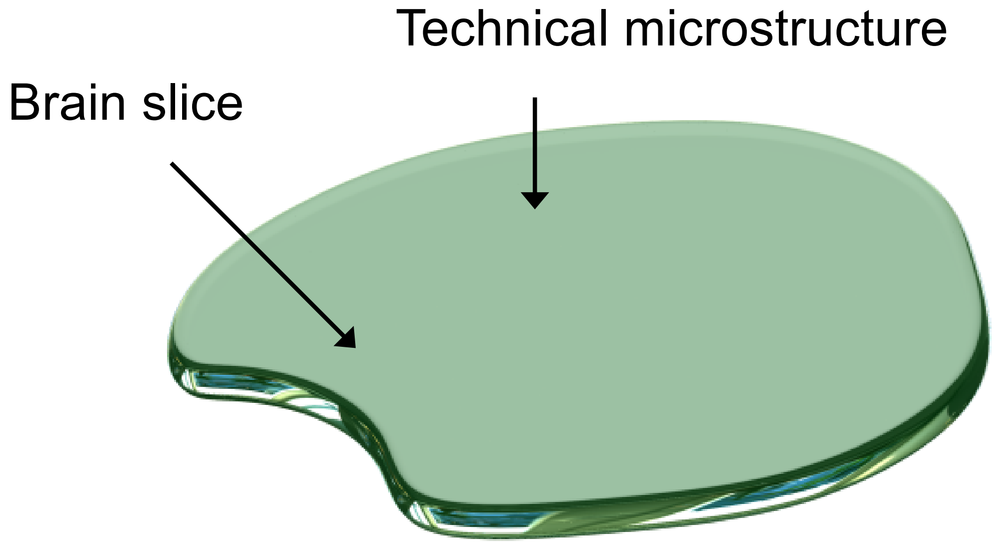

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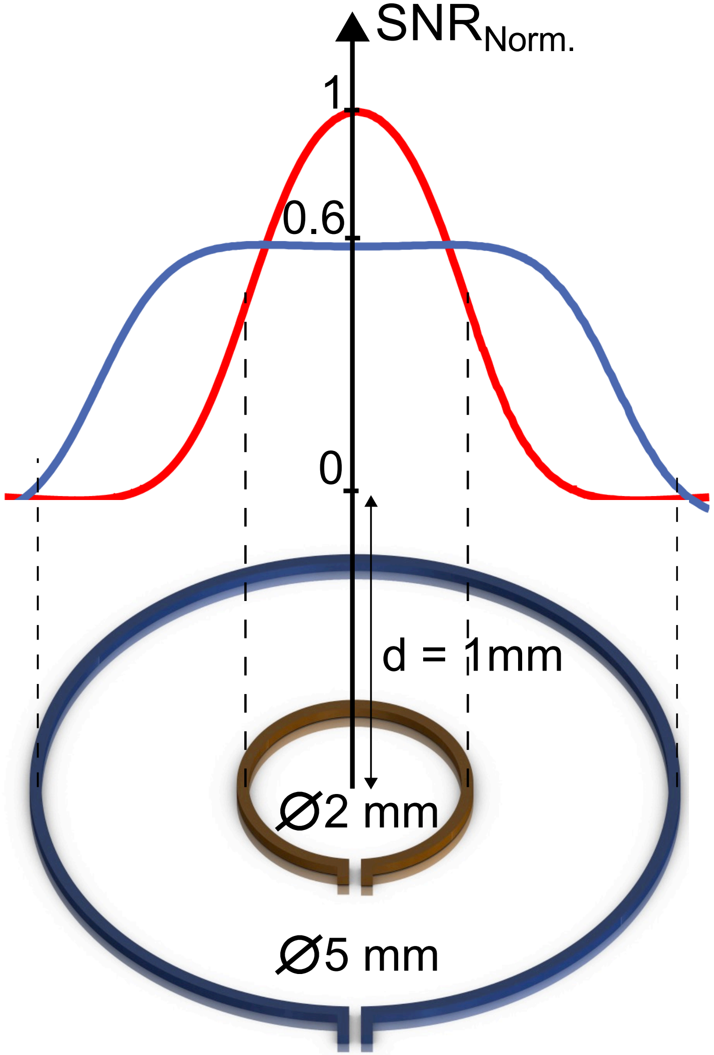
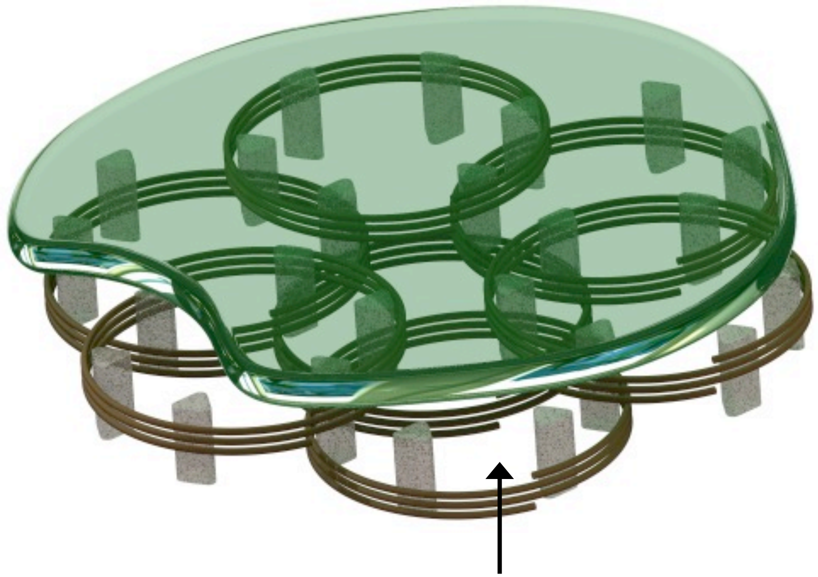


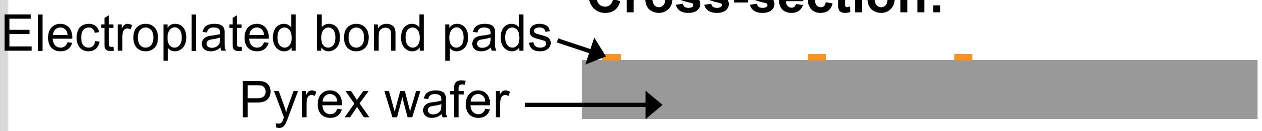


Phased array of microcoils

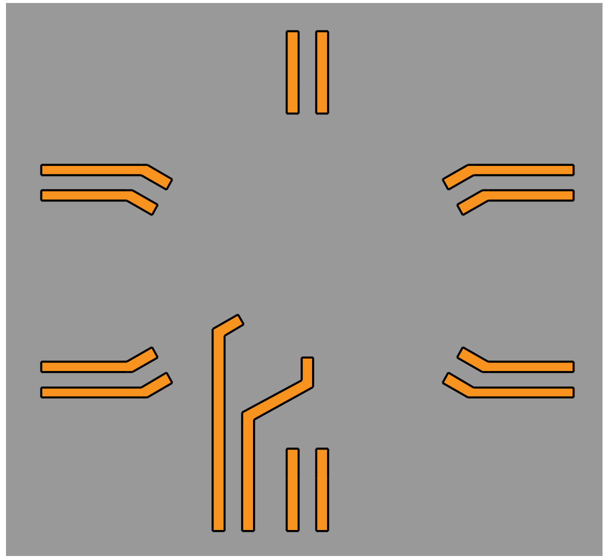
Gruschke et al., Lab Chip, 2012, 495

Wirebond wound multilayer process

Cross-section:



Top view:



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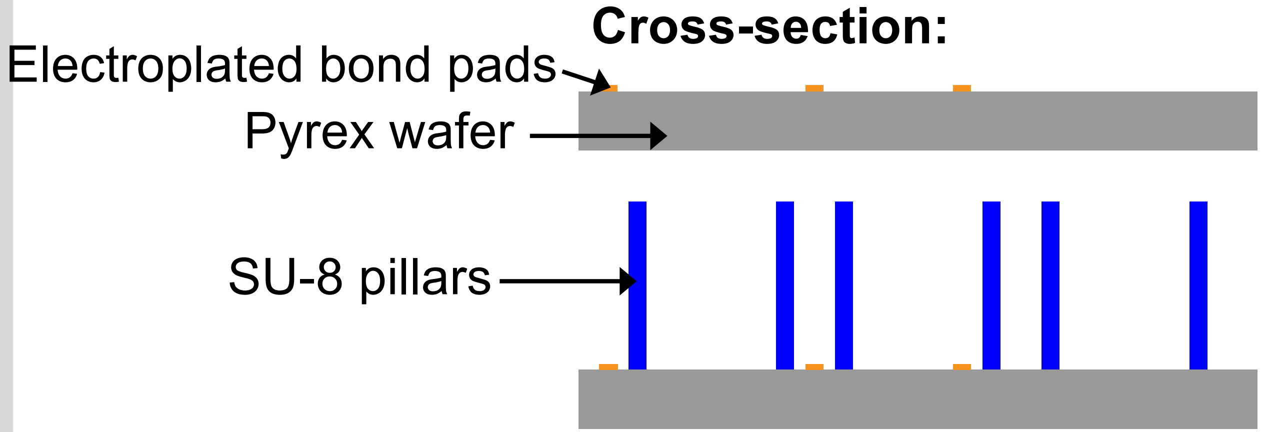

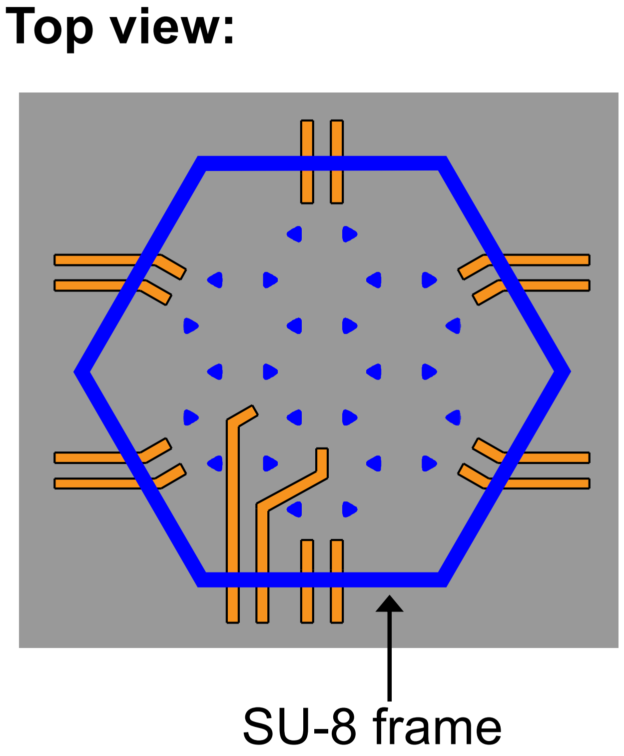

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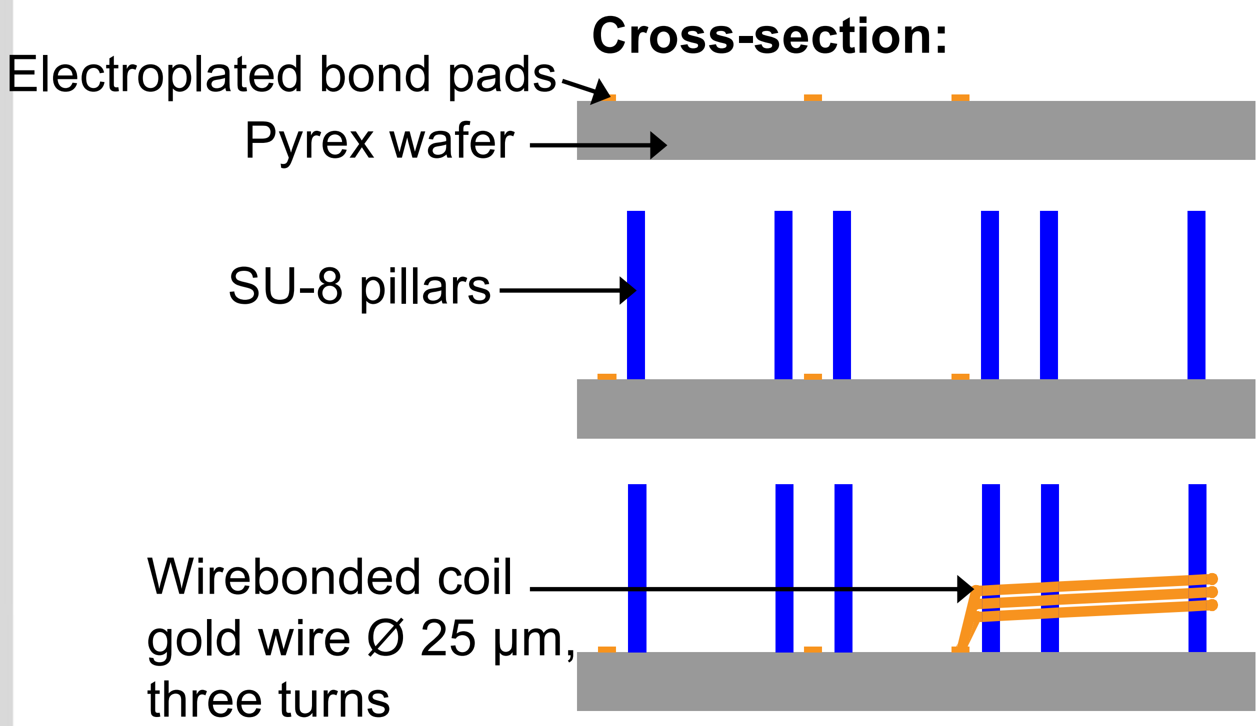

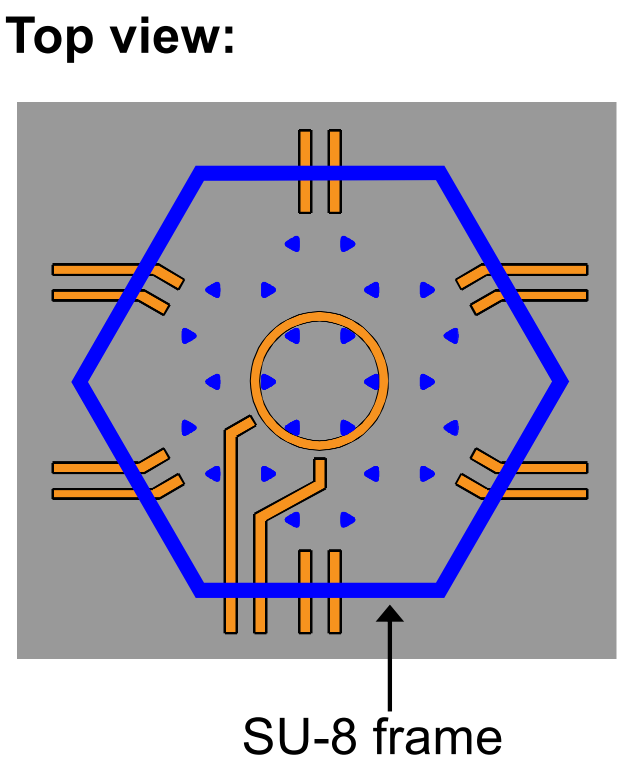

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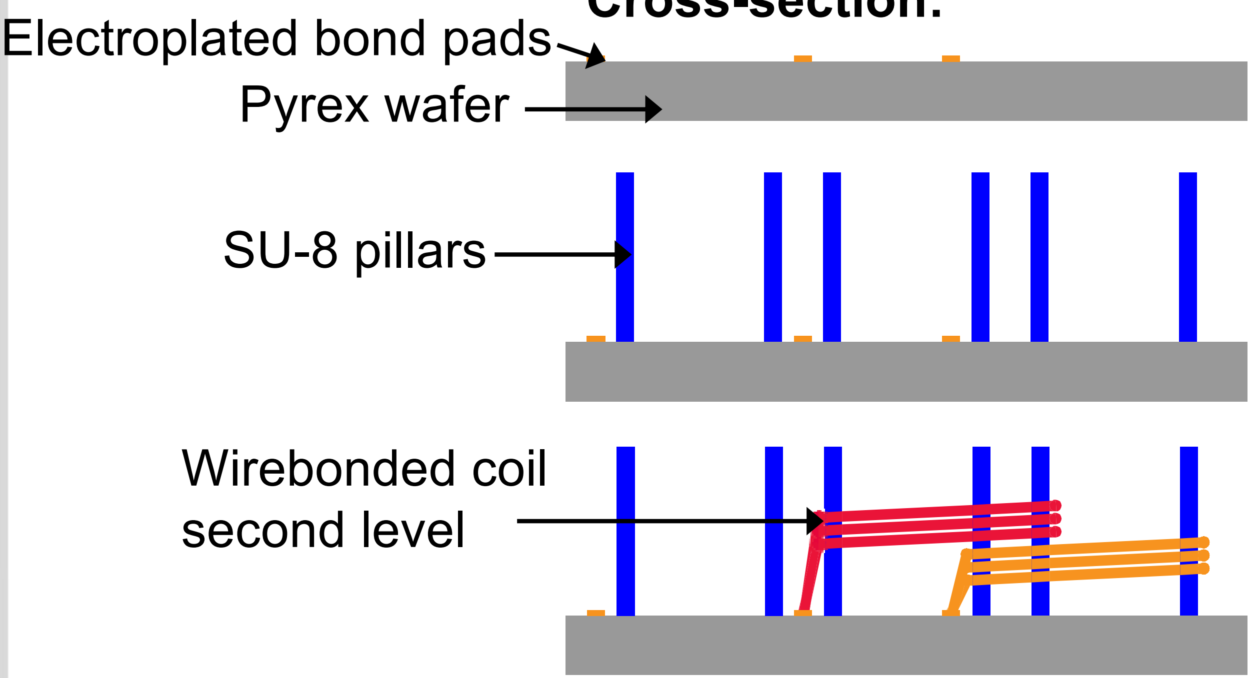

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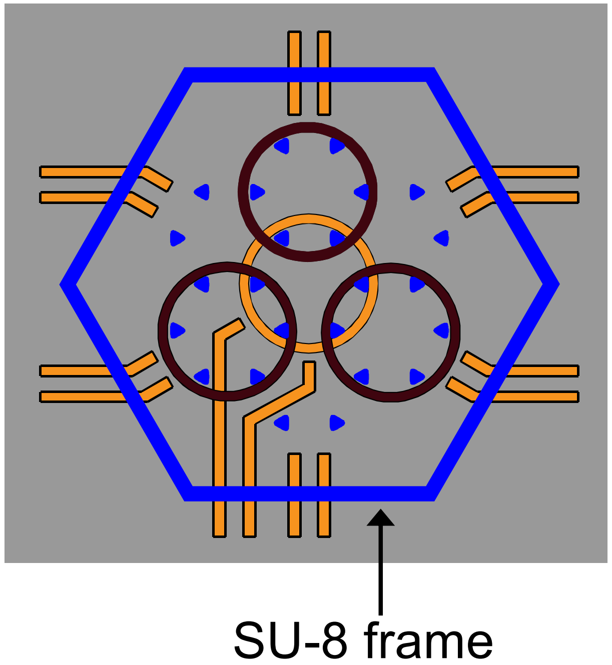

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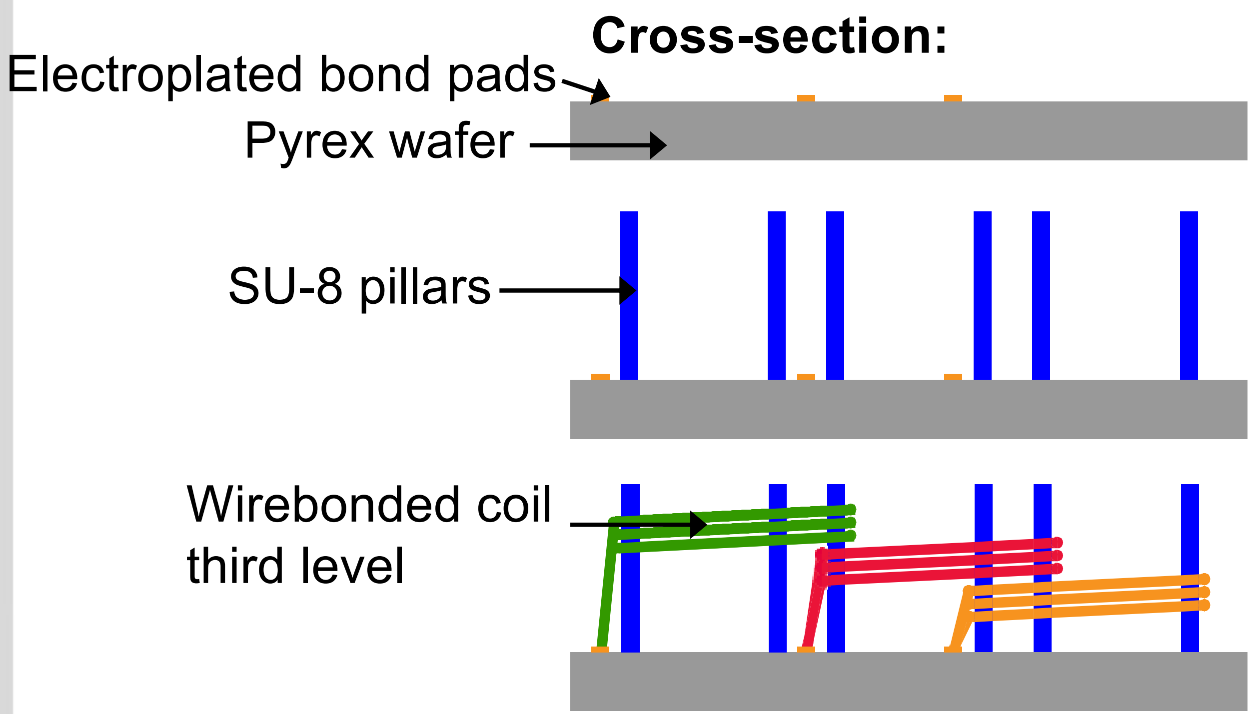
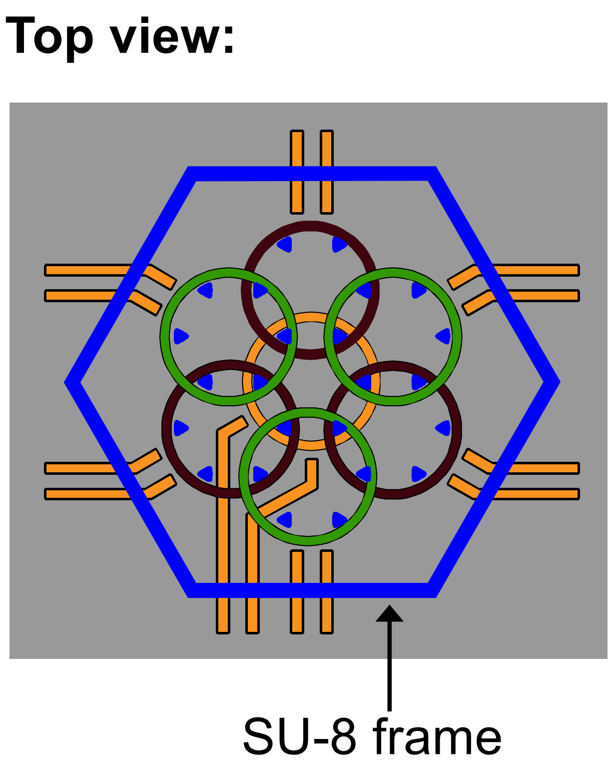
Wirebond wound multilayer process





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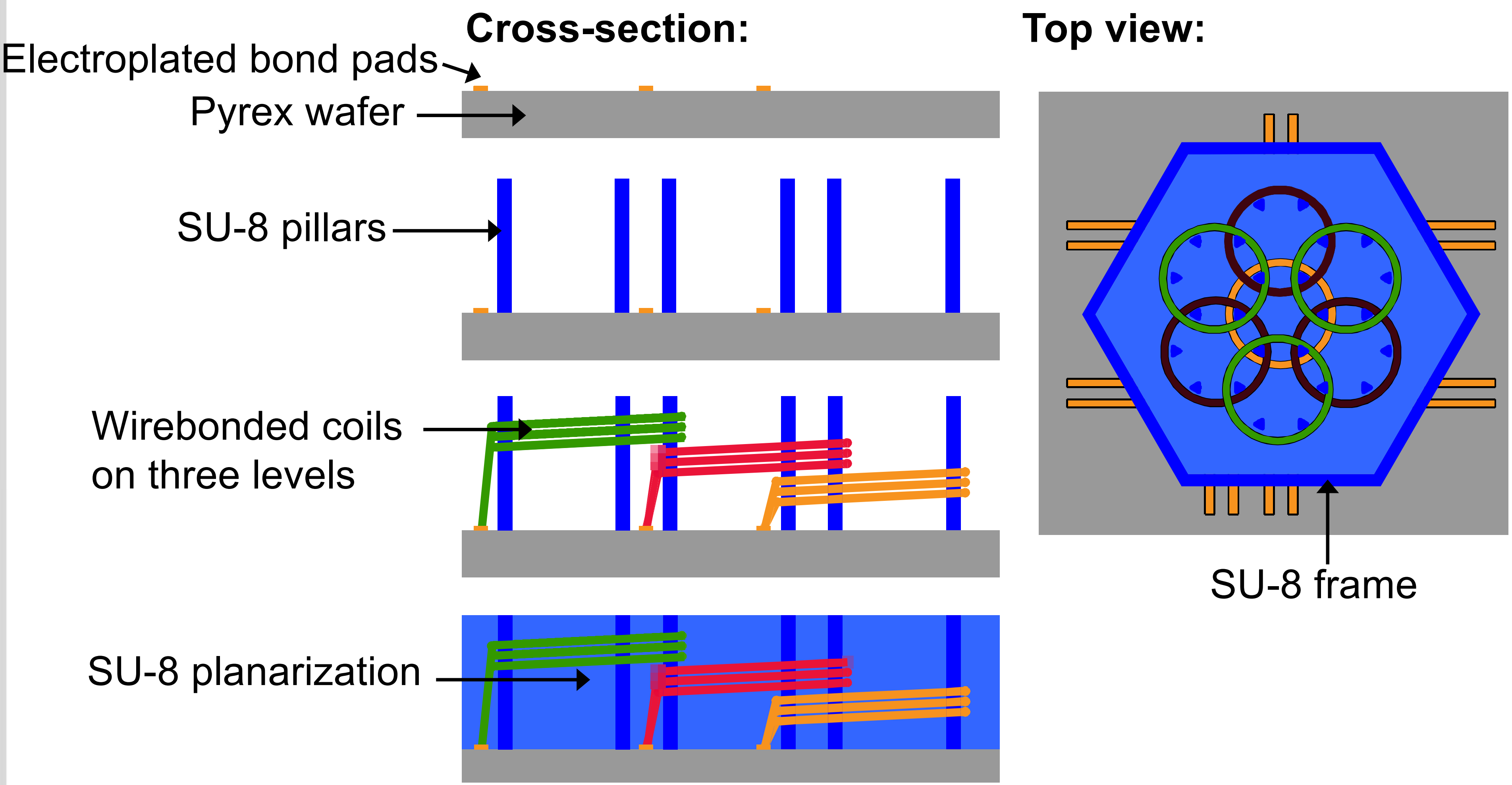

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Wirebond phased array of microcoils

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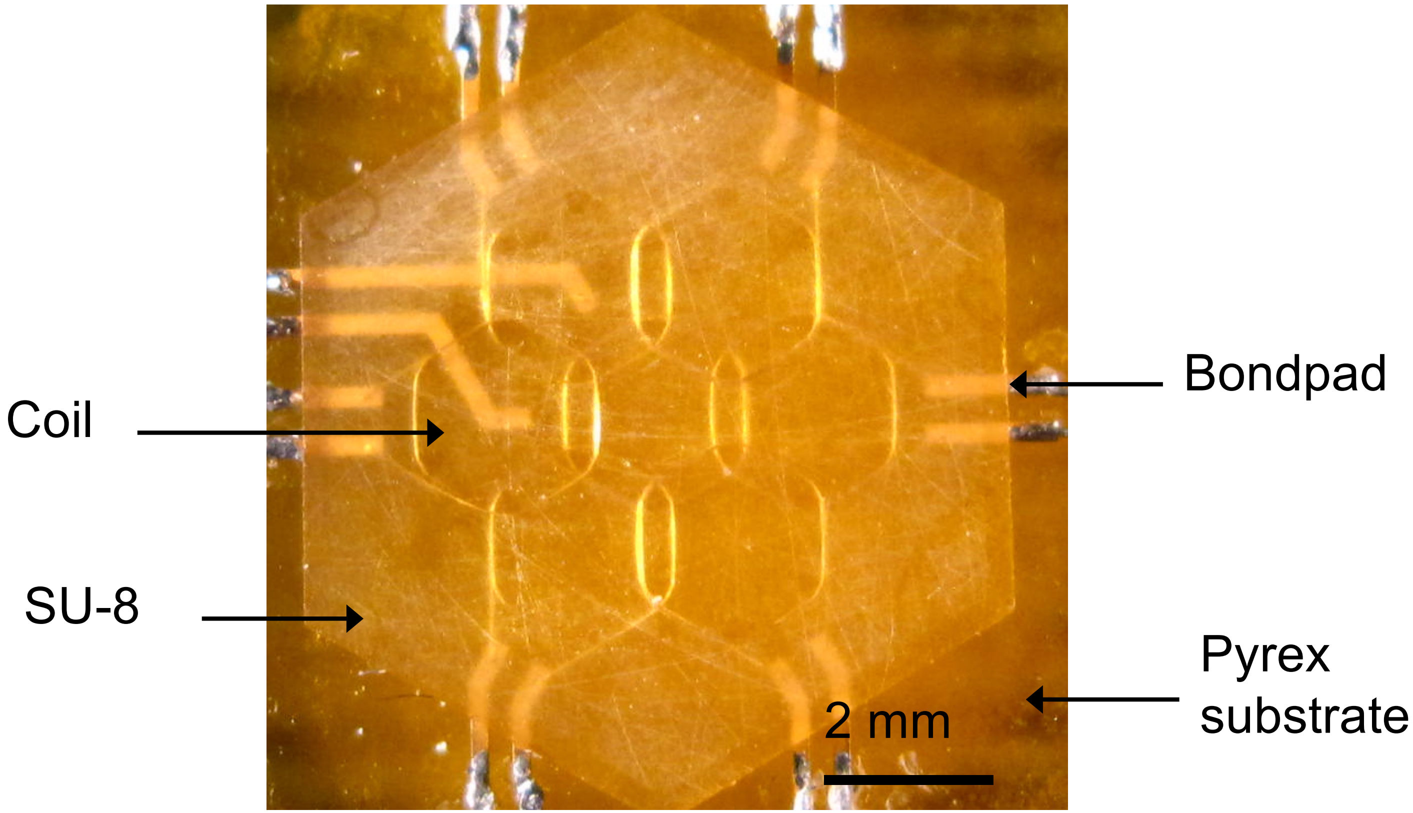

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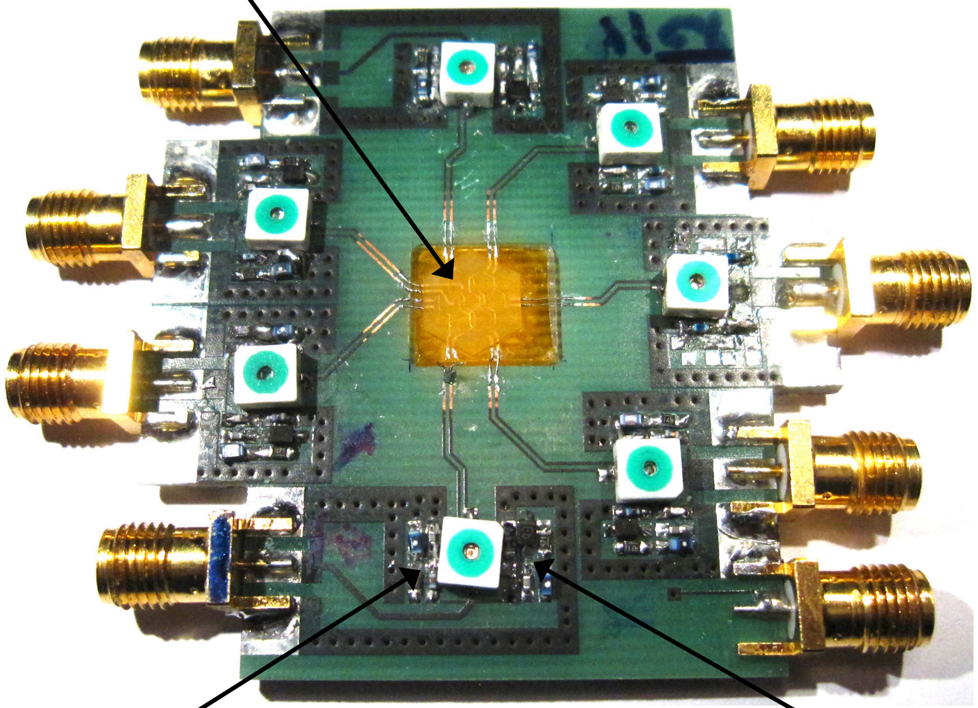
Phased array circuitry

Wirebond phased
array of microcoils



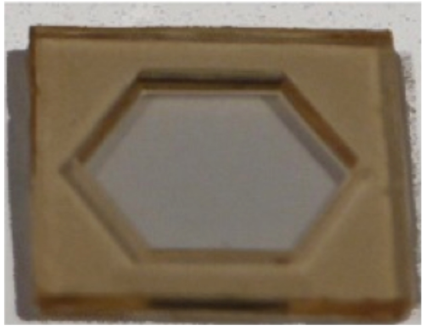
Noise matching circuit

Circuit for decoupling
of transmit coil and phased array

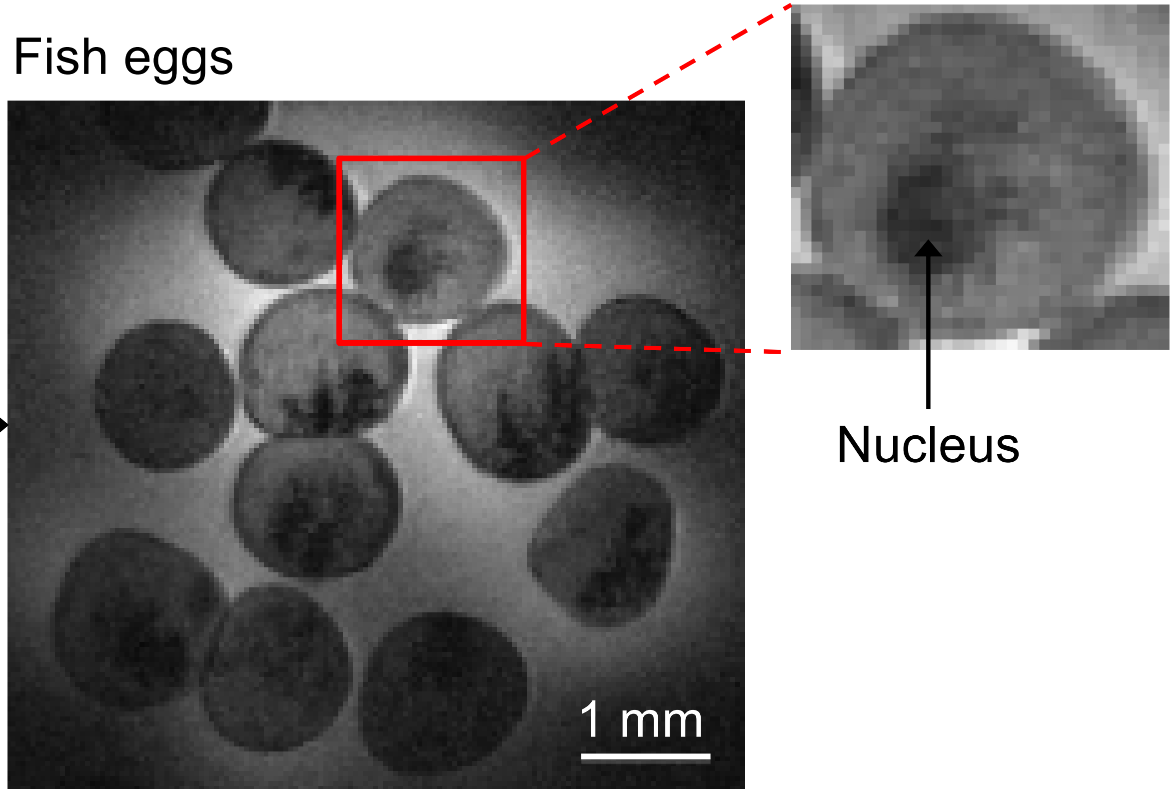
Gruschke et al., Lab Chip, 2012, 495

Results – Imaging

Sample container:



Fish eggs



In-plane resolution of 30 x 30 μm^2 →

Contrast to noise ratio 10

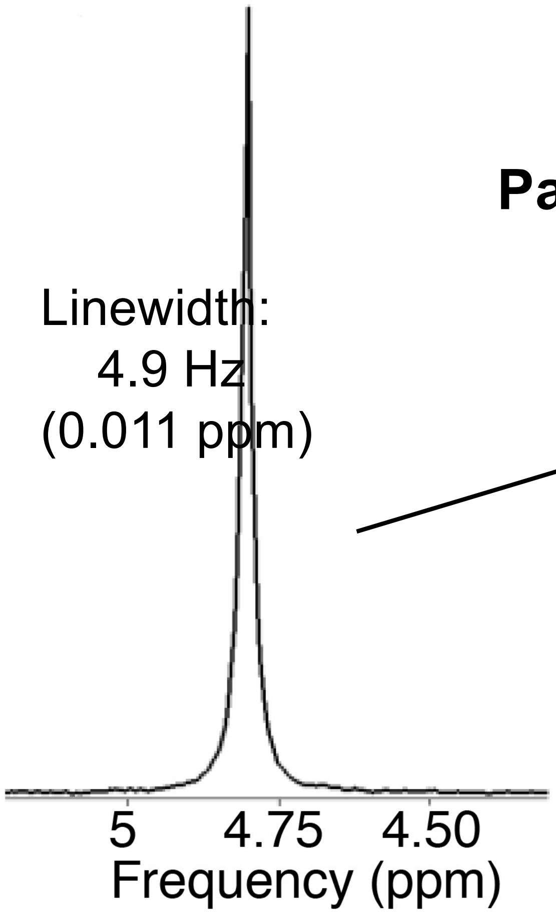
Measurement time 13 min 49 s

FOV 0.55 cm

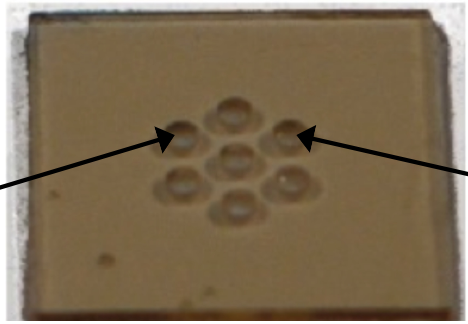
Gruschke et al., Lab Chip, 2012, 495

Results – Spectroscopy

DI water:

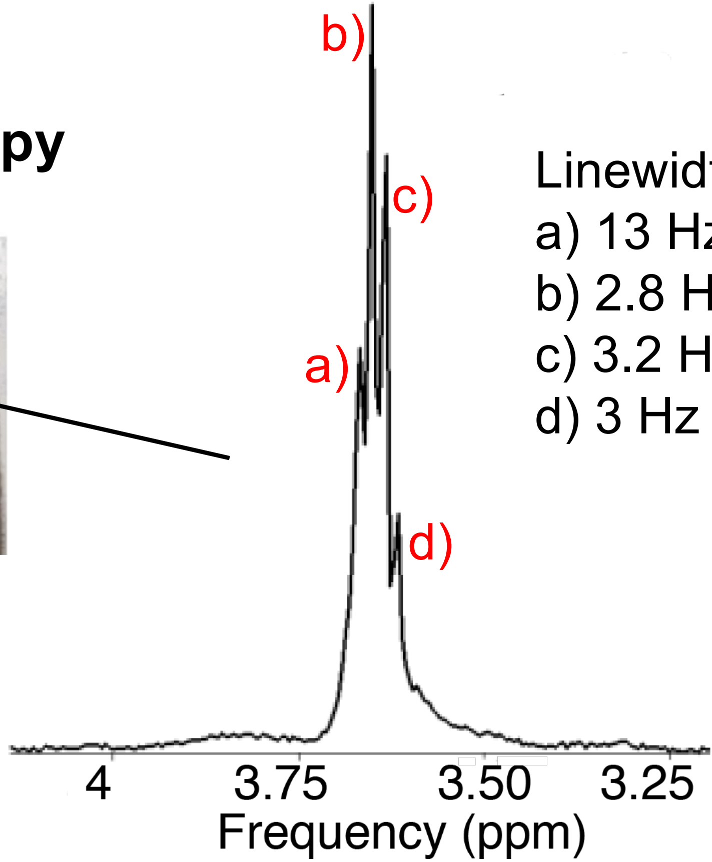


Parallel spectroscopy



Ethanol (5M solution):

CH_2 group



Linewidths:
a) 13 Hz
b) 2.8 Hz
c) 3.2 Hz
d) 3 Hz

Centre frequency: 400 MHz

Gruschke et al., Lab Chip, 2012, 495

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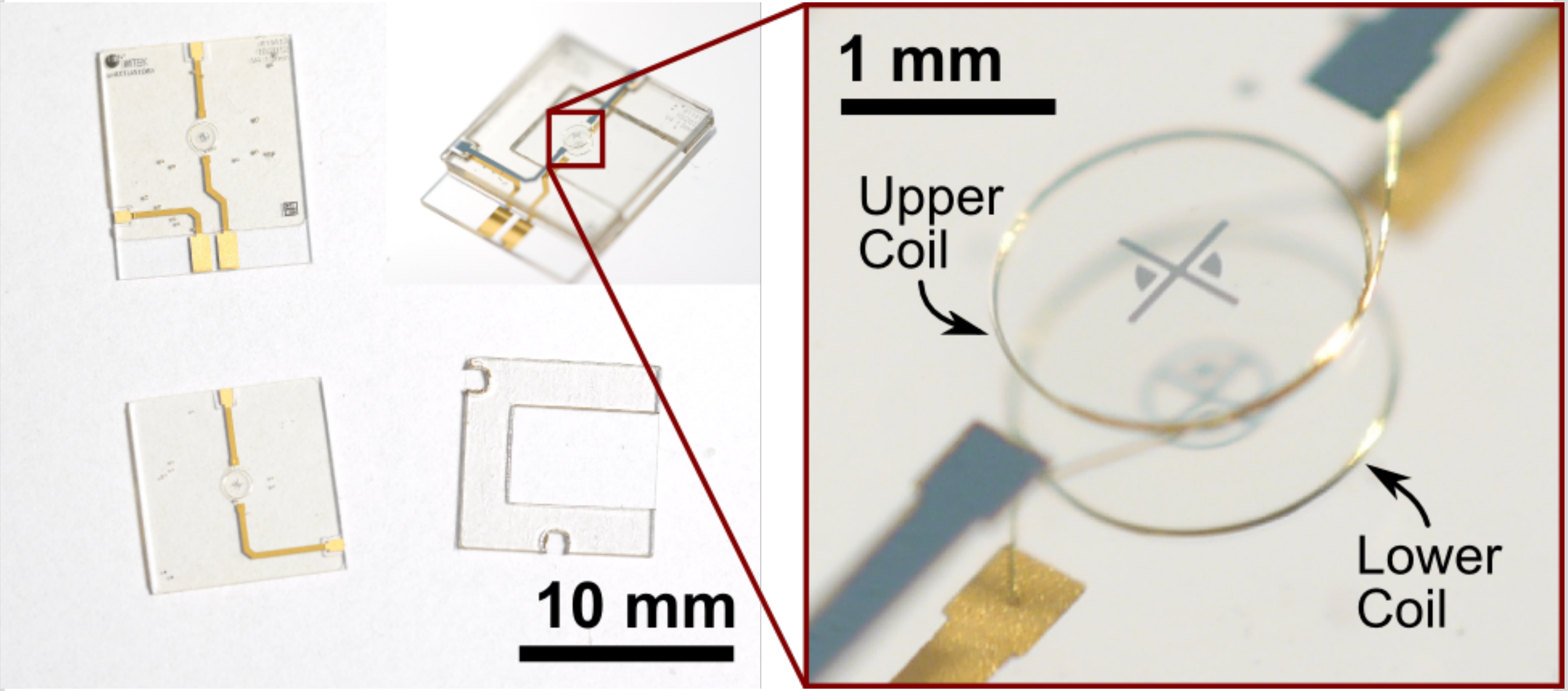
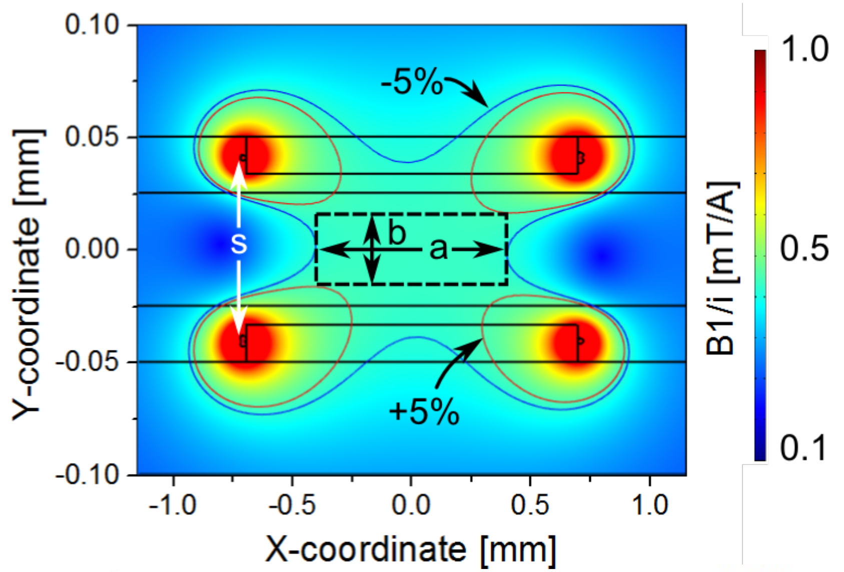
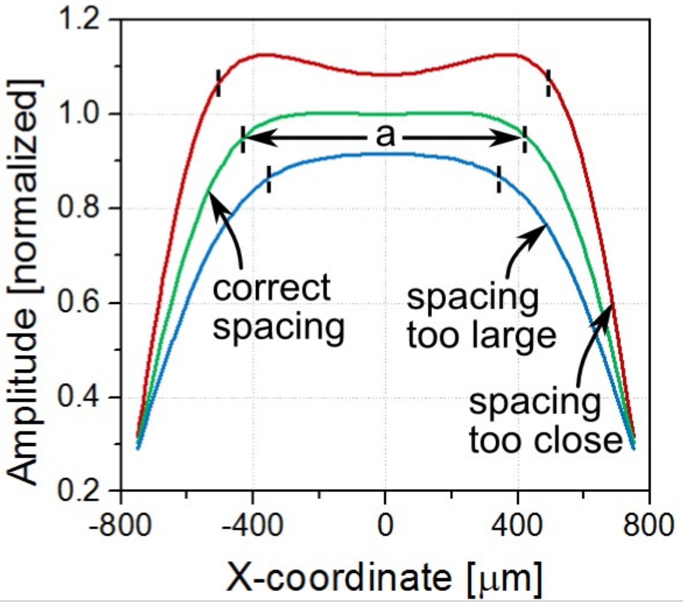
Helmholtz coil detector

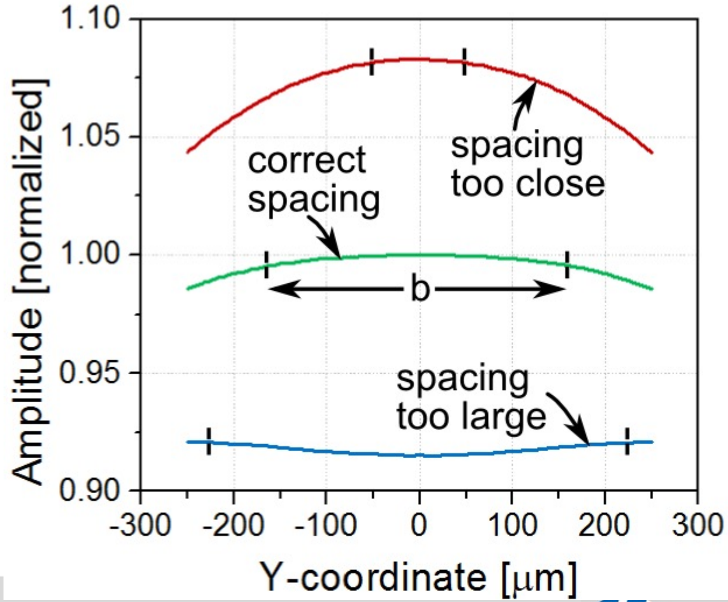


Spengler et al., JMM, 2014 (in press)

Helmholtz coil detector







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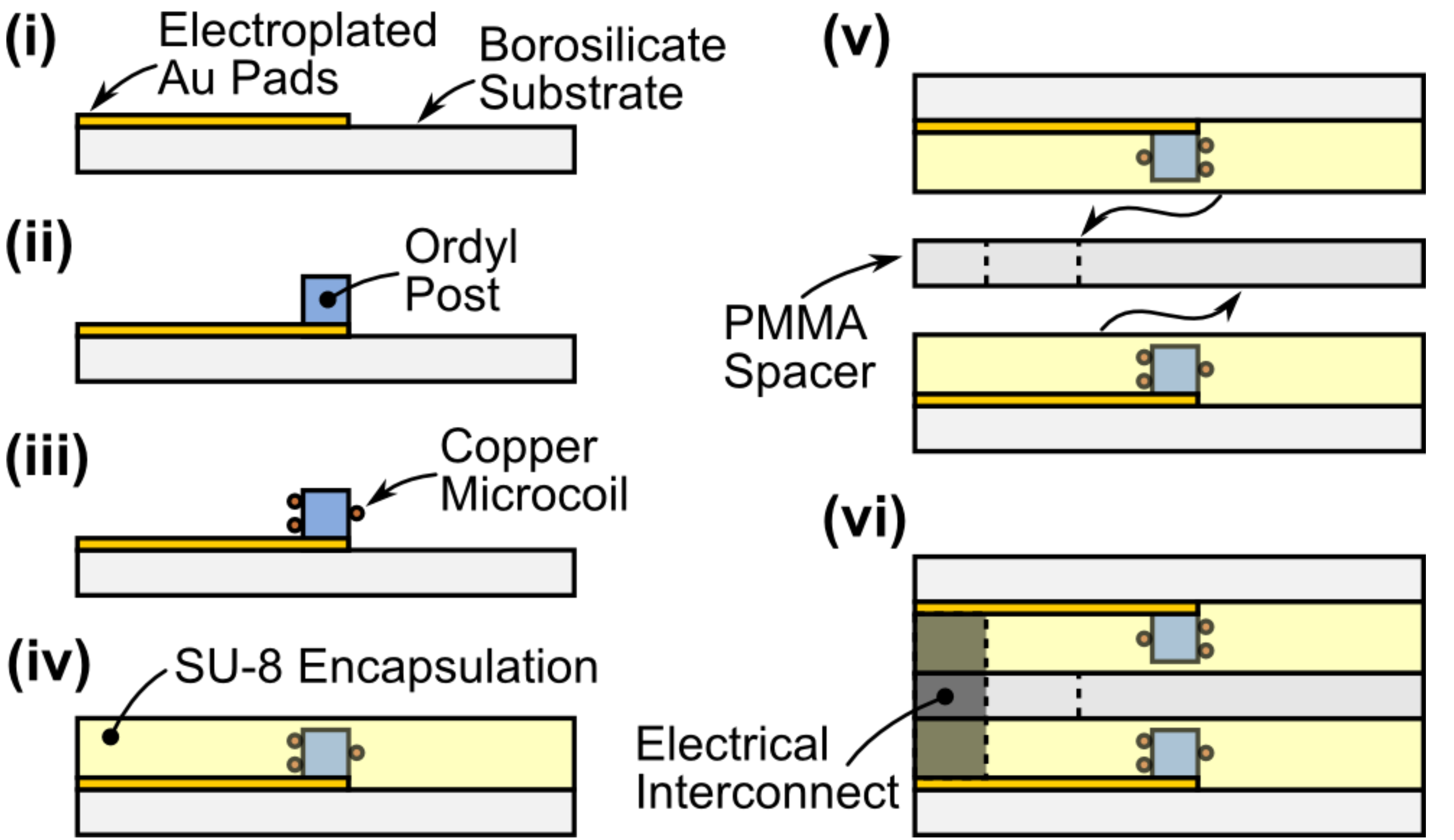

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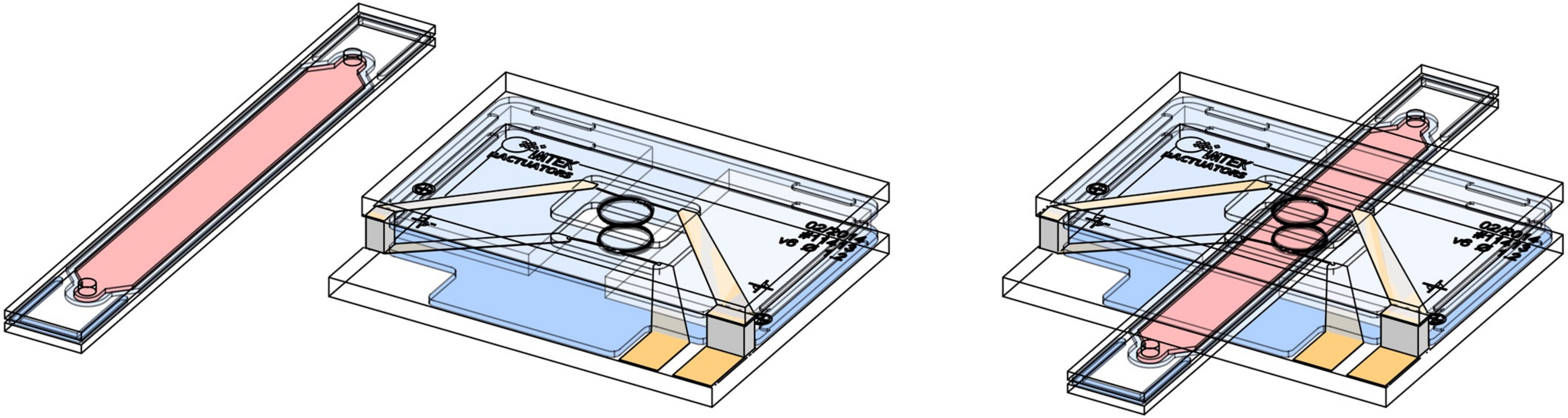

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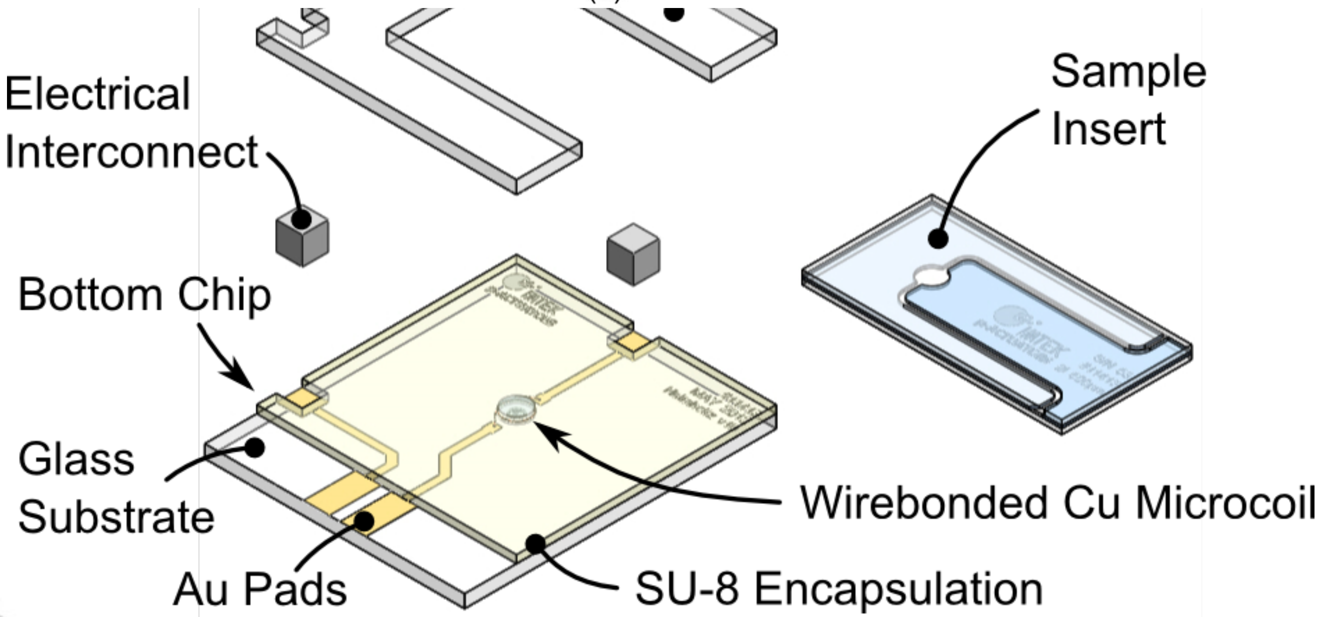
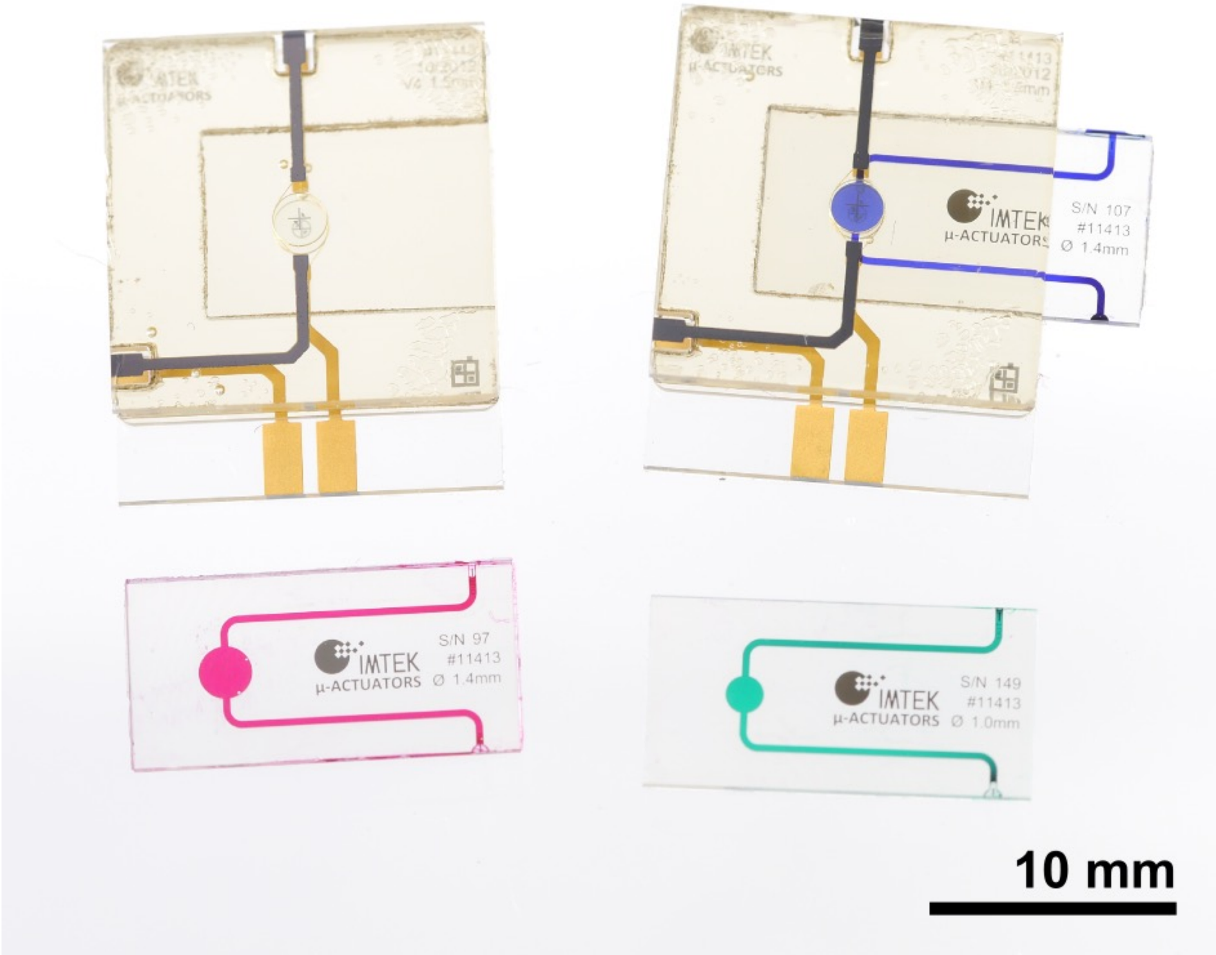
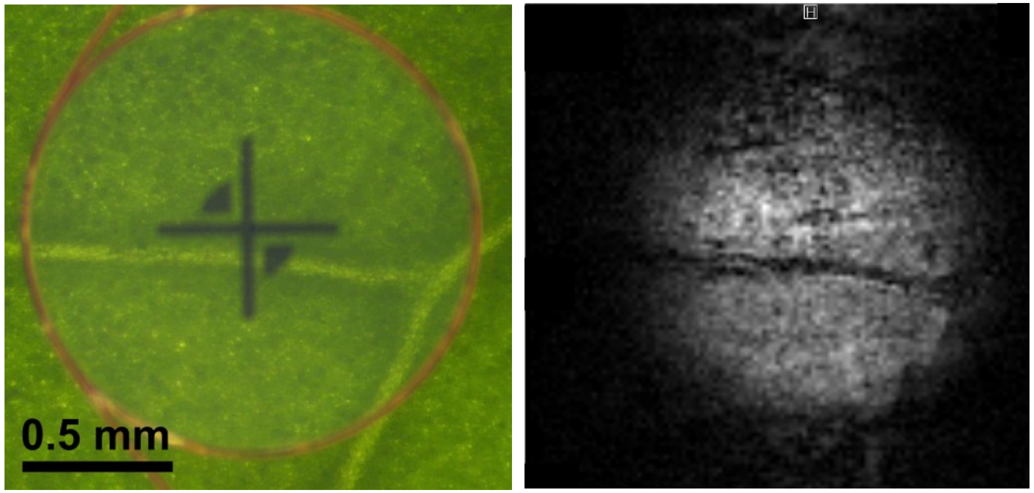


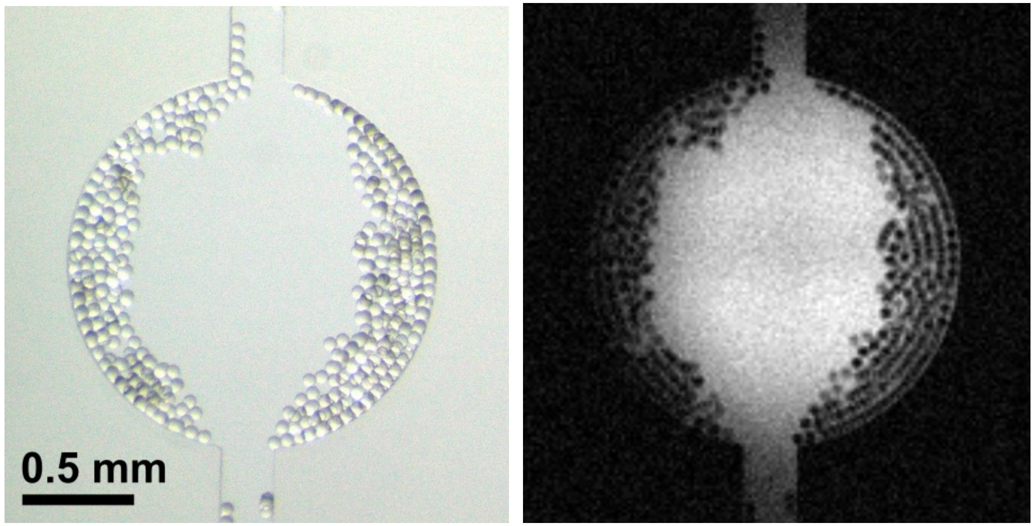
Helmholtz coil– disposable sample holders



Helmholtz coil detector – MRI

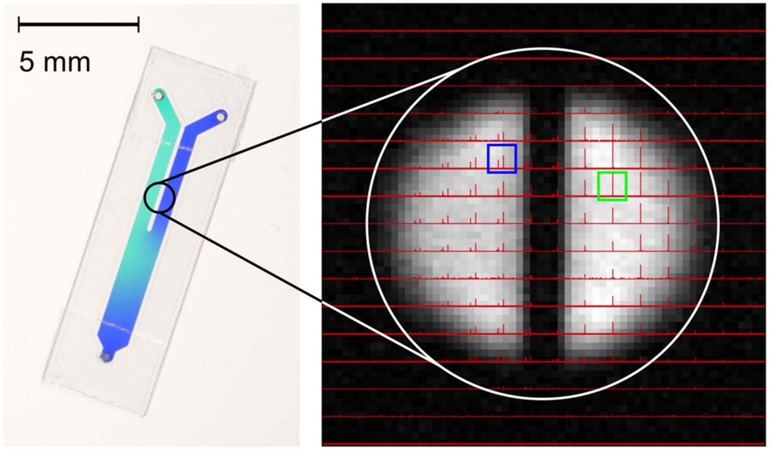


Piece of leaf:
LEFT: optical photograph
RIGHT: MRI – coronal view
Resolution: 20µmx20µmx400µm
2h 8min

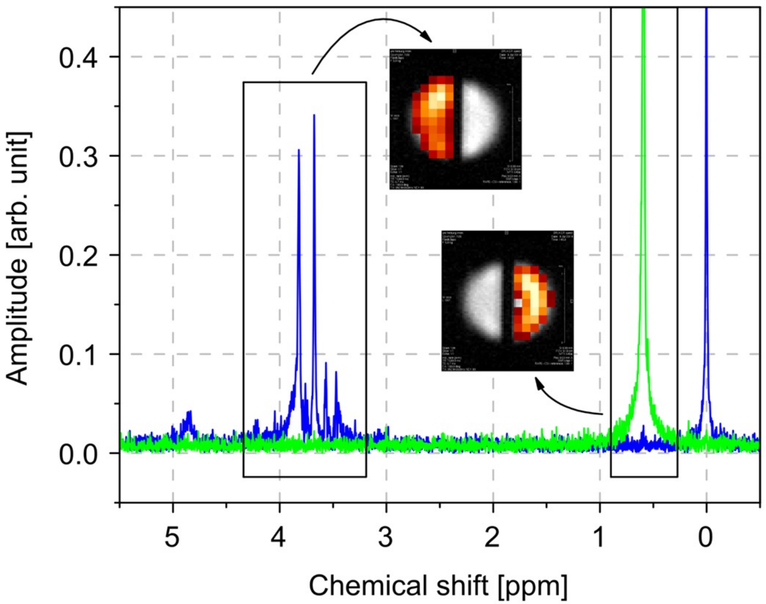


Polymer beads – 50 µm
LEFT: optical photograph
RIGHT: MRI – coronal view
Resolution: 10µmx10µmx100µm
11h 22min

Helmholtz coil detector – imaging + spectroscopy



(a)



(b)

one voxel = 1.44 nl !!

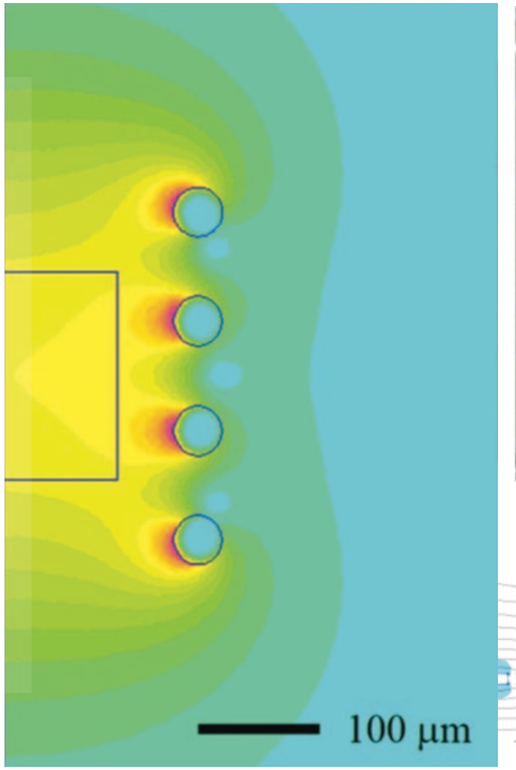
Extracted and assigned spectra from the two voxels marked in the right half of (a)

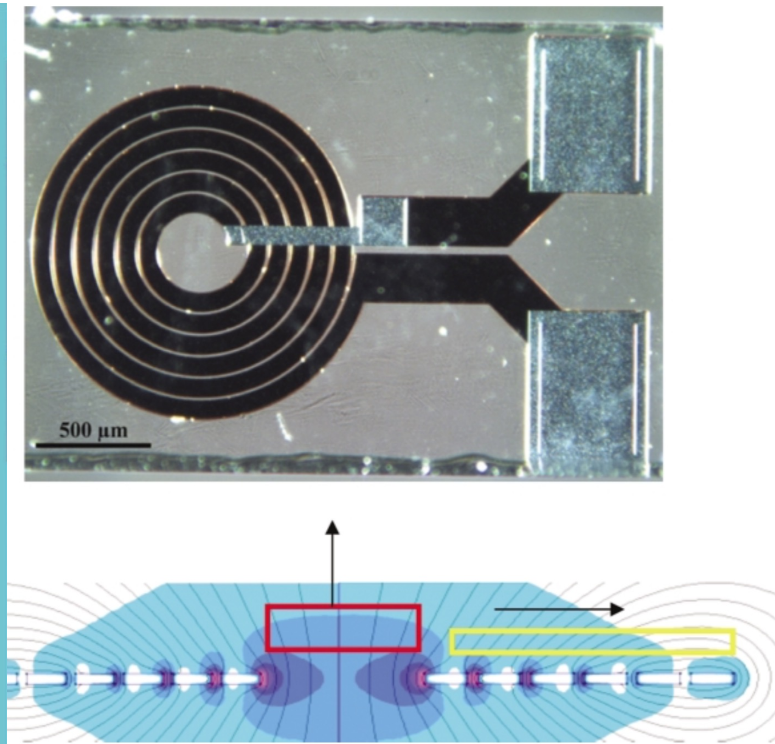
~~Four~~ Two micro-detectors today + BONUS

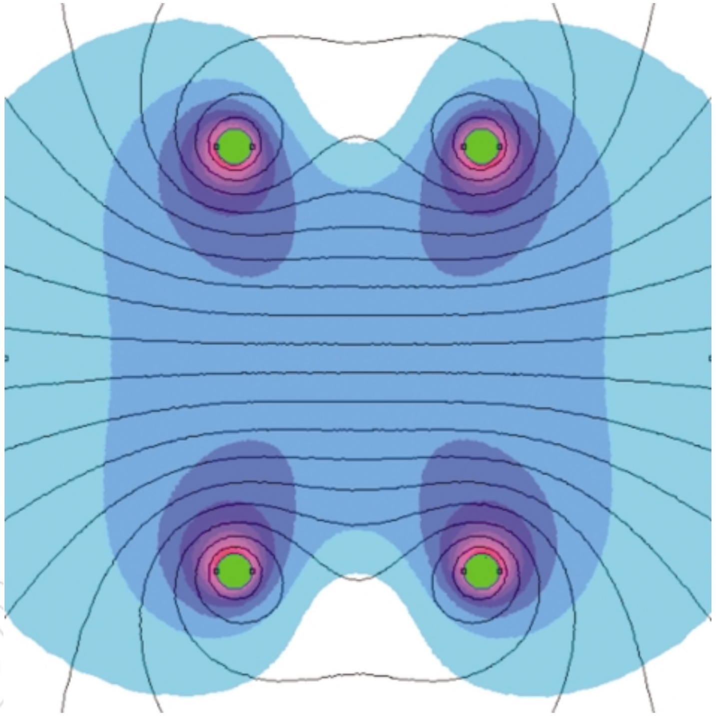
Karlsruhe Institute of Technology

- wirebonded solenoidal microcoil
  - imaging and spectroscopy
- on-chip *MACS* micro-resonator
  - for magic angle coil spinning applications
- **planar array of micro-coils**
  - **for planar samples**
- **Helmholtz coil micro-detector**
  - **for lab-on-a-chip applications**
- **Other geometries**
  - **stripline detectors**

NMR detectors – various geometries







solenoid

planar

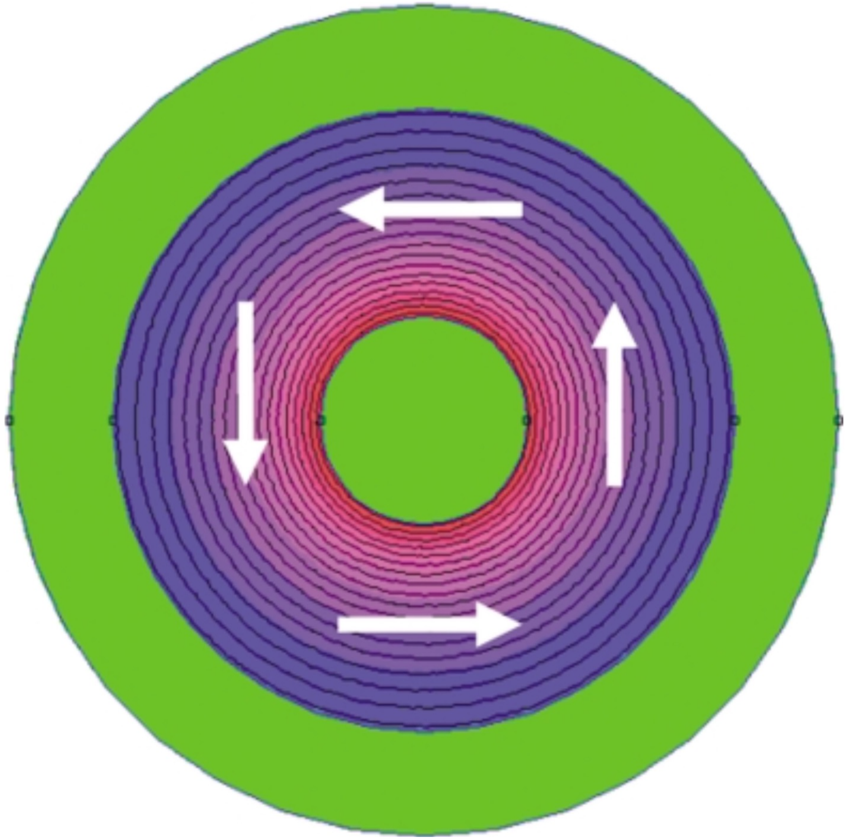
saddle

Kentgens et al., J. Chem. Phys. 128, 052202 2008

van Bentum et al., Analyst, 2004, 129, 793–803

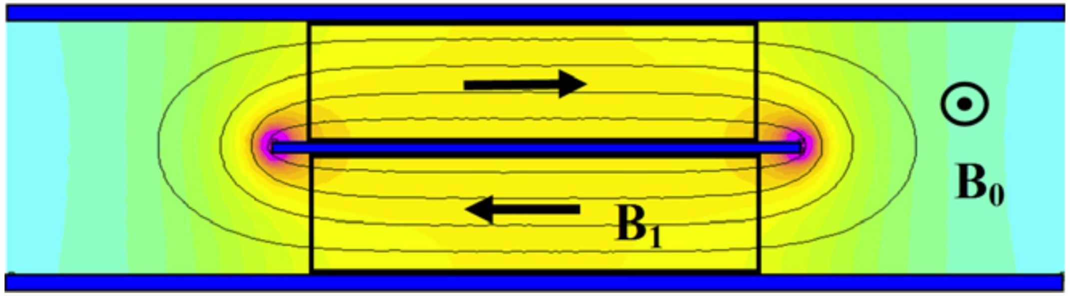
van Bentum et al., Analyst, 2004, 129, 793–803

A simple wire is an NMR detector



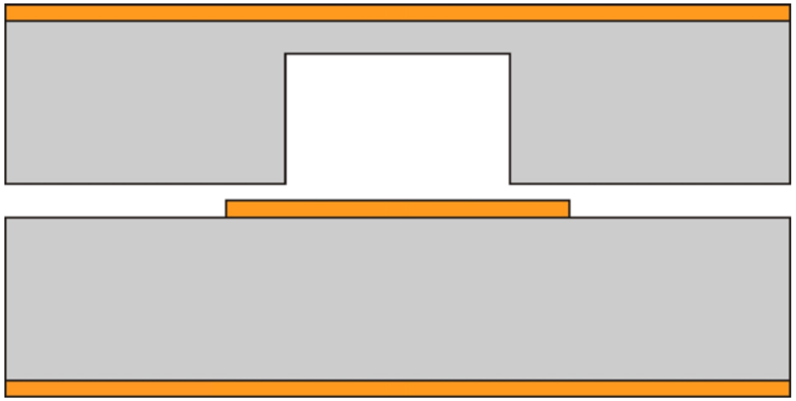
coax cable

van Bentum et al., Analyst, 2004, 129, 793–803



stripline

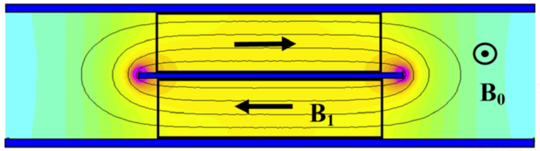
van Bentum et al., J. Mag. Res. 189 (2007) 104–113

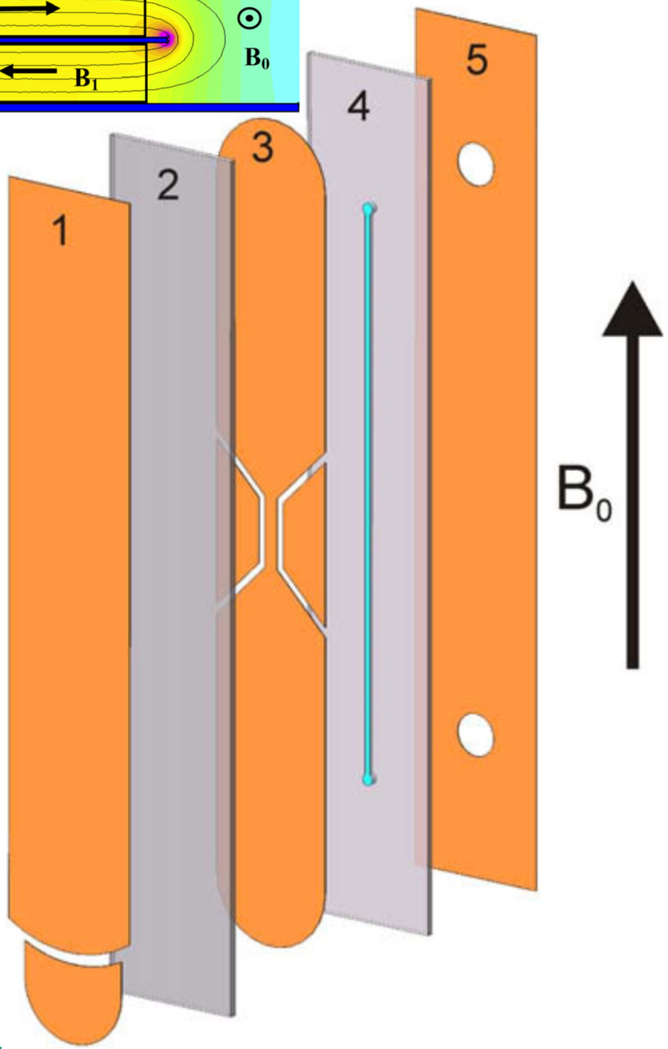


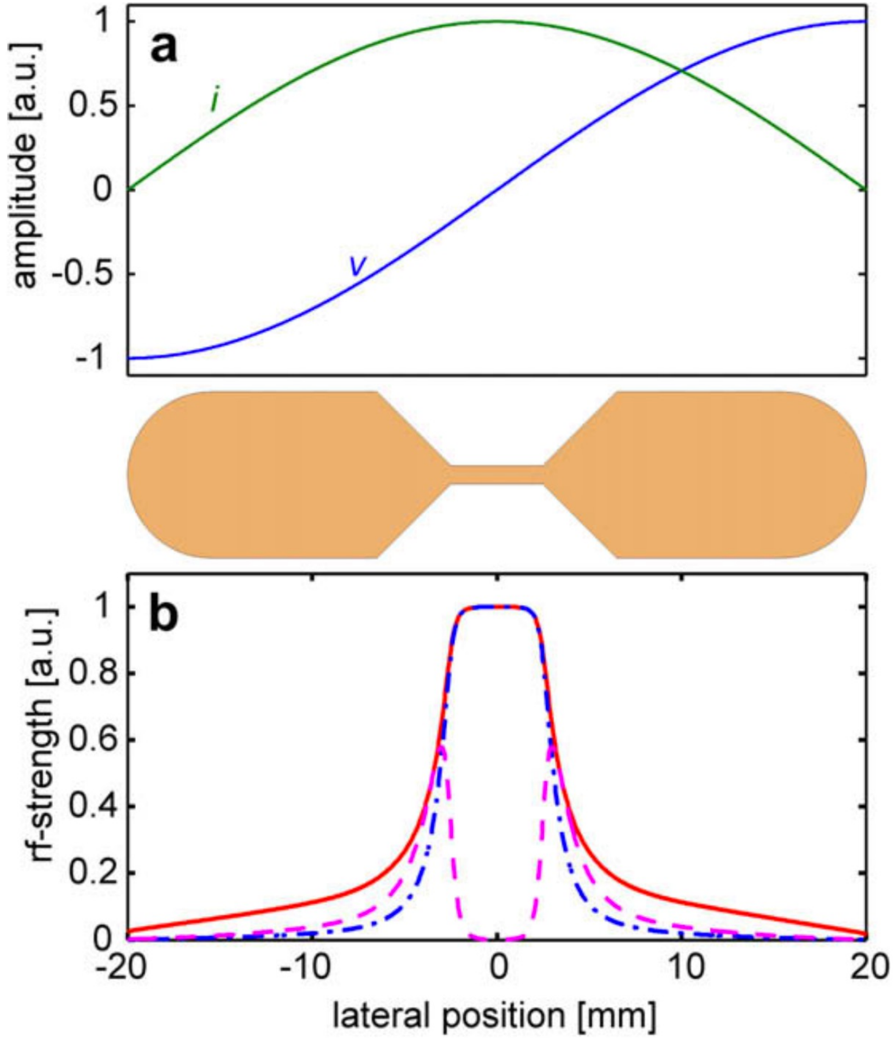
microfluidics + stripline

J. Bart et al., J. Mag. Res. 201 (2009) 175–185

Stripline NMR detector







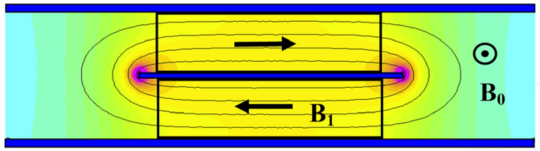
exploded view

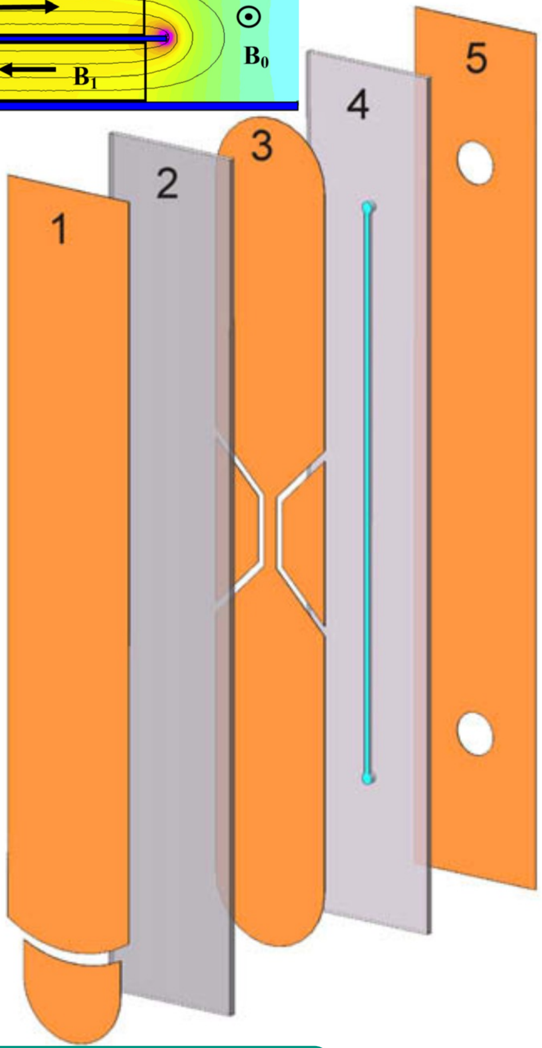
J. Bart et al., J. Mag. Res. 201 (2009) 175–185

voltage, current, rf-field distribution

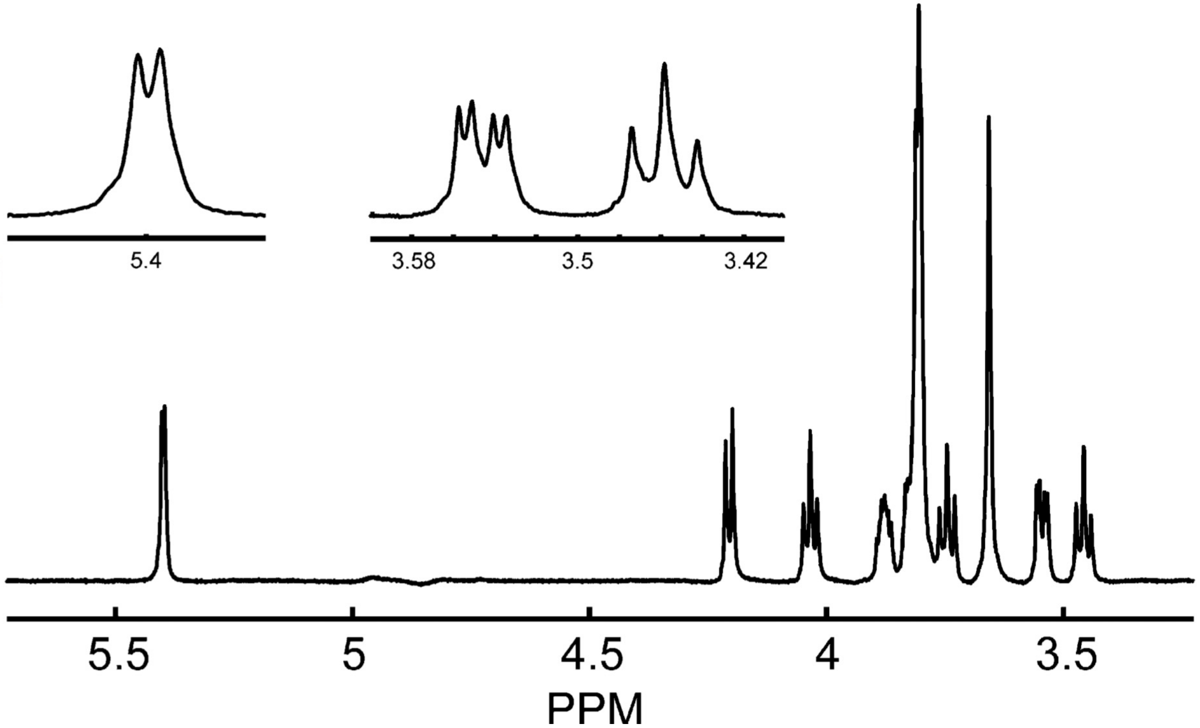
Stripline NMR detector

Karlsruhe Institute of Technology





- J-coupling resolved – 3.67 Hz



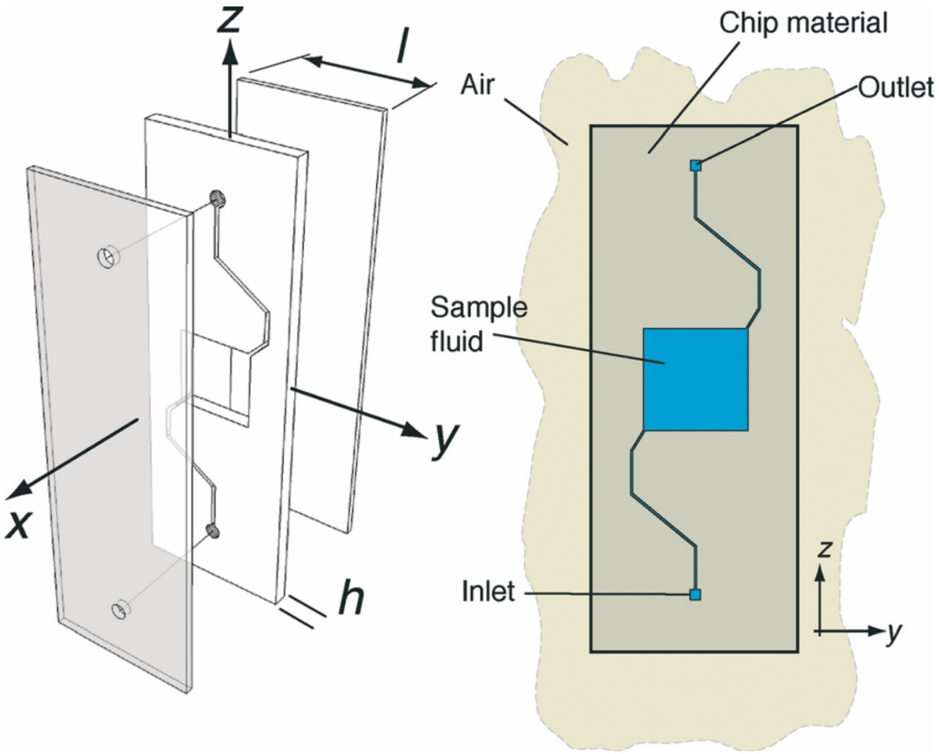
exploded view

sucrose spectrum

J. Bart et al., J. Mag. Res. 201 (2009) 175–185

Institut für Mikrostrukturtechnik
Institute of Microstructure Technology
IMT

B_0 uniformity – essential for high resolution

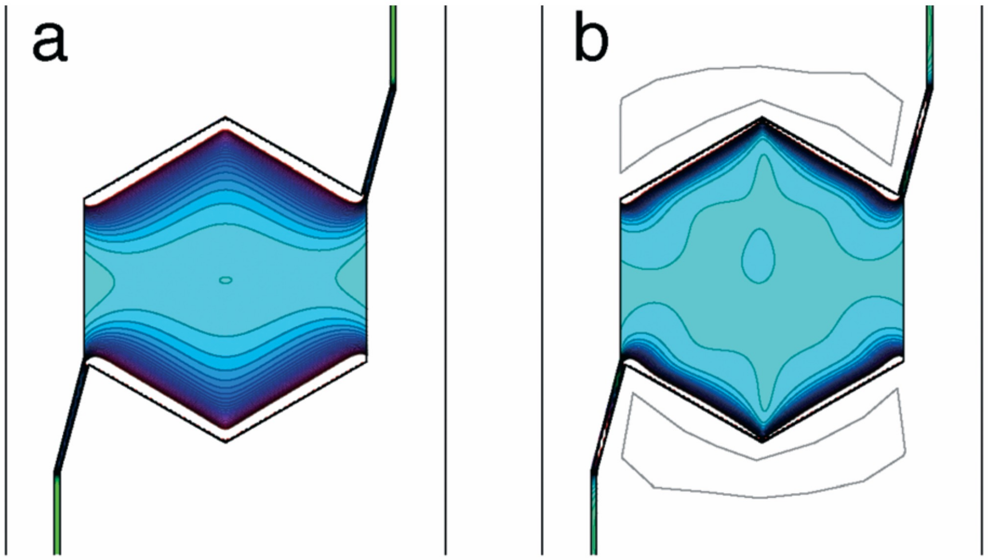


generic µ-fluidics design

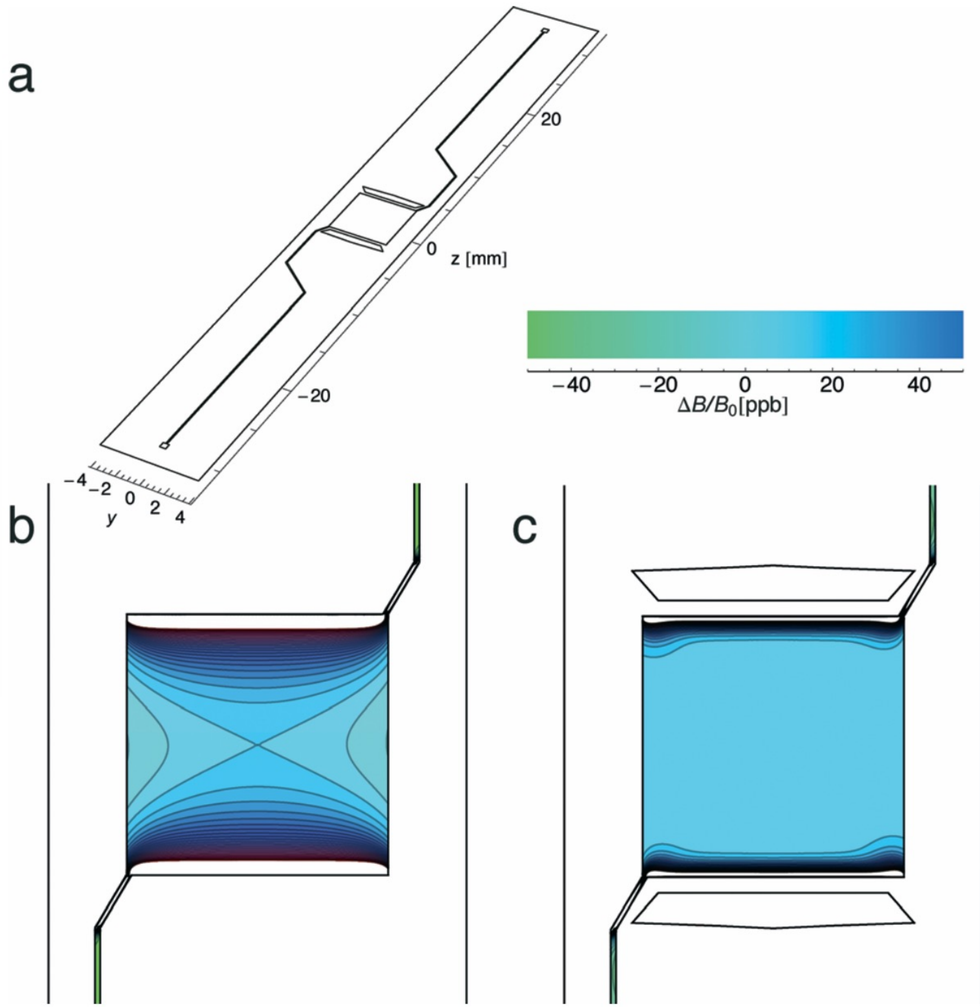
structural shimming

Ryan et al., Lab Chip, 2014, 14, 1678–1685

B_0 uniformity – essential for high resolution



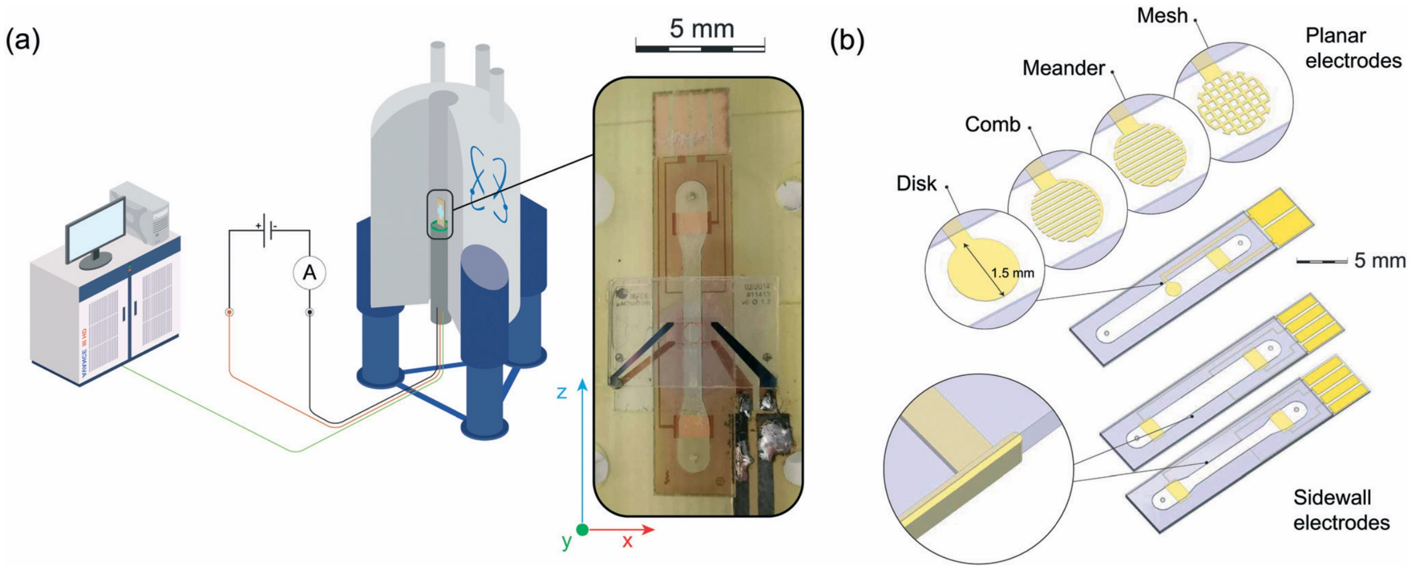
structural shimming through cavity shaping



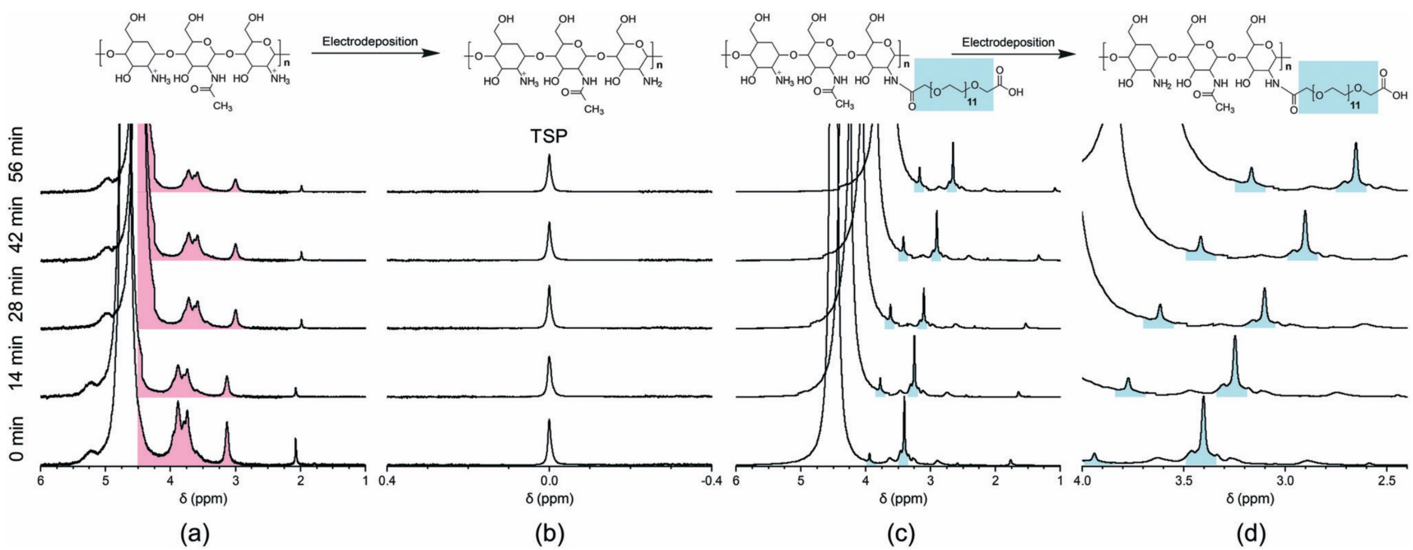
structural shimming

Ryan et al., Lab Chip, 2014, 14, 1678–1685

μ-fluidic platform for *in situ* NMR



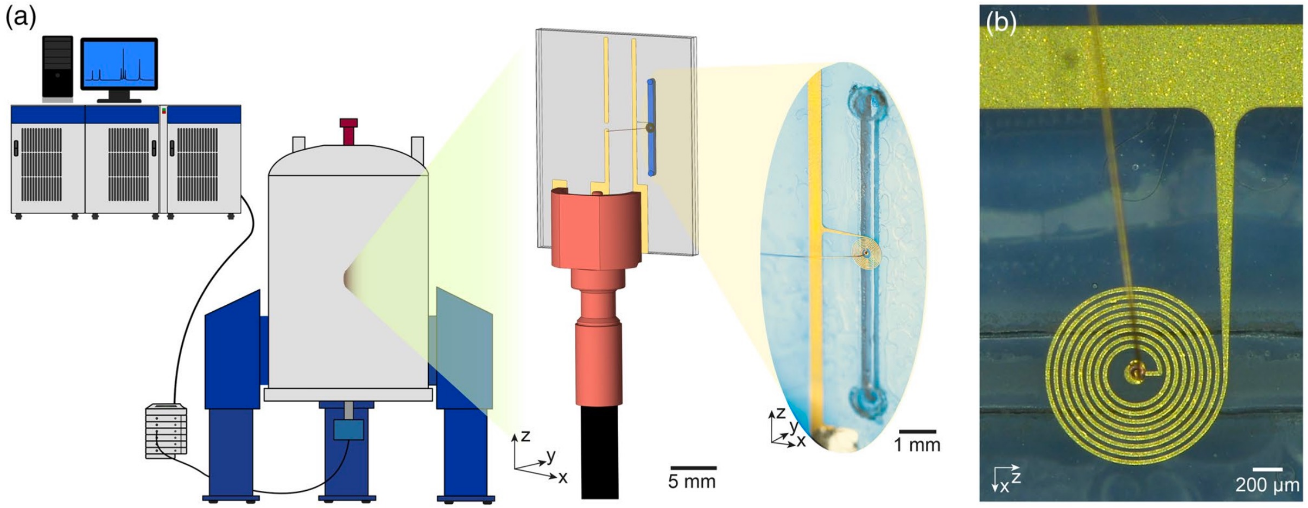
***in situ* NMR setup Helmholtz coil detector & electrodes**



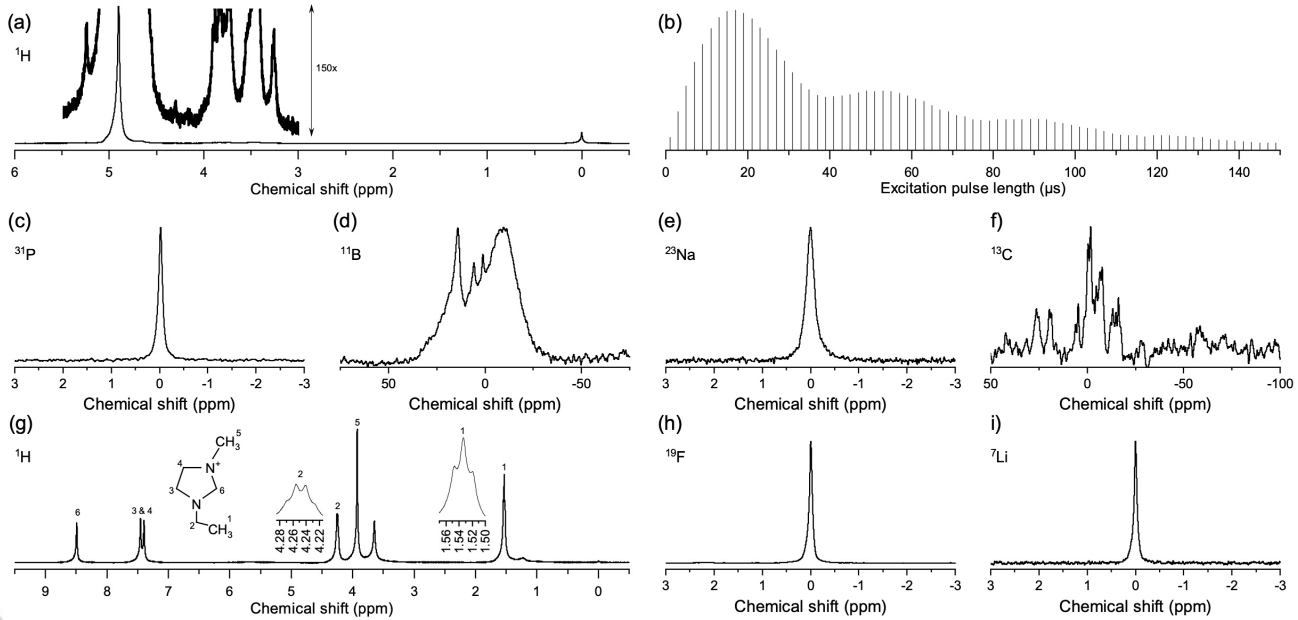
in situ NMR monitoring of chitosan electrodeposition

Davoodi et al., Lab Chip, 2020, 20, 3202–3212

Broadband detectors for multinuclear NMR



broadband spiral detector in a vertical bore superconducting NMR magnet



7 different nuclei observed using one optimized NMR detector

Davoodi et al., Sci. Rep., 2021, 11:7798

Thank you!