# Progress towards molecular-MRI with Signal Amplification by Reversible Exchange (SABRE) Hyperpolarisation

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- **Introduction:** Magnetic Resonance Imaging (MRI) is a widely used non-invasive method that uses the water pool as a diagnostic indicator of anatomy and function. However, the small thermal population difference between the quantum spin/energy states (polarization) makes it inherently insensitive, relying on the high abundance of water. The comparative low abundance of bio-molecules involved in cellular biochemistry limits the functionalisation of this important imaging technique. Hyperpolarised MR is an emerging method which meets this demand, generating short term increases in polarization, to enable the monitoring of molecular metabolism in health and disease through previously-inaccessible biochemical pathways.

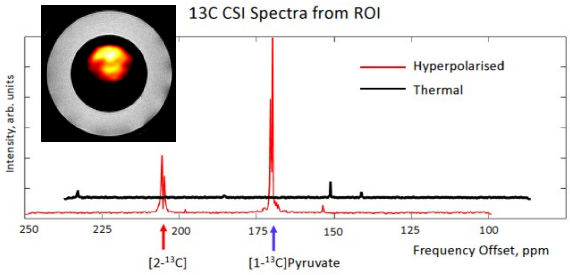


**Fig. 1:** Hyperpolarized pyruvate response taken from a ROI in a $^{13}$C CSI image of a phantom recorded at 9.4 T

The most common of these hyperpolarization methods is Dynamic Nuclear Polarisation (DNP), which is taking pyruvate through clinical trials associated with the diagnosis and treatment of cancer.[1] Here, we communicate progress using Signal Amplification by Reversible Exchange (SABRE) towards MRI applications. SABRE increases measurable hyperpolarisation levels in a wide range of molecules in seconds *via* catalysis and without expensive hardware.

- **Methods:** Molecular targets are brought into indirect contact with *para*hydrogen[3] *via* an Iridium catalyst during hyperpolarization transfer over 10-30 seconds in an optimal field (e.g. 60 mT for $^{1}$H nuclei) to create the improved NMR and MRI response. MRI measurements are made across a range of relevant field strengths (3 - 9.4T) using both clinical Siemens (Prisma) and high field Bruker (BioSpec) imaging hardware. Measurements utilize standard (RARE, FISP & FLASH) and spectroscopic (CSI & EPSI) imaging pulse sequences for $^{1}$H and $^{13}$C nuclei. *In-vivo* detection of SABRE polarized molecular agents is demonstrated at 7T (Bruker Biospec 70/30) in a rodent model where a 2.5 ml bolus (10 mg/ml) is infused into the sub-cutaneous space for detection.
- **Results and discussion:** Results are presented to show how SABRE can improve the MR detection of a variety of agents including nicotinamide, methyl-nicotinate, pyruvate, glucose and urea.[2,4] We also harness the power of SABRE to create a long lived spin isomer of pyruvate and show that its signals can be seen five minutes after the initial hyperpolarisation step (Fig. 1). These developments may lead to future applications where pyruvate hyperpolarisation can be used clinically in conjunction with this rapid and potentially low-cost delivery route. Although, functioanlisation has been proven, current key objectives to realize this technology *in-vivo* include increasing polarisation in bio-compatible solvents and complete de-gassing of hydrogen from the samples.
- **Conclusion:** This talk establishes that with further development SABRE could become a valuable weapon for metabolic monitoring, producing the hyperpolarized responses needed to enable *in vivo* MRI.

**References:** [1] Nelson, et. al. Sci. Trans. Med., (2013) 5, 10. [2] Adams, et al., Science, (2009) 323, 1708. [3] Bowers, et al., Phys. Rev. Lett., (1986), 57, 2645. [4] Iali, et al., *Sci. Adv.*, (2018), 4. eaao6250.