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3D ^{15}N visualization of a drug hyperpolarized by SABRE approach

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Outline

- Magnetic resonance imaging (MRI)
- Heteronuclear MRI
- Hyperpolarization
- Signal amplification by reversible exchange (SABRE)
- Fampridine (FAM)
- Results:
 - ^{15}N NMR of FAM with natural abundance of ^{15}N and ^{15}N -labeled FAM: explanation of the difference
 - 2D and 3D ^{15}N MRI of ^{15}N -labeled FAM
- Conclusions



Magnetic resonance imaging (MRI)

^1H

NA = 99.9885%
 $\gamma(^1\text{H}) \approx 42.6 \text{ MHz/T}$

^{31}P

NA = 100%
 $\gamma(^{31}\text{P}) \approx 17.2 \text{ MHz/T}$

^{19}F

NA = 100%
 $\gamma(^{19}\text{F}) \approx 40.1 \text{ MHz/T}$

For other nuclei: low sensitivity

Heteronuclear MRI: ^{15}N

Heteronuclear MRI can bring complementary and unique information



Pros

- Absence of background signal from protons
- Dispersion of chemical shift
- Long T_1 relaxation time



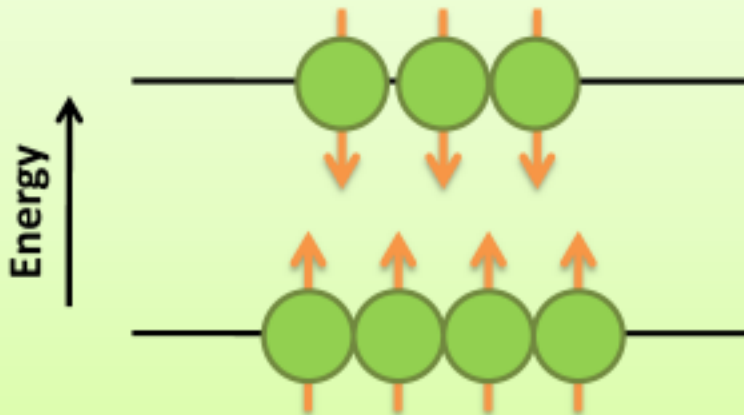
Cons

- Small natural abundance of ^{15}N isotope (0.364%)
- Small gyromagnetic ratio ($\gamma(^{15}\text{N}) = -4.32 \text{ MHz/T}$)

Hyperpolarization

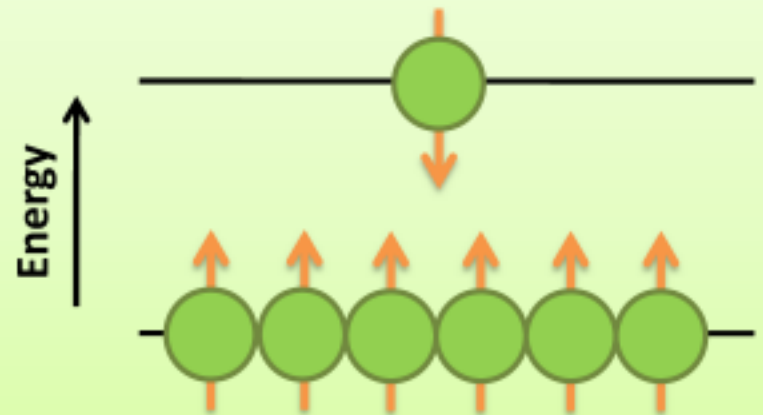
Thermal equilibrium

Problem: small difference of spin level populations

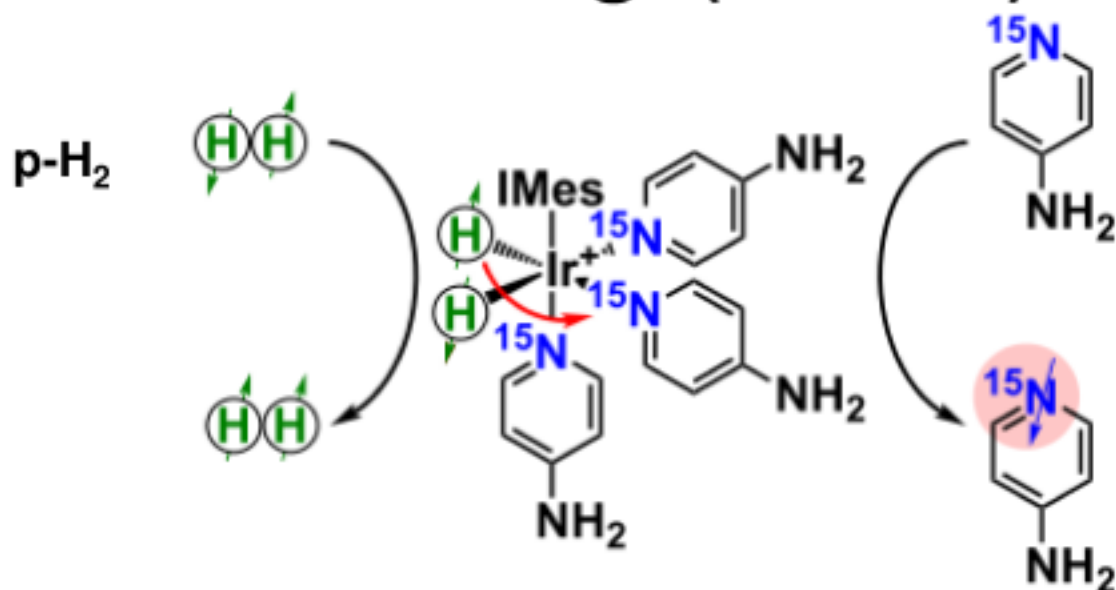


Hyperpolarization

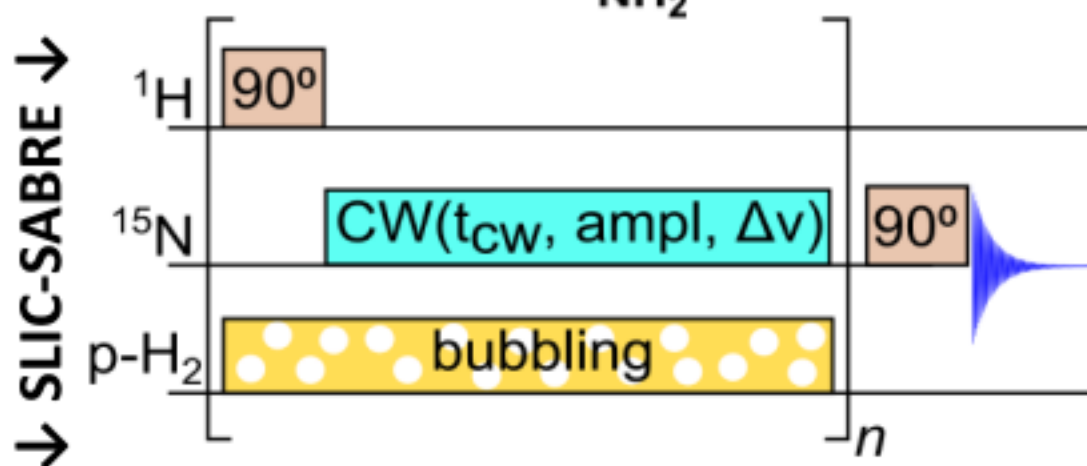
Increase of spin level population difference



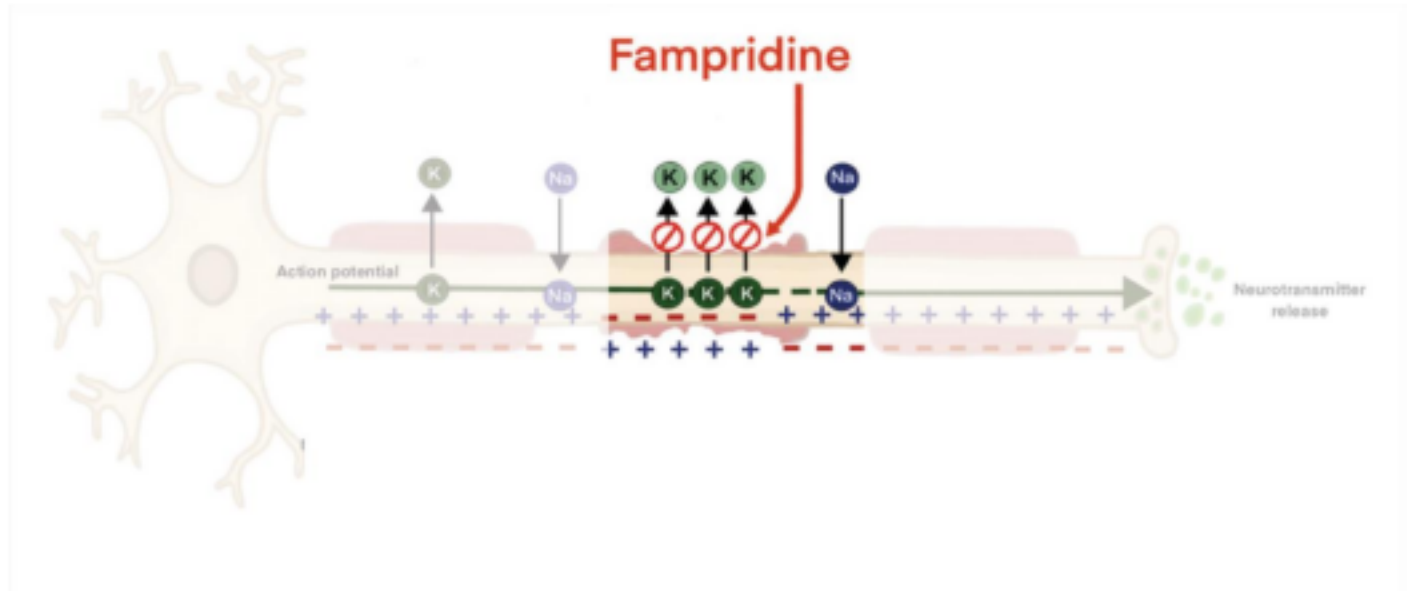
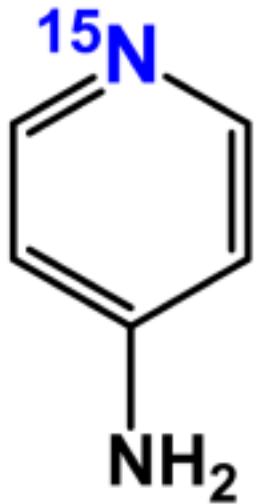
Signal amplification by reversible exchange (SABRE)



Polarization can be transferred to heteronuclei



[¹⁵N₁]fampridine, [¹⁵N₁]FAM

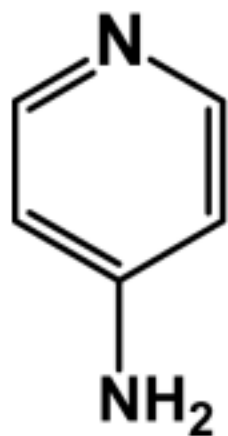


Blocks potassium channels in demyelinated axons

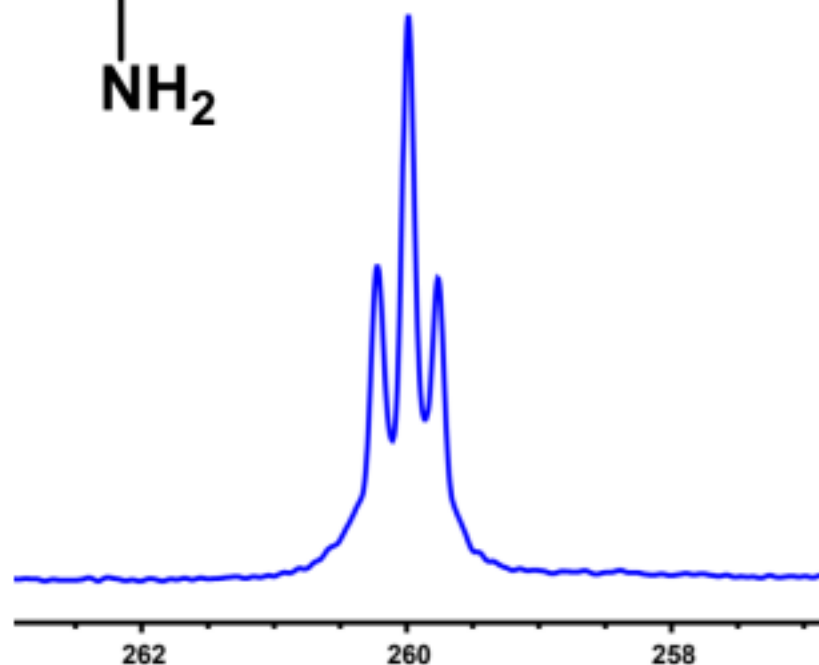
FAM is used in therapy for the treatment of symptoms of multiple sclerosis

Non-toxic

^{15}N NMR of fampridine at 7 T

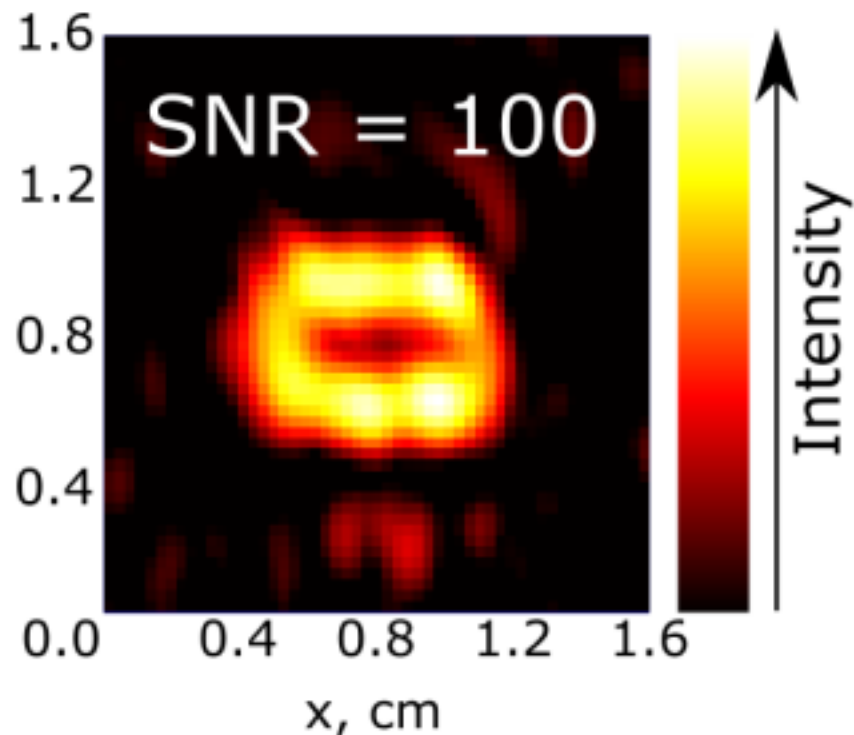


$\epsilon_{^{15}\text{N}} \approx 32000$
 $P(^{15}\text{N}) \approx 8\%$

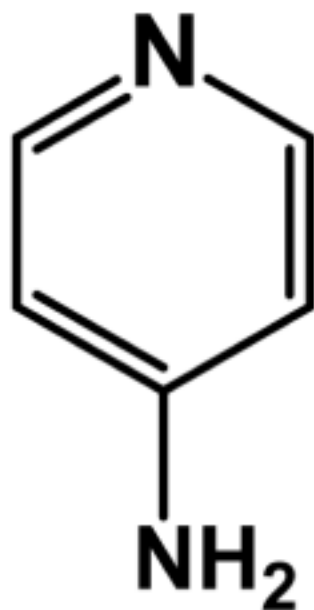


NS = 4

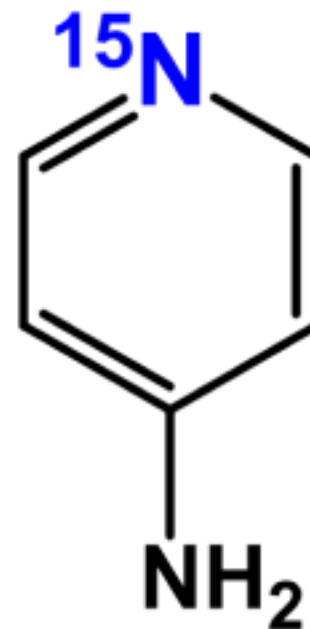
Spatial resolution: $0.3 \times 2.4 \text{ mm}^2/\text{pixel}$



[¹⁵N₁]FAMPRIDINE

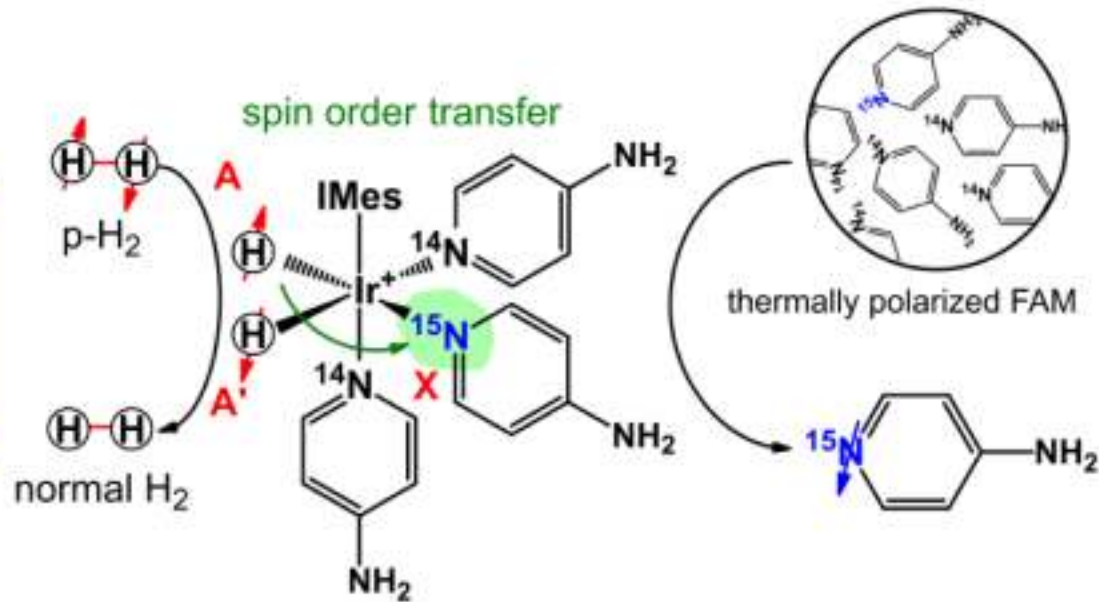


¹⁵N-labelling of
fampridine

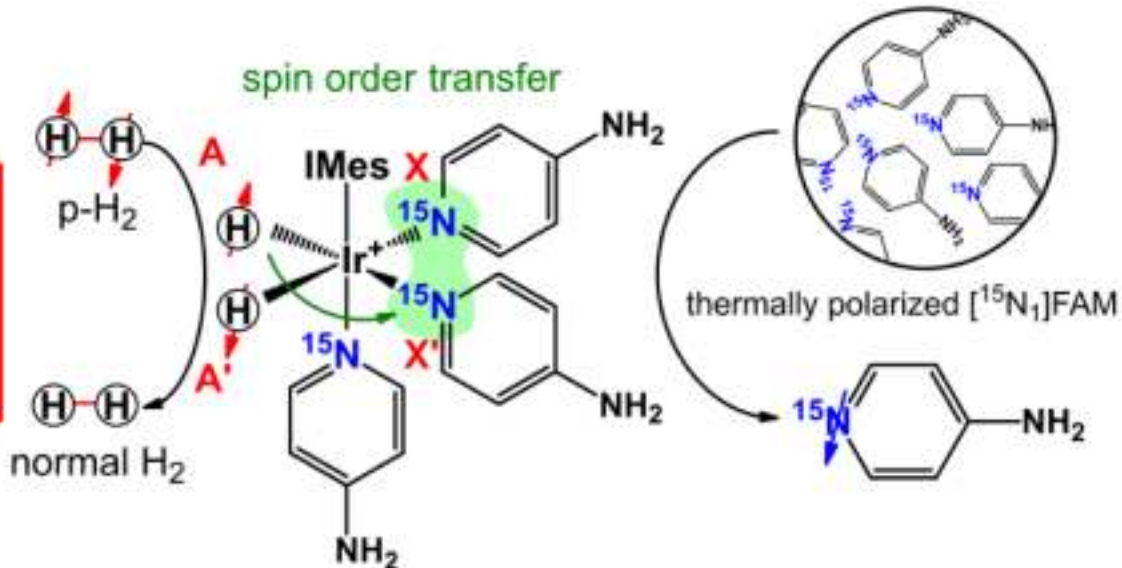


Difference in signal enhancements for FAM and $[^{15}\text{N}_1]\text{FAM}$ at 7 T

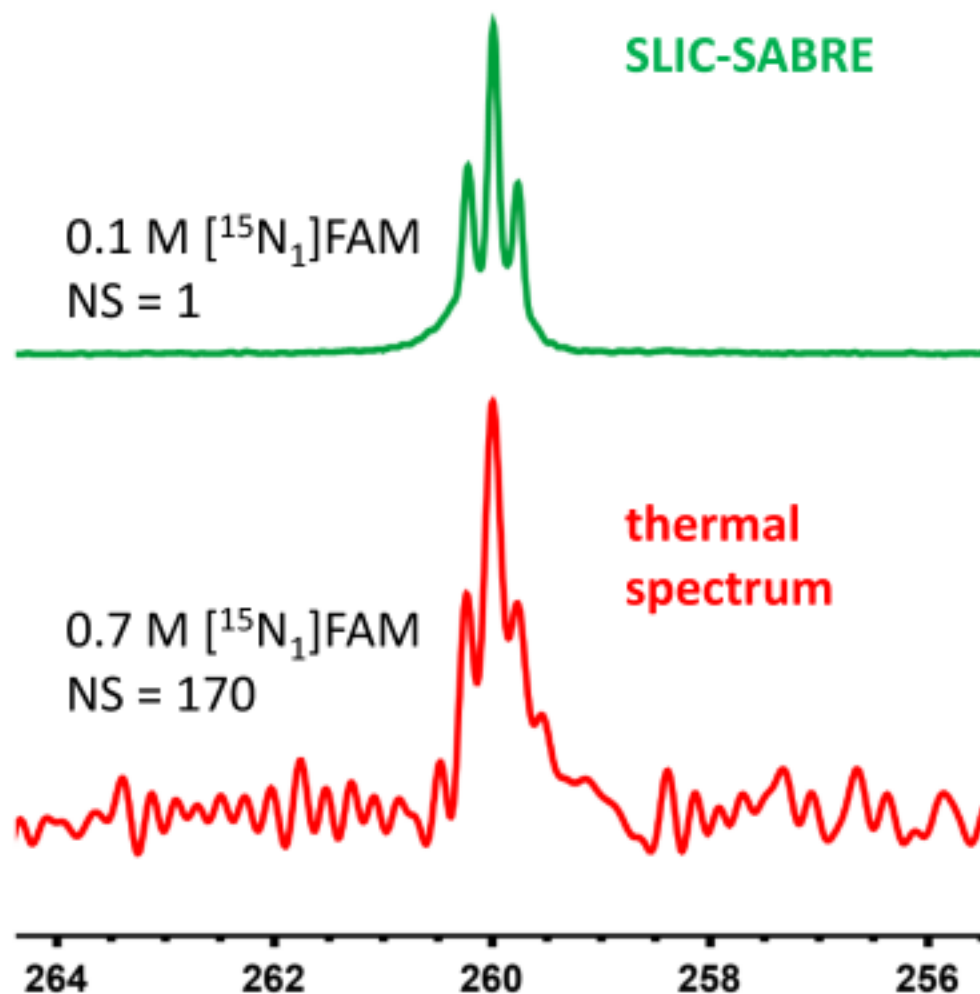
FAM
 $\epsilon_{^{15}\text{N}} \approx 32000$
 $P(^{15}\text{N}) \approx 8\%$



$[^{15}\text{N}_1]\text{FAM}$
 $\epsilon_{^{15}\text{N}} \approx 16000$
 $P(^{15}\text{N}) \approx 4\%$

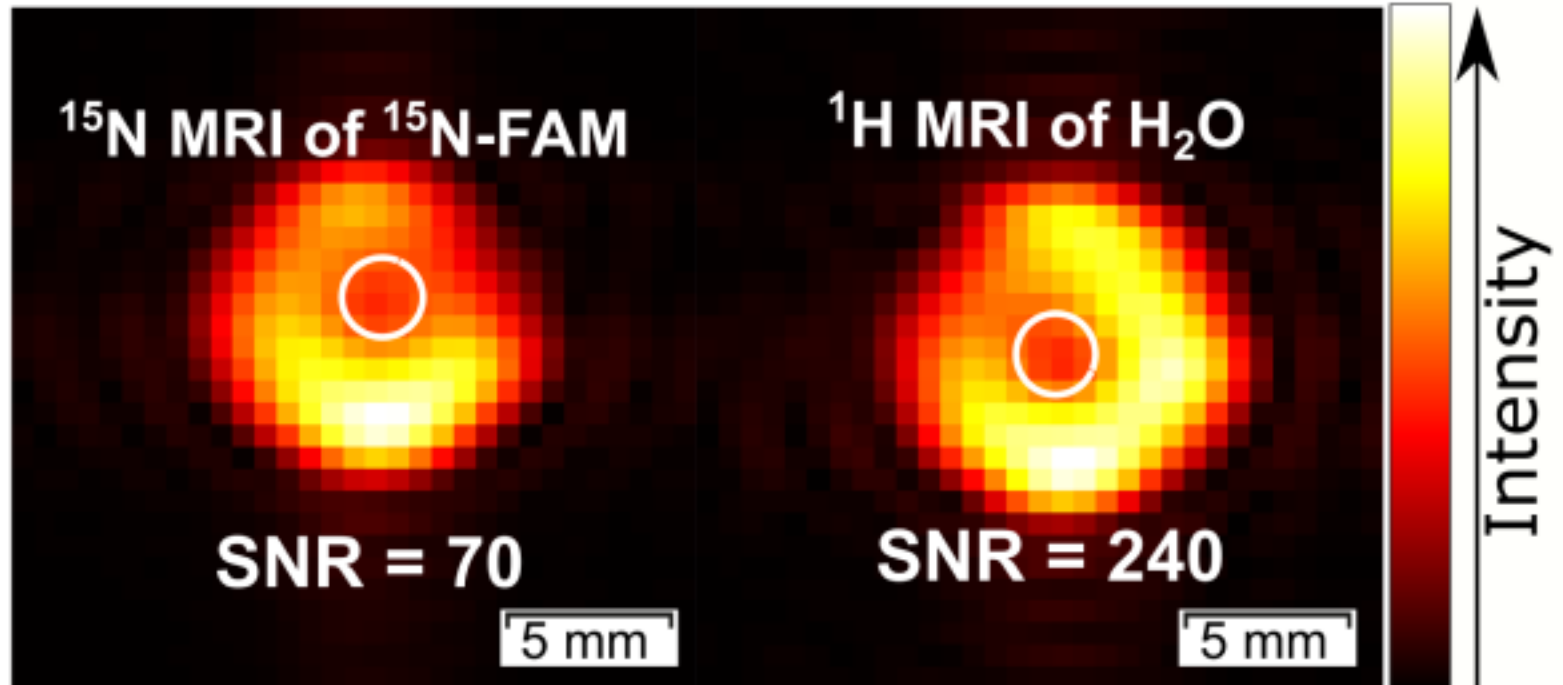
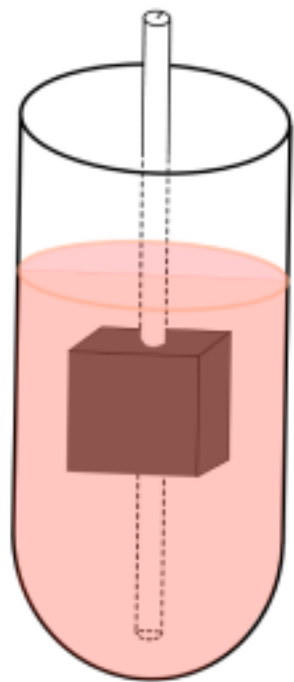


^{15}N NMR of $[^{15}\text{N}_1]\text{FAM}$ at 9.4 T

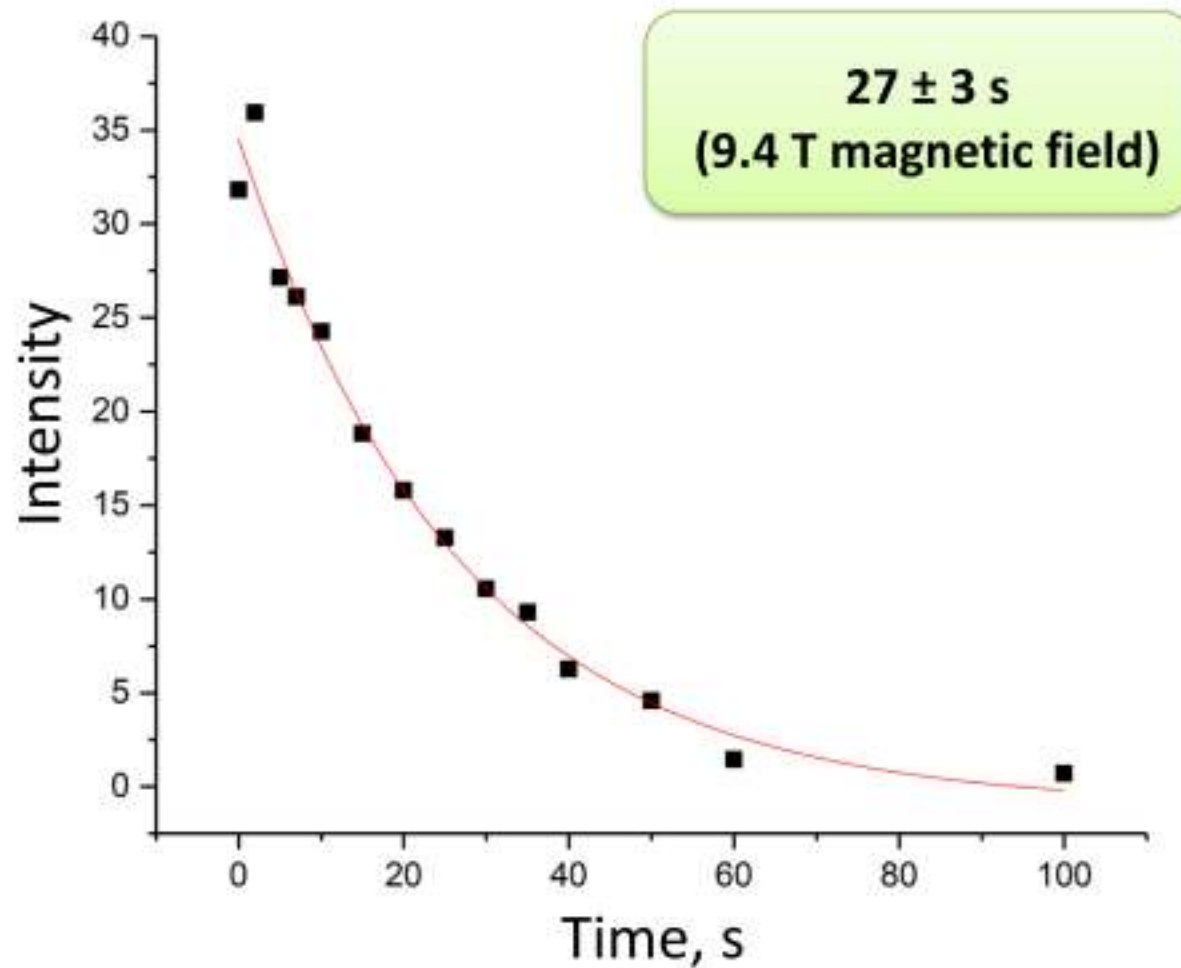


Signal enhancement ≈ 2000
Polarization(^{15}N) $\approx 0.7\%$
Magnetic field = 9.4 T

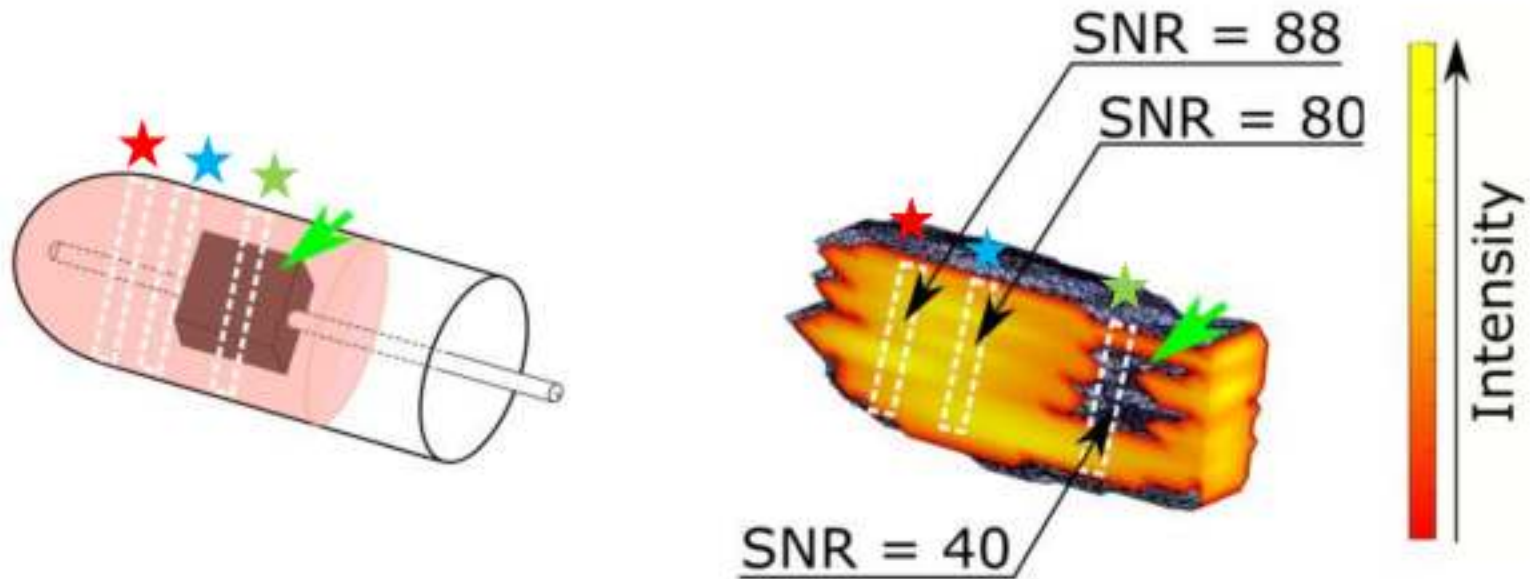
2D ^{15}N MRI: comparison with ^1H MRI of water



T_1 relaxation time



3D ^{15}N MRI



NS = 1

Spatial resolution:

$0.5 \times 5 \times 5 \text{ mm}^3/\text{pixel}$

Conclusions

- ^{15}N polarization level of $[\text{}^{15}\text{N}_1]\text{FAM}$ of 0.7% obtained using SLIC-SABRE allowed to acquire 2D ^{15}N MRI on 9.4 T MRI instrument. The resulting image has SNR of 70, which is only 3 times lower than SNR for 2D ^1H MRI of water dine under the similar experimental conditions
- 3D ^{15}N MRI with the presence of the phantom was done for the first time in the world practice
- The difference in polarization levels for ^{15}N -labeled fampridine and fampridine with natural abundance of ^{15}N is explained

Thank you for your attention!



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