Non-, or Minimally Invasive High Resolution ^{1}H NMR Metabolic Profiling Using Slow MAS

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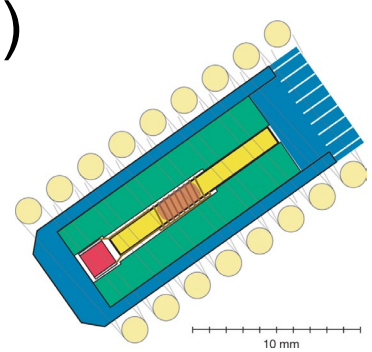
Research Objectives

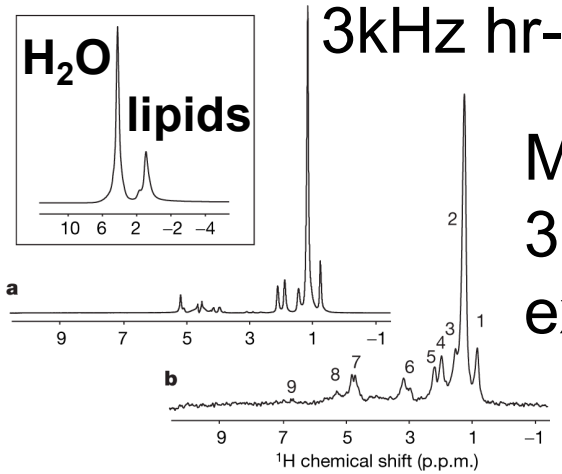
To develop a method

- Provide high resolution, high sensitivity ^{1}H NMR metabolic profiling on biological tissues
- Capable of non-, or minimally destructive detection
- Can easily work on samples with size as small as ~0.2 μl (200 nl) to as large as > 1 ml or 1.0 cm^3.

Previously Reported Nanoliter MAS NMR

Magic Angle Coil Spinning (MACS)





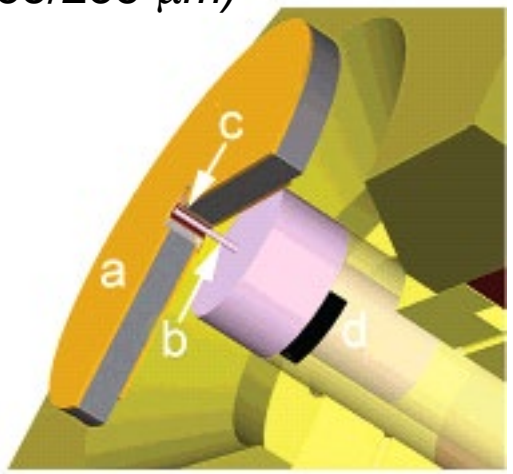
3kHz hr-MAS

MACS 33 s exp

0.3 mg bovine muscle

Sakellariou D, Le Goff G, Jacquinot JF. *Nature* 2007;447: 694-698; Wong et al. MRM 63, 269 (2010).

Static Microcoil MAS for solids (400/300 μm outer/inner diameter or 335/235 μm)



Janssen H, Brinkmann A, van Eck ERH, van Bentum PJM, Kentgens APM. *J Am Chem Soc* 2006;128: 8722-8723.

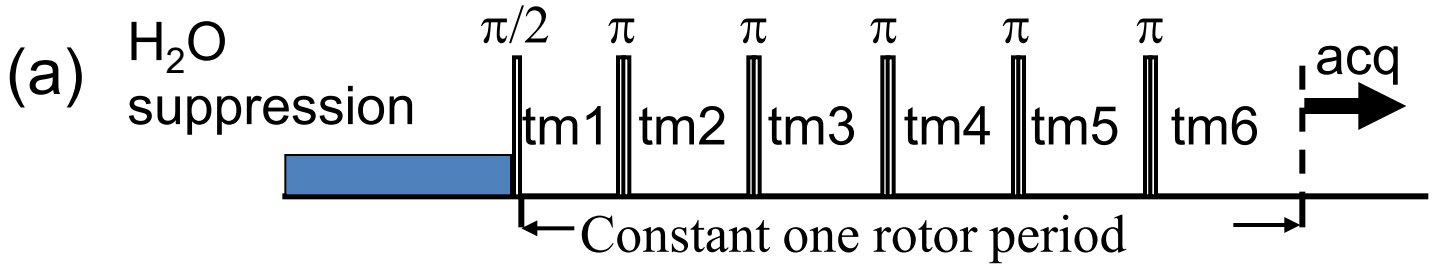
Difficult to scale up using a single probe

Our Approach

Combining the techniques of

- High resolution slow-MAS ^{1}H NMR and
- Switchable inductively coupled static micro-RF coil

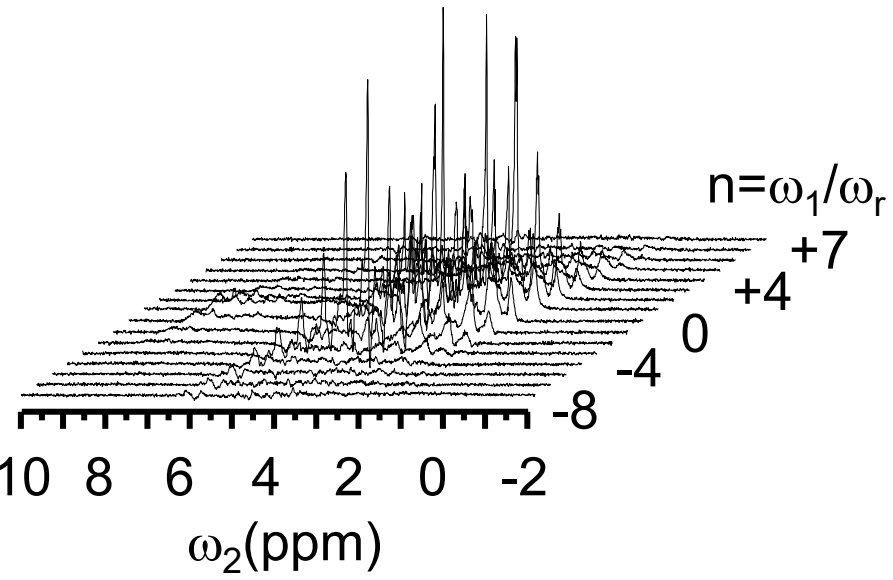
Slow-MAS using ^{1}H-PASS



Wind RA, Hu JZ, and Rommereim DN. *Magn. Reson. Med.* 2001; 46: 213-218.

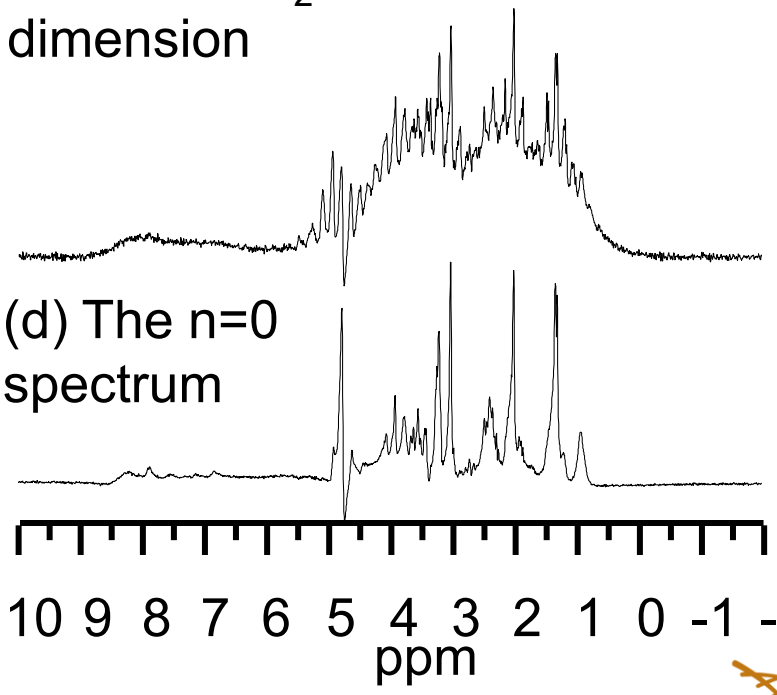
Antzutkin ON, Shekar SC, and Levitt MH. *J. Magn. Reson.* 1995; A115: 7-19.

(b) 2D 300MHz ^{1}H-PASS of 100 mg fresh mouse brain at sample spinning rate of 43Hz



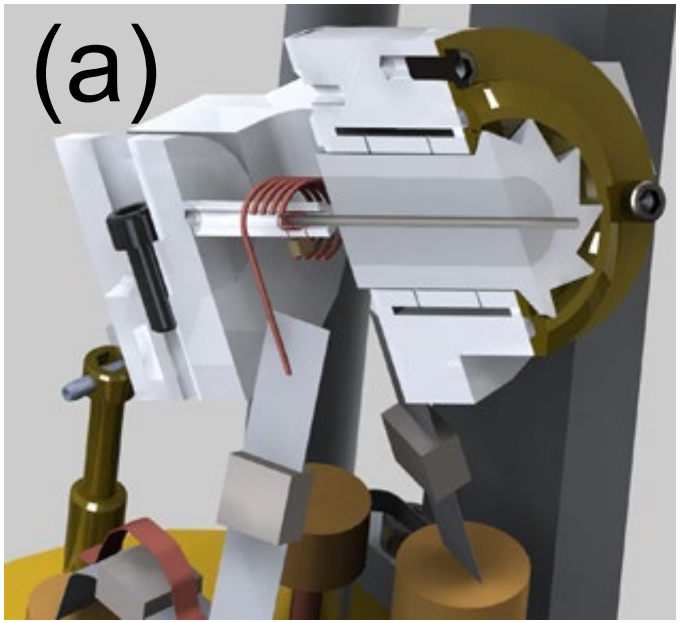
(c) Projection of the data on to ω_2 dimension

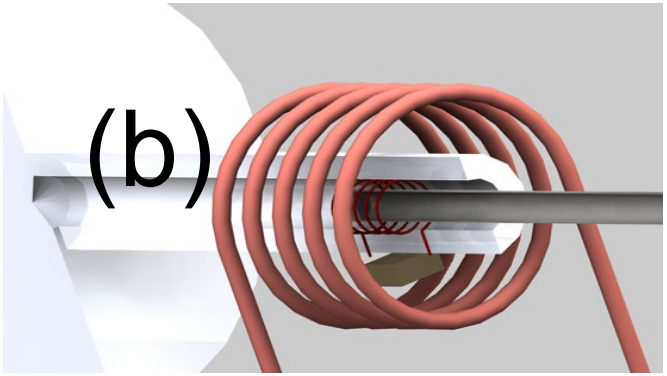
(d) The n=0 spectrum



16 evolutions steps using 52 minutes and a commercial 7.5 mm MAS probe.

The Switchable Microcoil Slow-MAS Probe

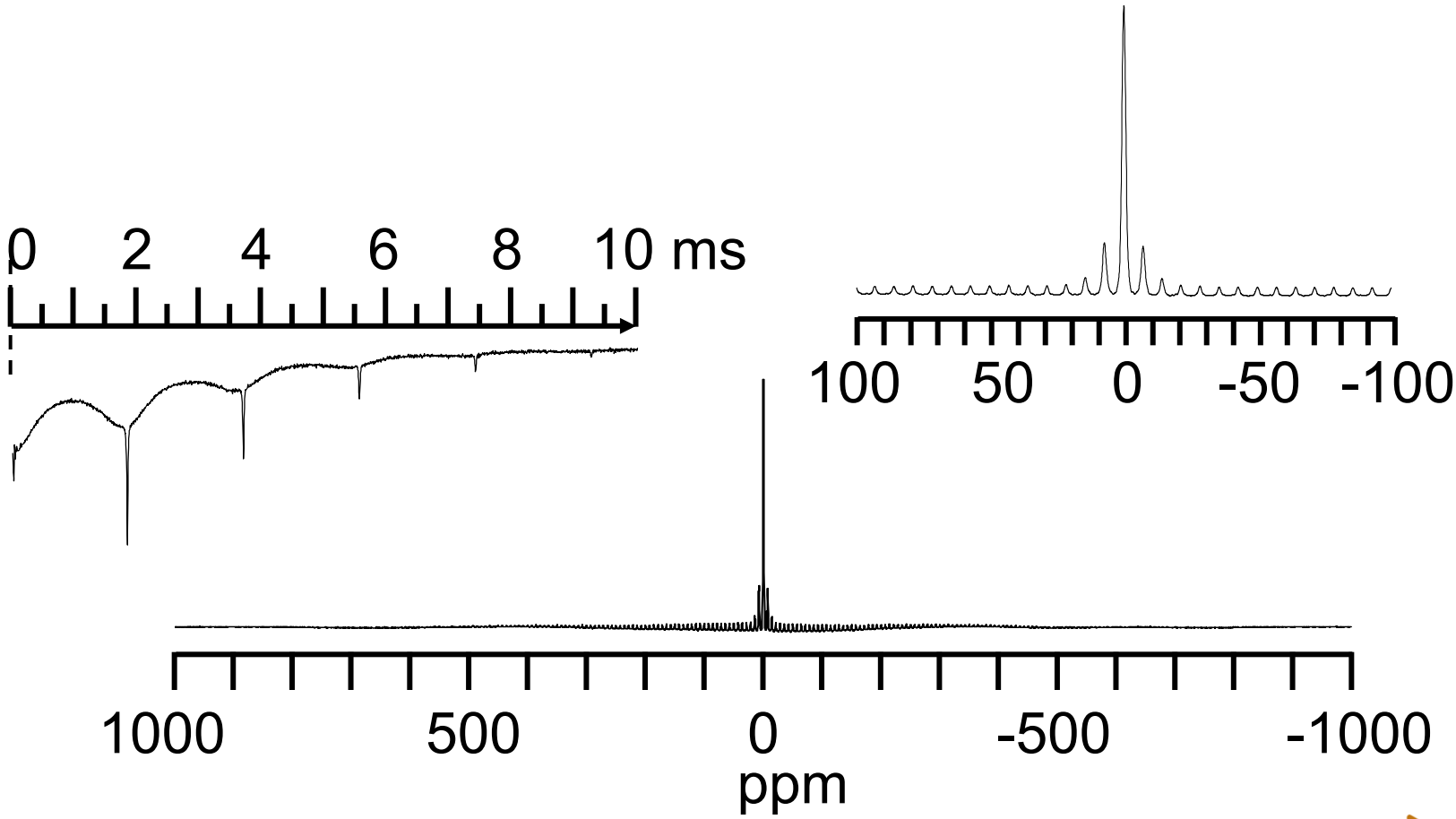




Features of the probe

- Static micro RF-Coil is wound inside the coil support for maximizing the filling factor.
- Inductive coupling between the micro coil and the outer coil for increased sensitivity due to increased sample filling factor from the micro coil.
- Magnetic susceptibility matched wires are used for winding the micro coil for best B_0 field homogeneity.
- Easily switch the plug with micro-RF coil of different ID to accommodate a range of sample sizes using a single probe.

Easy turning the magic angle without micro-RF coil using ~200 mg kBr at ~500 Hz at 7.05 T field



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Performance test results (one example)

Outer RF Coil: 3 turns flat; ID: 12.6 mm; OD: 13.8 mm; width: 1.2 mm; Coil length: 9 mm.

Inner micro RF Coil: 6 turns Pd plated OFHC Cu AWG wire; ID: 1.3 mm; OD: 1.7 mm; Length: ~2.7 mm.

$\pi/2$ pulse width for a given RF power at the probe
Without micro-coil: 12.5 μs at 28 W
With micro-coil: 3.75 μs at 0.6 W
Estimated S/N enhancement by using micro-coil: ~22

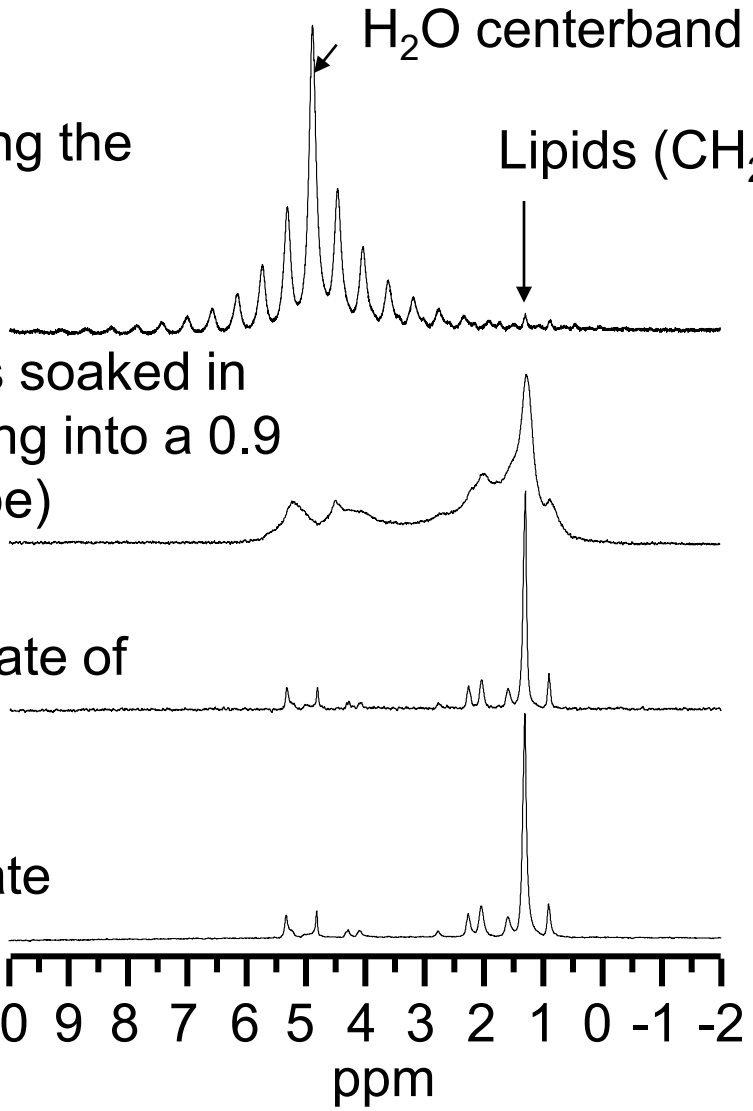
Nanolieters ^{1}H-PASS with micro-coil

(a) SP-MAS at 127 Hz, highlighting the relative ratio of H_2O to lipids

(b) Static (the 0.2 mg muscle was soaked in D_2O for 10 minutes before inserting into a 0.9 mm OD and ~0.7mm ID glass tube)

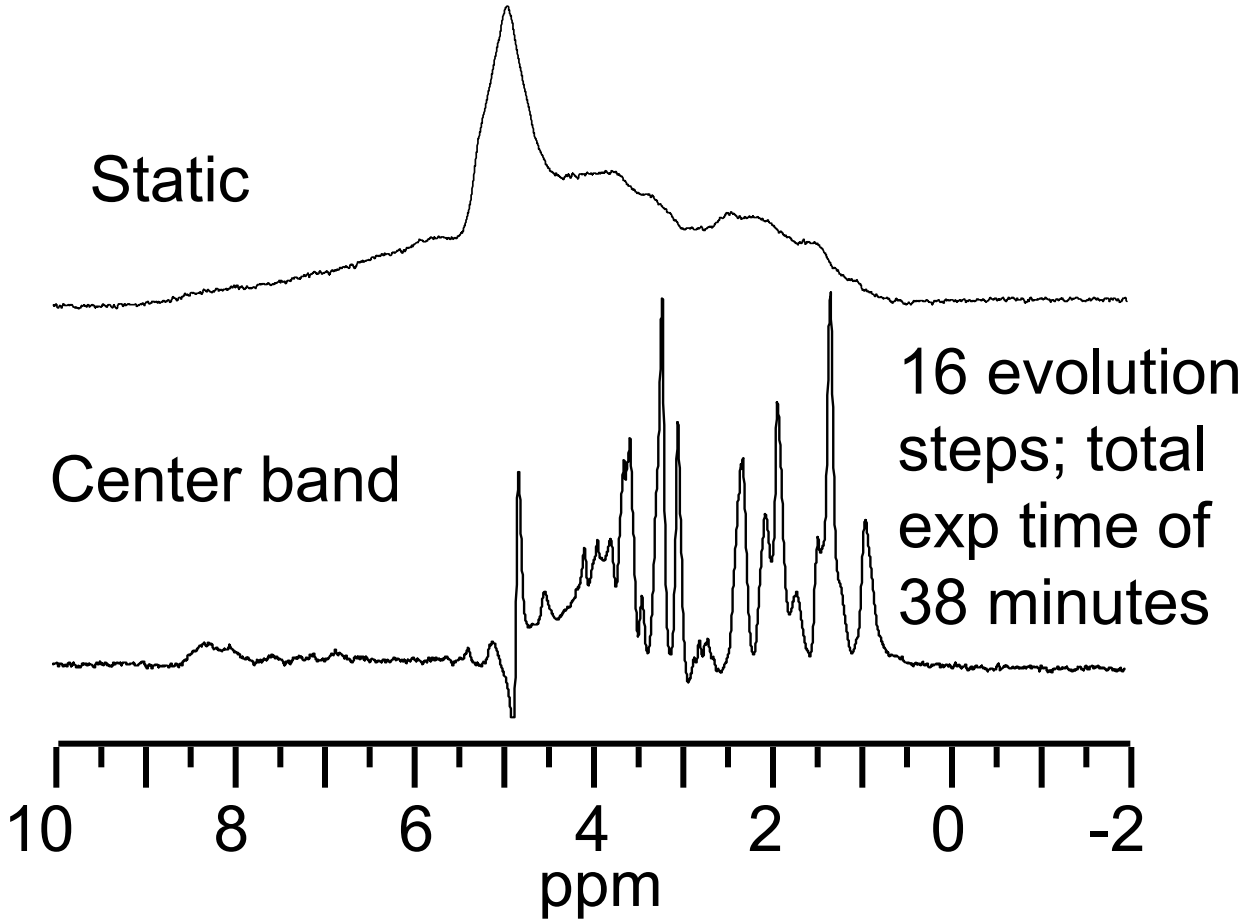
(c) 2.6 minutes ^{1}H PASS at spin rate of 147 Hz

(d) 31 minutes ^{1}H PASS at spin rate of 147 Hz



Nanolieters (200 nl or 0.2 mg) mouse muscle sample metabolic profiling with micro-coil inserted.

Large sample volume ^{1}H-PASS without microcoil



Large sample volume using only the outer RF coil. About 1005 mg (~1.005 cm^3) mouse brain ^{1}H-PASS at 83Hz. The tissue was left at RT for 24 hours before the EXP.

5.Summary

- A slow-MAS probe has been developed that allows high resolution ^{1}H NMR metabolic profiling on samples with volume as small as 0.2μl (200 nanoliters) to larger than 1 cm^3 investigated using a single probe.
- The nanoliter capability has the potential to follow the metabolic changes through a continued investigation on a single small laboratory animal over a long period of time using minimally invasive blood and tissue biopsy samples.
- The milliliter capability would allow minimally destructive studies of intact biological object with size as large as >1 cm^3.
- Slow-sample spinning avoids fluid leakage and keeps the integrity of the biological sample. It is a non-, or minimally invasive method and is also a safe method for working with hazardous biological samples.

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Probe body was machined at EMSL machine shop.