Optimization of ^{89}Y DNP

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Introduction

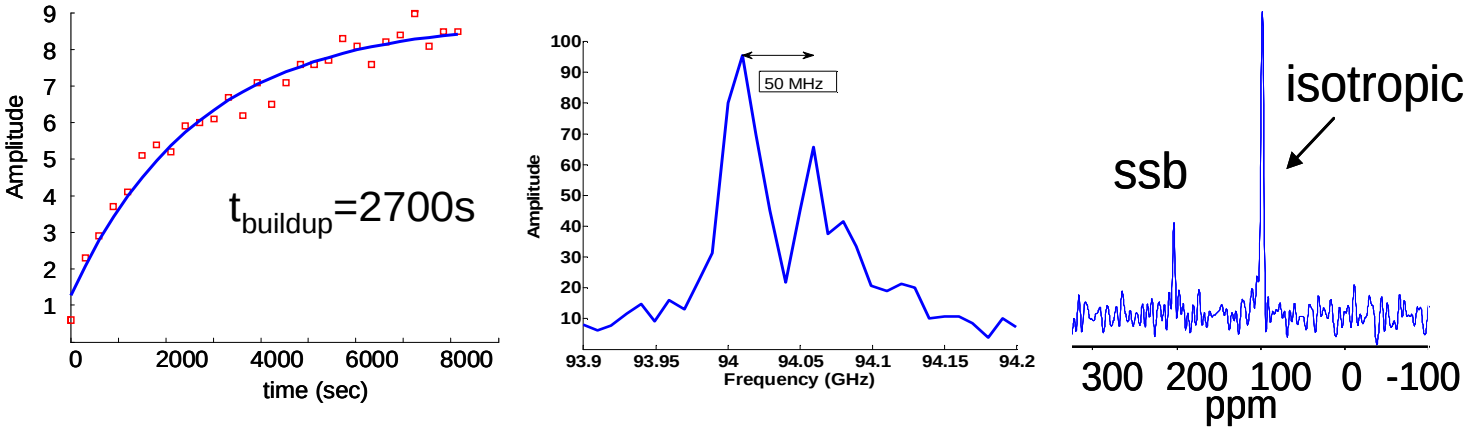
Molecular imaging with magnetic resonance using lanthanide-based contrast agents has shown great promise in measuring biologically relevant metrics such as pH, [glucose], temperature, etc. All of the methods developed so far have depended upon measuring secondary effects of the reagent, i.e. its effect on the T_1 of the bulk water, or the presence of bound water that can be saturated to introduce contrast through chemical exchange saturation transfer. Ideally, the contrast agent could be detected directly provided that sufficient sensitivity is obtainable at current field strengths. Previously we have reported on the use of dynamic nuclear polarization (DNP) as a method for increasing the sensitivity of yttrium based contrast agents.(1) The extremely long T_1's of ^{89}Y based compounds suggest they would make ideal DNP based molecular imaging agents. Further work discussed here characterizes the optimal parameters for yttrium DNP and suggests a new method for producing DNP polarized samples in a more time efficient manner.

Methods

Samples of either YCl_3 or Y^{3+} complexed with high affinity ligands (DOTA, DOTP, etc) were dissolved in 50:50 water/glycerol along with 16.6 mM trityl radical. Dynamic Nuclear Polarization (DNP) was carried out at 3.35T using an Oxford Hypersense DNP system. The samples were frozen at 1.4K and irradiated with a microwave frequency of 94.118 GHz at 100 mW for 2.5 hours. DNP microwave sweeps were recorded with 300 second build up times at each frequency point. Cross-polarization magical angle spinning (CPMAS) experiments were performed at 9.4 T using a Doty solids probe adapted for ^{89}Y irradiation. The CP transfers were carried at a nominal B_1 field strength of 15 kHz for ^{89}Y and ^{1}H.

Results

Figure 1 (left panel) shows the ^{89}Y DNP build up rate as measured with a 5 degree excitation pulse in the solid state. Despite the low gyromagnetic ratio of yttrium, 2.5 hours of DNP is sufficient for obtaining the maximum polarization. The center panel displays the ^{89}Y signal intensity as a function of microwave frequency irradiation. It is notable that the



maxima of the two enhancement peaks is split by a frequency that is ~7 times larger than the yttrium Larmor frequency at 3.35T (7 MHz), indicating that a standard thermal mixing explanation for ^{89}Y DNP is insufficient. The right panel shows the ^{89}Y CPMAS signal of NH_4Y(DOTA) obtained with a 4 ms cross-polarization sequence and 40000 scans with a total acquisition time of 11 hours. The ^{89}Y solid state NMR signal without cross-polarization would be 20 times less intense and would have to be collected with a T_r suitable for ^{89}Y. With cross polarization, the T_r is limited by the solid state proton relaxation time.

Conclusions

Optimal experimental parameters have been established for ^{89}Y DNP. Solid state NMR results point to a possible new method for producing hyperpolarized ^{89}Y samples; DNP to the protons followed by cross-polarization to the ^{89}Y nucleus. Construction of a cross polarization probe for the DNP instrument is in progress.

REFERENCES

1. Merritt ME, Harrison C, Kovacs Z, Kshirsagar P, Malloy CR, Sherry AD. Hyperpolarized ^{89}Y Offers the Potential of Direct Imaging of Metal Ions in Biological Systems by Magnetic Resonance. J Am Chem Soc 2007;129(43):12942-12943.