Achieving the Hyperpolarisation of Pyruvate, Glucose and Urea *via* SABRE

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Magnetic Resonance Imaging (MRI), as used widely in clinical diagnosis routinely relies on detecting a water response due to inherent low sensitivity. Hyperpolarisation methods that premagnetise agents such as pyruvate are currently receiving significant attention because they provide the potential to track disease directly through cellular metabolism. The most common of these methods is Dynamic Nuclear Polarisation (DNP), which is currently taking pyruvate through several clinical trials that are associated with the diagnosis and treatment of cancer.[1] Here, we communicate that Signal Amplification by Reversible Exchange (SABRE) readily provides strong pyruvate, glucose or urea responses in conjunction with novel molecular catalysis.[2]

SABRE uses low cost *para*-hydrogen (p-H_2) as the source of its hyperpolarisation and builds from earlier Parahydrogen Induced Polarisation studies (PHIP) that used a hydrogenation reaction to break the singlet nuclear spin order of p-H_2 to achieve sensitivity gains in the NMR experiment.[3] By working at low magnetic fields, like the ALTADENA[4]-PHIP approach, SABRE takes the original singlet spin order of p-H_2 and shares it in the strong coupling regime with spins in a target substrate. However, it does so without changing it chemically. In practice this is achieved by using a metal complex to bind simultaneously, and temporarily, both the substrate and p-H_2 so that the resulting J-coupling network allows spin order sharing. The results of this process can be remarkable, with >50% ^{1}H substrate polarisation levels being achievable in seconds.[5]

This talk focuses on explaining the basis of SABRE and a variation called SABRE Relay[6] which achieves the hyperpolarisation of protons, such as those in water. Subsequent proton exchange into urea or glucose provides a simple route to their hyperpolarisation. While pyruvic acid can be hyperpolarised in the same way, results are described that take a novel SABRE catalyst and rapidly hyperpolarise pyruvate itself. DNP results have been reported that show the 1,2 $^{13}C_2$ form of pyruvate can be created in a singlet state with a lifetime of seventy seconds.[7] We harness the power of SABRE to create this long lived spin isomer of pyruvate and show that signals can be seen five minutes after the initial hyperpolarisation step. These developments may lead to future applications where pyruvate hyperpolarisation is used clinically in conjunction with this rapid and potentially low-cost delivery route.

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